

THE  
PENROSE  
INQUIRY

# Final Report

**Volume 1:  
Patients' Experiences**

THE  
PENROSE  
INQUIRY

# Final Report

**Volume 1:  
Patients' Experiences**

Laid before the Scottish Parliament by the Scottish Ministers  
under section 26 of the Inquiries Act 2005.

March 2015  
SG/2015/15

© Crown Copyright 2015



This publication is licensed under the terms of the Open Government Licence v3.0 except where otherwise stated. To view this licence, visit [nationalarchives.gov.uk/doc/open-government-licence/version/3](https://nationalarchives.gov.uk/doc/open-government-licence/version/3) or write to the Information Policy Team, The National Archives, Kew, London TW9 4DU, or email: [psi@nationalarchives.gsi.gov.uk](mailto:psi@nationalarchives.gsi.gov.uk).

Where we have identified any third party copyright information you will need to obtain permission from the copyright holders concerned.

This publication is available at [www.penroseinquiry.org.uk](http://www.penroseinquiry.org.uk).

ISBN: 978-0-85759-022-0  
(Volume 1 of 5)

Published on behalf of The Penrose Inquiry by APS Group Scotland, 21 Tennant Street, Edinburgh EH6 5NA  
DPPAS43828 (03/15)

# THE PENROSE INQUIRY

Area 2J South  
Victoria Quay  
Edinburgh, EH6 6QQ  
Tel: 0131 528 5221  
[www.penroseinquiry.org.uk](http://www.penroseinquiry.org.uk)

Shona Robison MSP  
Cabinet Secretary for Health, Wellbeing and Sport  
St Andrew's House  
Regent Road  
Edinburgh  
EH1 3DG

March 2015

Dear Ms Robison

## **PENROSE INQUIRY- FINAL REPORT**

On 12 January 2009, I was appointed by the then Cabinet Secretary for Health and Wellbeing, Nicola Sturgeon MSP, to hold a public inquiry into Hepatitis C/HIV acquired infection from NHS treatment in Scotland with blood and blood products.

I published a Preliminary Report in 2010. I now present to you my Final Report, which reflects the amount of work required to address the Terms of Reference.

Yours sincerely



**Rt Hon Lord Penrose**  
Chairman

## HOW TO READ THE FINAL REPORT

### *Availability of the Final Report*

The Final Report is published by the Inquiry in this printed version and on the Inquiry website <http://www.penroseinquiry.org.uk/>

In 2010 Lord Penrose published a Preliminary Report which is available at <http://www.penroseinquiry.org.uk/preliminary-report/>

### *The printed version*

The printed version of the Final Report consists of five volumes and an Executive Summary, which has also been printed as a separate document. There is also a DVD included in the box which holds these volumes as well as the Executive Summary, in both HTML and PDF versions.

### *The website version*

The Final Report is available in HTML and PDF versions. It is fully searchable.

### *Structure of the Final Report*

The Final Report consists of five volumes which represent five parts as set out in the contents page. The five parts cover: Patients' Experiences; Knowledge of HIV/AIDS and Hepatitis C; Blood and Blood Products; Donor Selection and Screening of Donated Blood; and Information to Patients.

The Executive Summary is printed as a separate document. There are conclusions within each chapter where appropriate. There is one recommendation which can be found at the end of Chapter 35, *An Investigation into the Steps Taken to Identify the Individuals who were Infected (Look-back)*.

### *Footnotes*

Footnotes in the Report include details of documents which provide the supporting evidence for points made in the text. The Inquiry assigned unique 10-character identifiers to every page in the evidence collected. These are in the form of three letters, followed by a three-digit number and a four-digit number, for example: SNB.002.1537. The reference for the document as a whole is simply the identifier of its first page. The three-letter prefix indicates the origin or nature of the document. 'SNB', for example, indicates a document from the archives of the SNBTS, and 'PEN' indicates a document or statement collected by the Inquiry during its own investigations. No significance attaches to this prefix in the context of the Final Report. In many cases the same document was recovered from several sources and the choice of which one to publish has been made on the basis of which was most complete or most readable.

In the electronic versions of the Report the document identifiers have been made into active links so that readers can click on the link and open the document to read the evidence for themselves.

Links are not included for some documents of a sensitive nature. These are generally the statements or medical records of patients and their family members. Some of the linked documents have also been redacted. This has been done to remove sensitive personal data or personal data that is not relevant to the Inquiry. The Inquiry's policy has been to leave as much text visible as possible so that the reader will understand the nature of the material that has been redacted.

The footnotes also contain references to the transcripts of the Inquiry's public hearings. These references give details of the witness, particularly where this may not be obvious from the text, the hearing day, and the page number or numbers where the relevant evidence appears. The transcripts are available on the Inquiry website and on the DVD attached to the printed version of the Report.

### ***Reference period***

The reference period for the Inquiry was 1 January 1974 to 1 September 1991. Some material necessarily pre- and post-dates this period in order to help fully understand the context in which events took place.

### ***Names and designations***

Each person mentioned in the Report is identified by his or her full name and title. Some of the people mentioned in the Report have had more than one designation during the reference period, a doctor, for example, becoming a professor. Their most recent title has generally been used in the text of the Report, except when quoting from contemporaneous documents.

The evidence given by patients and their relatives has been anonymised, except for the four named individuals whose deaths were investigated as part of the Terms of Reference: Reverend David Black, Mrs Eileen O'Hara, Mr Alexander Black Laing and Mr Victor Tamburrini. Those patients and relatives who gave oral evidence were given pseudonyms to protect their privacy.

# CONTENTS

<b>Volume 1: Patients' Experiences</b>		Page
	Chairman's Letter to the Cabinet Secretary	iii
	How to Read the Final Report	v
	Foreword	ix
1	Introduction	1
2	Patients at Risk	7
3	Statistics	25
4	Experiences of the Patients and Their Families – Witness Statements	113
5	An Examination of the Effects of Infection with HIV on Patients and their Families, including Treatment	139
6	An Examination of the Effects of Infection with Hepatitis C on the Patients and their Families, including Treatment	217
7	An Investigation into the Deaths of the Reverend David Black, Mrs Eileen O'Hara, Mr Alexander Black Laing and Mr Victor Tamburrini	307
<b>Volume 2: Knowledge of HIV/AIDS and Hepatitis C</b>		
8	Knowledge of HIV/AIDS Now	399
9	Knowledge of the Geographical Spread and Prevalence of HIV/AIDS 1	415
10	Knowledge of the Geographical Spread and Prevalence of HIV/AIDS 2	449
11	HIV/AIDS Aetiology	491
12	HIV/AIDS: Response and Clinical Practice	535
13	Knowledge of Viral Hepatitis Now	589
14	Knowledge of Viral Hepatitis 1	627
15	Knowledge of Viral Hepatitis 2 – 1975 to 1985	649
16	Knowledge of Viral Hepatitis 3 – 1986 Onwards	691
<b>Volume 3: Blood and Blood Products</b>		
17	Blood and Blood Products Management	709
18	Collection of Blood – General	735
19	Production of Blood Products – Facilities	763
20	Haemophilia Therapy – The Period up to the Early 1980s	785
21	Haemophilia Therapy – Use of Blood Products	805
22	Haemophilia Therapy – Use of Blood Products 1985–1987	897
23	Viral Inactivation of Blood Products for Haemophilia Therapy up to 1985	933
24	Viral Inactivation of Blood Products for Haemophilia Therapy 1985–1987	1013

**Volume 4: Donor Selection and Screening of Donated Blood**

25	Screening of Donated Blood for Hepatitis B	1075
26	Donor Selection – Higher Risk Donors	1105
27	Surrogate Testing of Donated Blood for non-A, non-B Hepatitis	1177
28	Donor Selection – AIDS	1281
29	The Discovery of HIV and the Development of Screening Tests	1307
30	Screening of Donated Blood for HIV	1321
31	The Introduction of Screening of Donated Blood for Hepatitis C	1383

**Volume 5: Information to Patients**

32	An Investigation into the Systems in Place for Informing Patients about the Risks – Ethical Context	1489
33	An Investigation into the Systems in Place for Informing the Patients about the Risks – HIV/AIDS	1537
34	An Investigation into the Systems in Place for Informing the Patients about the Risks – Hepatitis C	1639
35	An Investigation into the Steps Taken to Identify the Individuals who were Infected (Look-back)	1689

**Appendices**

	Appendix 1: Inquiry Procedures	1749
	Appendix 2: Inquiry Organisation and Administration	1763
	Appendix 3: Core Participants	1769
	Appendix 4: Inquiry Witnesses	1771
	Appendix 5: Inquiry Procedure Directions, Guidance Notes and Restriction Orders	1779



## FOREWORD

When I was appointed as Chair of this Inquiry in January 2009, I did not know how many years the Inquiry would take, nor did the loyal members of my team who have remained with the task. Some inquiries relate to a single event. In others, as in this Inquiry, there are multiple factors that evolve over time. This creates a complexity that can only be resolved by critical analysis to define the particular areas for study, followed by ingathering and evaluating evidence with a view to reaching conclusions on matters of fact and opinion. This type of Inquiry can lead to an investigation of immense scope and so it has proved.

Both the duration and the cost of Inquiries are often matters of public concern, but until the evidence is ingathered, it is impossible to know the full scope of the task. Terms of reference only intimate the direction of the investigation: it is the evidence which dictates the necessary journey.

The terms of reference required a wide-ranging investigation into Hepatitis C and HIV/AIDS. That investigation involved people with bleeding disorders and those who had received blood transfusions: two very different groups, and those who had received blood transfusions are members of an extremely diverse group. With a timeframe of 1974 to 1991, the amount of material was vast.

The terms of reference also involved a requirement to investigate four specific deaths: Reverend David Black, Mrs Eileen O'Hara, Mr Alexander Black Laing and Mr Victor Tamburrini. The deaths of the Reverend Black and Mrs O'Hara played an important role in the genesis of the Inquiry as their relatives pursued the right to an independent investigation which ultimately led to this Inquiry being set up. Much effort has been expended in the investigation of the four deaths and it is to be hoped that their relatives obtain some comfort from this work.

It soon became apparent that the amount and complexity of the factual material alone for this Inquiry represented a significant challenge. I took the decision to write a Preliminary Report, setting out the factual narrative, which was published in September 2010. The Preliminary Report also contained the proposed topics for the hearings. The oral hearings commenced in March 2011. The Preliminary Report stood us in good stead and saved us a great deal of time during the hearings.

The oral hearings took place over 89 days and examined the controversial topics. They concluded in March 2012. We had over 13,000 pages of transcript, in addition to 200 witness statements and 120,000 documents in our database. The task of writing the Final Report has been demanding. Some topics were particularly challenging. More evidence had to be taken for the Statistics topic. The numbers of people affected are clearly important and this is reflected in the efforts made to ensure they were as accurate as possible.

Once the Final Report was in draft form in December 2013 there was a requirement under the Inquiries Act 2005 to issue warning letters to anyone subject to significant or explicit criticism. This included not just criticisms made by the Inquiry but also those made of individuals in evidence, if repeated in the Report. Again the warning letter process constitutes unknown territory as the impact of the responses cannot be known until they

are seen. As currently framed, the statutory requirement is far-reaching, with inevitable consequences for the time required to complete the Report.

The Final Report is long because of the amount of evidence and the need to understand the development of the diseases and their impact not just on people with bleeding disorders but also on anyone who had become infected with Hepatitis C or HIV through a blood transfusion.

Much of the comment made over the years on the topics discussed in the Final Report has reflected strongly-held beliefs. Some commentators believe that more could have been done to prevent infection in particular groups of patients. Careful consideration of the evidence has, however, revealed few respects in which matters could or should have been handled differently.

One area where it is concluded that more could have been done is in the delay in the introduction of screening for Hepatitis C. In relation to AIDS, it appeared to the Inquiry that, once the risk had emerged, all that could reasonably be done, was done. When actions in Scotland were subjected to international comparison, they held up well.

This was always going to be an Inquiry about what happened in the past as opposed to a commentary on current practice with recommendations for change. Indeed there is only one recommendation – the need to make further efforts to assist anyone who received a blood transfusion before September 1991 and who has not had a test for Hepatitis C. The Scottish Government must take action to address this.

The length of time which had passed since the events addressed by this Inquiry was unusually long. We were constantly aware of the need to understand the conditions prevailing at the time and not to judge events by today's standards. This was found to be true especially in relation to the doctor-patient relationship which was acknowledged to be paternalistic at the beginning of the period. There was a great deal of dissatisfaction on the part of patients about the information provided to them. This was found to be a combination of genuine lack of information as the understanding of the conditions developed, and the nature of the relationship in which doctors were not used to sharing all information available with patients as they do today.

Much of this Inquiry has been about the adverse consequences experienced by those who were infected by HIV/AIDS and or Hepatitis C. The impact on their lives and those of their loved ones has often been devastating, as set out in the Report. I would also comment on the often forgotten suffering of clinical staff, who were to discover that the treatments they thought were beneficial to patients actually caused them to become infected with life-threatening conditions. This is the stuff of nightmares, and they too have suffered, especially when accused of knowing or deliberate attempts to harm patients. One doctor eloquently described his experience of prescribing the new concentrate products which offered so much to patients with haemophilia only to discover the threat of AIDS as, 'waves of hope, followed by waves of despair'. Patients and doctors shared this experience.

The work of the Inquiry could not have been carried without the support and active participation of the administrative staff, lawyers and paralegals. I am grateful to the Medical Assessor to the Inquiry, Professor Oliver James, Emeritus Professor of Medicine, University of Newcastle, for his advice and guidance throughout the process.

Laura Dunlop, QC, worked with diligence and dedication. Maria McCann and her team provided the administrative support without which the process would have been impossible. The individual members of both teams are listed in Appendix 2. I wish to record my unqualified thanks and admiration for their work, sometimes carried out in trying circumstances.

Finally, I would like to thank all those who gave evidence to the Inquiry. The courage of the patients and relatives is manifest within the relevant chapters in the Final Report. I also pay tribute to those patients who gave evidence and who have sadly died during the course of the Inquiry. I offer my sincere condolences to their loved ones.



The Right Honourable Lord Penrose

# CHAPTER 1

## INTRODUCTION

**1.1** This is the Final Report of the Inquiry into the transmission of blood-borne viruses to people in Scotland in the course of medical treatment provided by the NHS. The viruses, HIV and Hepatitis C, cause life-threatening illness. Some of those who became ill following infection with one or both of these viruses died as a result, and others continue to live with serious ill-health. Why and how that occurred has been investigated in depth by the Inquiry and the results of that investigation are set out in full in this Report. A summary version of the Report is available separately.

### **Origins of the Inquiry**

**1.2** On 18 April 2006, the Health Committee of the Scottish Parliament called for a Public Inquiry into the infection of people with Hepatitis C from NHS treatment. The then Scottish Executive decided not to hold an Inquiry, but the Scottish National Party made a commitment in its 2007 manifesto to hold such an Inquiry if elected to form the government in Scotland.

**1.3** Separately, the personal representatives of Reverend David Black and Mrs Eileen O'Hara, two individuals who appeared to have acquired Hepatitis C from NHS treatment with blood or blood products in Scotland and who had since died, raised proceedings in the Court of Session to challenge decisions not to conduct investigations into those deaths. The challenges were successful, the court taking the view that, under Article 2 of the European Convention on Human Rights, the applicants were entitled to an independent Inquiry into the deaths of their relatives.

**1.4** On 23 April 2008, the then Deputy First Minister and Cabinet Secretary for Health and Wellbeing, Nicola Sturgeon MSP, announced to the Scottish Parliament that there would be a judicially led Public Inquiry, under section 28 of the Inquiries Act 2005, into the transmission of Hepatitis C and HIV from blood and blood products to National Health Service patients in Scotland. She informed Parliament that the Rt. Hon. Lady Cosgrove would chair the Inquiry. Lady Cosgrove subsequently withdrew for family reasons. The Inquiry was set up as the Penrose Inquiry on 13 January 2009 with 12 Terms of Reference.

### **Terms of Reference**

**1.5** The Terms of Reference required the Inquiry to investigate the deaths of named individuals who were thought to have acquired Hepatitis C from treatment with blood or blood products and, more generally, to investigate how patients in Scotland acquired HIV or Hepatitis C from blood or blood products, and the consequences of such infection. An amendment to the Terms of Reference was announced in November 2009 to include three additional deaths which were to be investigated and a further amendment to them was made in February 2011 to remove one of those individuals from the investigation. The Terms of Reference, as amended, are as follows:

1. To investigate the systems in place in Scotland for the collection, treatment, licensing, testing, preparation for supply and supply for use by the NHS of blood and blood products with particular reference to the risks of transmission of the Hepatitis C virus and HIV to patients treated by the

- NHS in Scotland, including the role of government in regulation and setting guidelines and standards.
2. To investigate the systems in place for informing patients treated by the NHS in Scotland of the risks associated with the use in their treatment of blood or blood products, with particular reference to the risks of infection with the Hepatitis C virus and HIV.
  3. To investigate the systems in place in Scotland for obtaining consent from, and testing for infection with Hepatitis C and HIV, patients treated with blood or blood products, and informing any patients found to be so infected.
  4. To investigate the systems for recording and monitoring the numbers of NHS patients in Scotland treated with blood and blood products, with particular reference to the numbers exposed to risk of infection with the Hepatitis C virus and HIV and the numbers contracting either or both such infections as a consequence of such treatment.
  5. To examine the circumstances generally in which patients treated by the NHS in Scotland became infected with Hepatitis C, HIV, or both through the use of blood or blood products in the course of their treatment, taking account of the development of scientific and clinical understanding and evidence internationally.
  6. To investigate the deaths of Reverend David Black, Mrs Eileen O'Hara, Alexander Black Laing and Victor Tamburrini, with particular reference to the circumstances in which they became infected with the Hepatitis C virus, HIV or both.
  7. To investigate the steps taken by those involved in, and those responsible for, the NHS in Scotland, including NHS Boards and the Scottish National Blood Transfusion Service (SNBTS), their officers and employees and associated agencies, once Hepatitis C and HIV were identified, to trace individuals who might have become infected with one or both of them as a result of receiving blood or blood products; and to identify any other or further steps that might reasonably have been taken to trace such individuals.
  8. To investigate the steps taken by those involved in, and those responsible for, the NHS in Scotland including NHS Boards and SNBTS, their officers and employees and associated agencies, to prevent the provision of infected blood and blood products.
  9. To investigate the steps taken by those involved in, and those responsible for, the NHS in Scotland including NHS Boards and the SNBTS, their officers, employees and associated agencies to inform individuals who might have received infected blood or blood products of the risks associated with their treatment for themselves and their families; and to offer treatment to any individual at risk, and to identify any other or further steps that might reasonably have been taken to inform and to treat such individuals.
  10. To examine any particular adverse consequences for patients treated by the NHS in Scotland and their families of infection through blood and blood products with Hepatitis C and HIV, including the treatment offered.

11. To identify any lessons and implications for the future, and make recommendations.
12. To report as soon as practicable.

**1.6** The period scrutinised by the Inquiry began on 1 January 1974, although in many respects, it was necessary to make some study of earlier events in order to provide context for the principal examination. The period ended on 1 September 1991, when screening of donated blood for the Hepatitis C virus was introduced throughout the UK. As occurred with the commencement date, it was not possible to adhere to a fixed point for termination of the period investigated. Some parts of the Report therefore make reference to events after 1991, in order to explain the outcome in relation to specific aspects of the investigation.

### **Work of the Inquiry**

**1.7** The Inquiry discharged its remit in four stages: gathering information and documents and familiarisation of the Inquiry Team with the issues; preparing, and publishing in September 2010, a Preliminary Report setting out the evidential background to the matters covered in the Terms of Reference; hearings in relation to defined topics; and the writing and publication of this Final Report. It was recognised that additional factual material was likely to emerge during the hearings stage of the Inquiry's work, and so it proved; in consequence of this, a fuller factual background is set out in this Report, with references to the Preliminary Report where appropriate.

**1.8** The selection of topics for oral hearings was made following research carried out by the Inquiry Team up to, and including, the writing of the Preliminary Report. The process whereby a virus was transmitted from donor to recipient offered several stages at which infection could have been prevented: selection of blood donors; screening of donations for viral infection; treatment of blood products (although not whole blood) to destroy viruses present; and the approach adopted to use of blood and blood products in the treatment of individuals. The extent of information communicated to patients about the hazards of treatment, primarily before treatment was given but also after it had occurred, was also an important part of the story. The topics selected for exploration at hearings reflected all these aspects. They are listed in Appendix 1.

### **Oral hearings**

**1.9** The hearings took place between 8 March 2011 and 30 March 2012. The presentation of evidence was led by the team of Counsel to the Inquiry. Counsel representing (i) patients, families and the Haemophilia Society; (ii) National Health Service interests and (iii) the Scottish Government were also present throughout, and able to question witnesses. Evidence was led from 67 witnesses, and 120,000 documents were introduced. Submissions were made by Counsel during the hearings, on various matters, and closing submissions were presented by those listed in (i) to (iii) above.

**1.10** It will be obvious that the period into which the Inquiry was conducting its examination was more than 20 years ago. This inevitably affected the quality of recollections. Some key witnesses had died. On the other hand, the database assembled by the Inquiry held many thousands of documents, and it was frequently possible to reconstruct events from a combination of written material and the testimony of those involved. Where the Inquiry has not found it possible to resolve questions of fact, that is stated in the Report. These instances are few.

**1.11** The approach adopted, of examining individual topics, meant that certain key NHS personnel had to attend to give evidence on more than one occasion. Two clinicians attended on 10 occasions each. Every witness who testified, whether physician or lay person, will have experienced inconvenience and a degree of stress. The Inquiry was and is aware of this, and is grateful for the contribution made by all those concerned.

### **Warning letters**

**1.12** During the final stage of the Inquiry's work, it was necessary to prepare and send warning letters in accordance with Rule 12 of the Inquiries (Scotland) Rules 2007. Rule 12(7) provides:

The inquiry ... must not include any significant or explicit criticism of a person in the report ... unless –

- (a) the chairman has sent that person a warning letter; and
- (b) the person has been given a reasonable opportunity to respond to the warning letter.

**1.13** To comply with this Rule, it was necessary to send 103 warning letters. One hundred replies were received, running to over 1000 pages of material. The points made in these responses were considered by the Chairman and his team and, in some instances, changes were made to draft text of the Report in order to reflect points that were considered well-founded.

### **Structure of Final Report**

#### ***Part one***

**1.14** The first part of the Report gives an indication of the patients primarily at risk of viral infection from blood and blood products, and covers the effects of Hepatitis C or AIDS, or both conditions, and their treatment, on patients and their families. As Term of Reference 4 required the Inquiry to investigate the numbers of patients exposed to the risk of contracting either or both conditions through treatment with blood and blood products and the numbers who actually contracted the conditions, Chapter 3 entitled *Statistics* provides the results of that investigation. Part one also contains a chapter concerned with the investigation of the deaths of certain named individuals which, in consequence of Term of Reference 6, the Inquiry was specifically required to investigate (see Chapter 7).

#### ***Part two***

**1.15** The second part of the Report deals with knowledge, past and present, of HIV/AIDS, covering its aetiology, geographical spread, prevalence, and the response to it in clinical practice. This part of the Report is also concerned with knowledge of viral hepatitis, as at the beginning of the reference period and from 1975 until the present day.

#### ***Part three***

**1.16** The third part of the Report provides information on blood collection and the production of blood products, including details of the management of such activities and the facilities relating to collection and production. It also provides information on haemophilia therapy, including the use of blood products, up until 1987. Finally, it contains chapters on the viral inactivation of blood products for such therapy up until 1987.

### *Part four*

**1.17** The fourth part of the Report considers the discovery of HIV and the development of screening tests for it; screening of donated blood for, respectively, Hepatitis B, C and HIV; donor selection; and surrogate testing of donated blood for what was then known as non-A, non-B Hepatitis, later recognised as largely due to Hepatitis C.

### *Part five*

**1.18** The fifth part of the Report is devoted to a consideration of the information given to, or withheld from, patients by the medical profession, and the ethical principles governing the provision of, or withholding of, such information at the relevant time and currently. The relevant information concerned, primarily, the risks of HIV/AIDS and Hepatitis C and patients' test results. This section of the Report also covers 'look-back', the Inquiry's investigation into the steps taken to identify individuals infected by HCV as a result of treatment with blood donated prior to HCV screening. A glossary is also contained in this part of the Report.

### *Appendices*

**1.19** The Report has five appendices. Appendix 1 details the processes followed by the Inquiry, including the governing law and the specific procedures adopted, and outlines the Core Participants and how they were selected. Appendix 2 covers Inquiry organisation and administration, including the provision of IT for the preparatory phase and for the hearings, and the processing of documents. Appendix 3 details the individuals and organisations which were designated as Core Participant. Appendix 4 lists the witnesses who gave evidence at the oral hearings. Appendix 5 gives details of all the Inquiry Procedure Directions, Guidance Notes and Restriction Orders which were issued during the course of the Inquiry.

### **Recommendation**

**1.20** There were four groups of people in Scotland affected by this tragedy: those who acquired the Hepatitis C virus (HCV) from blood transfusion; those who acquired HCV from treatment for bleeding disorders; those who acquired HIV from blood transfusion; and those who acquired HIV from treatment for bleeding disorders. As the Report explains, the risks which materialised in relation to individuals in these groups do not now exist in the same way. Donated blood is screened for HIV and HCV, and blood products used in the treatment of bleeding disorders are artificially synthesised and do not pose a risk of transmission of blood-borne viruses.

**1.21** Owing to the significant changes which have taken place, it was not necessary for the Inquiry to identify measures required to prevent recurrence of infection with HIV and HCV through blood transfusion or therapy for bleeding disorders. The primary focus for the Inquiry's work was retrospective: posing and answering questions relating to how infection in the reference period occurred, and whether steps which might have prevented these events were available and were taken timeously. Answering these questions is of paramount importance to those who acquired infection, and to those who lost loved ones.

**1.22** In conclusion, there is one respect in which the Inquiry has identified action still required to deal with past transmission of HCV. In the look-back chapter (see Chapter 35), the Inquiry sets out its recommendation that people who received a blood transfusion in the period before screening of donated blood for HCV was introduced, on 1 September 1991, but who have never been tested for HCV, should now be offered such a test.





## CHAPTER 2

### PATIENTS AT RISK

#### Introduction

**2.1** NHS patients with bleeding disorders and medical and surgical patients requiring transfusion of blood or blood components formed small cohorts only of the total UK populations exposed to risk of infection with Hepatitis C and HIV/AIDS. Reports from 2014 estimated that there were 214,000 chronically infected individuals with HCV, and 107,800 with HIV/AIDS in the UK.<sup>1</sup> The numbers of NHS patients infected in Scotland are discussed in Chapter 3, *Statistics*. In summary, around 2500 individuals are thought to have been infected with HCV by transfusion and a small number of transfusion patients, estimated at 18 minimum, with HIV. 478 bleeding disorder patients are thought to have been infected with HCV, and 60 with HIV.

**2.2** As this Report will discuss, there was research of unprecedented intensity into the aetiology and natural history of AIDS and into the development of forms of therapy for infected individuals, resulting in the effective treatment of HIV and control of its progression to AIDS. AIDS appeared to be a genuinely new disease when it was first reported and commitment by governments, public sector scientists and the pharmaceutical industry in response to it achieved these results in a very short time, reflecting the common perception that the disease threatened to achieve pandemic proportions, with high mortality. HCV proved to be a more intractable problem but, in that context also, the efforts of researchers led to the identification of enough of the genetic structure of the virus to allow for the development of tests for infection, a developed understanding of the natural history of the disease and, in due course, treatment of those infected.

**2.3** The NHS patients with whom this Report is primarily concerned benefited from these scientific and technological developments, as did other groups at risk, and it has been necessary to discuss them at some length in later chapters of this Report. The common element affecting the various groups exposed to risk was that infection was transmitted by blood. That applied as much to intravenous drug users as to blood disorder patients receiving blood component or blood product therapy. It is important to bear in mind that the medical and other scientists conducting research and developing technology for identifying infection in blood, for example, were often concerned with the interests of the larger populations at risk and were not narrowly focused on blood disorder and transfusion patients.

**2.4** In this chapter, the focus is on the groups of people who were potentially at risk from infection and the procedures that gave rise to risk. The patient groups exposed to risk were:

- Patients receiving transfusions of blood or blood components in the course of medical care or surgical procedures.
- Patients with bleeding disorders, such as haemophilia, who received whole blood, blood components and products manufactured from human plasma in the course of therapy for their primary disease.

---

<sup>1</sup> <https://www.gov.uk/government/statistics/hiv-in-the-united-kingdom> & <https://www.gov.uk/government/publications/hepatitis-c-in-the-uk>

**2.5** The topic was discussed in Chapter 3 of the Preliminary Report. Since the writing of that chapter, subsequent investigation and the oral evidence led at the public hearings, particularly from experts in the field, have added significantly to the Inquiry's understanding both of the scope of the risks and of the impact of infection on individuals and on their families. The account which follows is therefore fuller than the account in the Preliminary Report and varies from it in part.

**2.6** This chapter discusses, with the benefit of hindsight, the causes of risk and the practices that gave rise to risk generally, without reference to a time line of developing knowledge. The chronology of the developing knowledge of individual diseases is discussed later.<sup>2</sup>

## **Patients receiving transfusions of blood and blood components**

### *Historical overview*

**2.7** As noted in the Preliminary Report<sup>3</sup>, safe transfusion, in the broadest sense, is a relatively modern procedure. Dr Derek Norfolk, a Consultant Haematologist practising mainly in Leeds, provided oral evidence and a witness statement on the use of blood components in clinical medicine.<sup>4</sup> Dr Norfolk developed a particular interest in blood components and patient safety and, in 2006, took up a joint appointment with NHS Blood and Transplant and Leeds Teaching Hospitals NHS Trust. He is a member of the National Blood Transfusion Committee of the Chief Medical Officer for England and Wales. In the last decade he has written frequently on transfusion medicine.<sup>5</sup>

**2.8** Dr Norfolk gave an insight into the hazards of nineteenth century transfusion practice:

Following early, but often ill-fated, attempts at blood transfusion in the 17th century, the first well-documented successes were those of the Edinburgh and London obstetrician Dr James Blundell ... who '... appalled at my own helplessness at combating fatal haemorrhage during delivery...', reported 10 direct donor to patient transfusions between 1819 and 1829. However, the equipment was primitive, the volumes transfused were small and, with no knowledge of blood groups, serious reactions were common.<sup>6</sup>

**2.9** Direct transfusion involved connecting the donor and the recipient by a tube as they lay or sat together. In obstetric practice, the donor was usually the husband of a woman bleeding in childbirth.<sup>7</sup> The procedure was inherently hazardous and, in 1873, the Obstetrical Society of London concluded that transfusion should be used only as a last resort.<sup>8</sup> Real progress began only in the twentieth century.

**2.10** Karl Landsteiner, a biologist and physician working in Vienna, discovered the ABO blood group system in 1901, although it took some time before his discovery began to influence clinical practice.<sup>9</sup> Transfusion using donor blood advanced little until it was introduced into military practice towards the end of the First World War, although it was not used very much in civilian practice for another two decades. It was only during the

<sup>2</sup> Chapters 8–11 and 13–16

<sup>3</sup> Preliminary Report, paragraph 3.4

<sup>4</sup> Dr Norfolk's Report [PEN.010.0048]

<sup>5</sup> Dr Norfolk – Day 7, pages 57–59

<sup>6</sup> Dr Norfolk's Report [PEN.010.0048]

<sup>7</sup> Dr Norfolk – Day 7, page 59

<sup>8</sup> Dr Norfolk's Report [PEN.010.0048]

<sup>9</sup> Dr Norfolk – Day 7, page 60. (Landsteiner was also, with Alexander S Wiener, responsible for the discovery of the Rhesus factor in 1937. These two discoveries – ABO and Rhesus – were essential to the possibility of blood transfusion as currently practiced.)

Second World War that voluntary blood donation was established generally in the UK. It appears that war has always been a major promoter of advances in transfusion technology and medicine and that continues in modern conflict zones.<sup>10</sup>

**2.11** Until transfusion in medical and surgical practice came into general use, the risk of transmission of viral infection was relatively low. There were other risks associated with blood transfusion, such as haemolysis (the breakdown of red blood cells), that tended to have more immediate consequences.

### *Blood transfusion in the reference period*

**2.12** In the middle of the twentieth century, the relatively high risk of haemolysis was reduced by the development of sophisticated blood matching technology. With that reduced risk, however, the transmission of viral infection became more significant as transfusion became more common and as clinical practice tended towards the use of blood components. The use of continuous flow techniques (apheresis) that return unwanted components to the donor and collect only targeted components ensured an approach to collecting donations that was safer for the donor and clinically and economically more sensible,<sup>11</sup> although it appears that the procedure was not extensively used over much of the reference period for this Inquiry.<sup>12</sup> That change in technology did not, in any event, have a direct impact on the risk of transmission of any infection in the donor's blood, since such infections affected the component also.

**2.13** A change of practice that did have an impact on the spread of risk was the separation of whole blood into its major components after donation.<sup>13</sup> The major components are red cells, white cells, platelets and plasma. Plasma is the straw-coloured liquid portion of blood. It contains, in suspension, proteins, such as albumin, antibodies and clotting factors, as well as hormones, fats and dissolved salts and gases.<sup>14</sup> Blood cells are suspended in plasma and can therefore be removed by centrifugation.<sup>15</sup> The separation and use of blood components served a number of purposes. Most patients needing transfusion require the replacement of only one particular blood component, such as red cells for anaemia. Separation into components allows several patients to benefit from a single donation. Storage requirements vary: red cells survive for at least 35 days at 4°C while platelets are damaged by refrigeration and have to be stored at room temperature. Separation allows the different requirements of safe storage to be accommodated. The practice made and continues to make clinical and economic sense.<sup>16</sup>

**2.14** All of these blood components were in use in Scotland throughout the reference period and each of them, the red cell units and platelet and plasma preparations used in clinical practice, may transmit infection. Red cells contain a small amount of plasma and platelets are suspended in plasma and even the relatively small amount of plasma involved would be capable of transmitting a viral infection.<sup>17</sup> As the practice of component use

---

<sup>10</sup> Dr Norfolk's Report [PEN.010.0048]

<sup>11</sup> Dr Norfolk – Day 7, page 64

<sup>12</sup> The reference period for this Inquiry begins on 1 January 1974, the date selected by the Cabinet Secretary for Health and Wellbeing at the outset of the Inquiry's work. There is no specified end-date for the reference period, it having been necessary to consider aspects of the Terms of Reference which continue to operate until the present day.

<sup>13</sup> The use of blood components was promoted by SNBTS from the beginning of the 1970s: see Chapter 17, *Blood and Blood Products Management*, paragraph 17.55.

<sup>14</sup> Dr Foster's paper [PEN.013.1125] at 1127

<sup>15</sup> Dr Norfolk's Report [PEN.010.0048], section 2 from 0049 and section 3.3.1 from 0051.

<sup>16</sup> Ibid [PEN.010.0048] at 0049

<sup>17</sup> Dr Norfolk – Day 7, pages 65–66

increased during the reference period, the numbers of recipients correspondingly at risk of transmission of infection from a single donor increased.

**2.15** The clinical application of blood and blood components has changed over the reference period and it will be possible to identify only significant points of transition towards modern practice. The Preliminary Report traced the growing use of red cell concentrates between 1975 and 1990.<sup>18</sup> Between 1975 and 1981 use increased threefold. Growth continued until 1989, by which point it had reached almost five times its 1975 level. Simple partition into the components most frequently used in clinical practice, without further virucidal treatment, would not have increased the risk of introducing infected blood into the system: the proportion of blood donors who were carriers of infection would not have been altered by the sub-division of donations into blood components. On the other hand, the components of a single infected donation had the capacity to infect more patients than transfusion of the donation as whole blood from one individual donor to a single recipient, and risk overall increased.<sup>19</sup> In that sense, changing clinical practice did change risk.

### *Red cell transfusions*

**2.16** The clearest indication for a red cell transfusion is in patients who have dangerous bleeding after trauma, surgery or childbirth. In those cases, the urgent transfusion of red cells may be required. The body replaces platelets and plasma much more quickly than red cells and the production of red cells may fall short of what is required to replace those lost or consumed in coagulation.<sup>20</sup> In many of these cases transfusion of red cells is essential to maintain life and the prompt replacement of red cells can be life-saving in some cases.<sup>21</sup>

**2.17** There are many causes of anaemia (decreased red cells in the blood), not associated with bleeding, that require medical intervention. The bone marrow may fail to produce enough healthy red cells or the cells produced may have a shortened lifespan in circulation. Genetic diseases such as thalassaemia and sickle cell disease, a lack of essential nutrients such as iron or vitamin B12, serious bone marrow diseases such as leukaemia or aplastic anaemia and anaemia due to inflammation or cancer, all require transfusion of red cells.

**2.18** Particular types of patient receive more transfusions than others. Recent studies have shown that, in the case of red cell transfusions, there is an early peak in sick newborn babies, mainly in the first month of life. In the 20–40 age group red cell transfusion is more common in females than in males because of obstetric and gynaecological indications. All studies have shown that the transfusion of red cells increases sharply over the age of 60: the median age of patients receiving red cell transfusion in one study was 69 years.<sup>22</sup> In a later study, carried out in 2004, it was found that 62% of all red cell transfusions were received by medical patients; 33% by surgical patients; and 5% by obstetric patients. The most common surgical indications were orthopaedic surgery, gastrointestinal and liver surgery and cardiac surgery (16.7% in aggregate). A further 5.9% of red cell transfusions were used in treating trauma patients. These percentages are not absolute, as between

<sup>18</sup> Preliminary Report, paragraph 5.52 and Figure 1.

<sup>19</sup> An extreme example was reported from Italy where a single donation divided into 31 aliquots and administered as mini-transfusions infected 18 neonatal patients with Hepatitis. Castiraghi *et al* 'Long term outcome (35 years) of hepatitis C after acquisition of infection through mini transfusions of blood given at birth', *Hepatology* 2004 (39:90–96) [LIT.001.4027] See Chapter 13, *Knowledge of Viral Hepatitis Now*, paragraph 13.70

<sup>20</sup> Dr Norfolk's Report [PEN.010.0048] at 0051

<sup>21</sup> *Ibid* [PEN.010.0048] at 0050

<sup>22</sup> The Epidemiological and Survival of Transfusion Recipients (EASTR) study discussed in Dr Norfolk's Report [PEN.010.0048] at 0053

2000 and 2004 the number of red cell transfusions used in surgery fell by around 25% despite significant increases in orthopaedic and cardiac surgery. The percentages given do, however, provide an indication of the order of magnitude of the use of the component.<sup>23</sup>

**2.19** In modern practice, red cells remain the most commonly transfused blood component.<sup>24</sup> Improvements in surgical and obstetric techniques in western countries have reduced the use of blood for surgery and during childbirth. Some orthopaedic procedures, such as knee replacements, involve a lot of bleeding during surgery. Modern clinical practice, however, uses technology to re-infuse the patient's own blood, collected during an operation by 'cell saving' techniques, so reducing dependence on transfusion.<sup>25</sup> When liver transplantation was first carried out it was not uncommon for patients to need massive blood transfusions, up to 50 or even 100 units of red cells, to support the patient during the procedure. Re-infusing the patient's own blood has reduced transfusion in many cases to two or three units of blood.<sup>26</sup> With these new techniques, such residual risk of the transmission of infections, like the Hepatitis C virus (HCV) and HIV, as subsists notwithstanding modern screening techniques, was reduced. The emerging risks of transmission of as-yet unidentified viruses were also reduced. The use of transfusion in surgery has now reduced to the extent that in most modern hospitals more than half of all red cells are transfused to medical patients (those not undergoing surgery), typically patients with anaemia.<sup>27</sup>

### *Platelet transfusions*

**2.20** Platelet transfusion became readily available in the UK from the late 1970s.<sup>28</sup> Significant quantities were produced by Regional Transfusion Centres (RTCs) in Scotland before the beginning of the reference period. Production increased after the mid-1970s. Patients with very low platelet counts are at increased risk of bleeding and, at extremely low levels, may die of serious internal bleeding. Low platelet counts (thrombocytopenia) are a feature of bone marrow diseases such as leukaemia and are often a temporary effect of cancer chemotherapy or cardiac bypass surgery. The condition is also commonly seen in patients in intensive care and in sick newborn babies, often caused by serious illness. In modern practice prophylactic platelet transfusions are used to try to avoid bleeding.<sup>29</sup> The pattern of usage of platelets is broadly similar to the pattern of red cell usage.<sup>30</sup>

### *Other components and products*

**2.21** Clinical use of plasma and products derived from plasma predates the reference period. Plasma for clinical use is separated from the cellular components of blood soon after collection and quickly frozen as fresh frozen plasma (FFP). The pattern of usage of FFP is broadly similar to the pattern of red cell usage.<sup>31</sup> The main use of FFP is in the treatment of patients who are bleeding as a result of major tissue trauma, as occurs in road traffic and other serious accidents, military trauma or obstetric complications, when the natural clotting system cannot produce new clotting factors fast enough to replace those consumed in clotting. This condition, disseminated intravascular coagulation, is also

<sup>23</sup> Dr Norfolk's Report [PEN.010.0048] at 0053

<sup>24</sup> Ibid [PEN.010.0048] at 0049

<sup>25</sup> Dr Norfolk – Day 7, pages 82–83

<sup>26</sup> Day 7, pages 83–84

<sup>27</sup> Dr Norfolk's Report [PEN.010.0048] at 0050

<sup>28</sup> Ibid [PEN.010.0048] at 0051

<sup>29</sup> Dr Norfolk's Report [PEN.010.0048] at 0051

<sup>30</sup> Ibid [PEN.010.0048] at 0055

<sup>31</sup> Ibid [PEN.010.0048] at 0056

a potentially life-threatening complication of many acute illnesses, and is commonly seen in very sick newborn babies and in patients with cirrhosis.<sup>32</sup>

**2.22** Current usage of all components and products reflects major changes over time. For example, cryoprecipitate, a derivative of FFP initially developed as a source of Factor VIII<sup>33</sup> for the treatment of clotting factor deficiencies, has been used over the last two decades primarily as a source of fibrinogen for the treatment of patients with major haemorrhage.<sup>34</sup>

## Patients with Bleeding Disorders

### *Patients at risk*

**2.23** Individuals with haemophilia and related coagulation disorders who received whole blood, blood components and blood products were at risk of transmission of infection by treatment.<sup>35</sup> Haemophilia and its treatment were discussed in detail at paragraphs 3.9–3.82 of the preliminary report, and readers are referred to that discussion for more background on the condition and its effects. There is a broad relationship between the risk of transfusion-related transmission of viral infection and the severity of the patient's underlying condition. There are necessary qualifications of this statement which will emerge in the course of this chapter, but current classification criteria are inevitably part of the context in which risk to these patients has to be considered.

**2.24** The World Federation of Haemophilia has graded the severity of Haemophilia A and B according to the quantity of clotting factor (Factor VIII for Haemophilia A and Factor IX for Haemophilia B) in a given patient's blood,<sup>36</sup> as follows:

- <1 international unit per decilitre (iu/dl) - Severe
- 1 – 5 (iu/dl) - Moderate
- 5 – 50 (iu/dl) - Mild

**2.25** Dr Brian Colvin, until 2007 Director of the Haemophilia Centre at Barts and The London Hospital, observed, however, that diagnosis at the edges of normality can be difficult.<sup>37</sup>

**2.26** The normal range of Factor VIII is between 50 and 150 iu/dl. In practical terms, at below 50 iu/dl a degree of abnormal bleeding is found in haemophilia patients and in women who are carriers of haemophilia. Below this level people can have significant clinical problems at times of dentistry or surgery or following trauma.<sup>38</sup> There are other classifications, for example The International Society on Thrombosis and Haemostasis defines the upper limit of mild haemophilia at 30 iu/dl,<sup>39</sup> but for NHS purposes 50iu/dl is accepted.<sup>40</sup>

<sup>32</sup> Ibid [PEN.010.0048] at 0052

<sup>33</sup> Factor VIII is a protein essential for the normal clotting of blood. Haemophilia A is a deficiency of this 'clotting factor'.

<sup>34</sup> Dr Norfolk – Day 7, page 73

<sup>35</sup> Preliminary Report, paragraph 3.1

<sup>36</sup> Dr Colvin – Day 2, page 80; Witness Statement of Dr Winter [PEN.015.0292]

<sup>37</sup> Ibid, page 82

<sup>38</sup> Dr Winter – Day 15, pages 58–59

<sup>39</sup> Ibid, pages 69–70

<sup>40</sup> Some NHS clinicians continue to prefer older formulations, while conforming to the official policy: see, for example, Professor Ludlam's Witness Statement [PEN.015.0385] at 0388 and Professor Ludlam's evidence on Day 18, Pages 23–25. For present purposes it is not necessary to resolve these differences.

**2.27** Traditionally, the classification of a patient's haemophilia as mild, moderate or severe has been based on the level of Factor VIII or Factor IX found on assay using the technology available at the time. Some patients who have extremely low levels of Factor VIII, including some who do not produce Factor VIII at all, do not bleed excessively, however, and therefore do not require replacement therapy as often as might be expected, or in a few cases do not require it at all. In some cases it has been discovered that the patient has acquired another gene that develops clotting. Dr Mark Winter, Kent and Canterbury Hospital, described the case of a child who had acquired a severe haemophilia gene from his mother and a thrombosis gene from his father. The clinical result was that, although the child had no natural Factor VIII, his father's thrombosis tendency made his bleeding less than expected. Clinically, he behaved like a patient with mild haemophilia.<sup>41</sup>

**2.28** Quite apart from such exceptional cases, the level of Factor VIII or Factor IX in an individual case is not determinative of exposure to risk of bleeding: the level of physical activity of the patient is a much more common indicator.<sup>42</sup>

**2.29** It is now possible to precisely identify the genetic defect responsible for haemophilia.<sup>43</sup> Generally speaking, haemophilia breeds true within a family: those who are affected within the family tend to be affected to a similar degree. However, people's characters do differ and individuals of a sedentary disposition are less likely to bleed than those who are physically active. Bleeding in the first years of life is a strong determinant of subsequent bleeding. An active child who falls off his bike from time to time is more likely to have trouble than a sibling who sits at home.<sup>44</sup> A child who is very active in the first few years of life and has had, by the age of two or three, multiple bleeds into one particular joint, may develop a 'target' joint. In that event, the child is much more likely than other children with haemophilia to get bleeds later on in life.<sup>45</sup> Lifestyle can also affect older patients. Playing football as goal keeper in a Sunday league, for example, can expose that individual to a greater risk of bleeding than other mildly affected haemophilia patients with the same factor levels.<sup>46</sup>

**2.30** When patients suffer recurrent untreated haemarthroses (bleeding within a joint), the joints are rapidly destroyed by secondary osteoarthritis.<sup>47</sup> When this occurs in knee joints walking becomes slow and painful.

**2.31** On the other hand, it is a mystery why some severely affected patients do not bleed more often. Dr Winter said:

We don't know why ... [severely affected haemophilia patients] don't bleed more often. They have no Factor VIII, so why do they only bleed naturally 30- to 40-ish times per year? We have evidence they are more likely to bleed when they are infected. That's probably because the infection affects the way their platelets work, which is the other part of the clotting mechanism apart from clotting factors.

<sup>41</sup> Dr Winter – Day 15, pages 61–62

<sup>42</sup> Ibid page 62

<sup>43</sup> Dr Colvin – Day 2, page 81

<sup>44</sup> Ibid page 87; Dr Winter – Day 15, page 62

<sup>45</sup> Dr Winter – Day 15, pages 62–63

<sup>46</sup> Ibid page 65. The example was not hypothetical.

<sup>47</sup> Professor Ludlam explained the difference between osteoarthritis and osteoarthritis (Day 18, page 28). He advised that most of the chronic changes in bones are osteoarthritis whereas osteoarthritis refers more to an inflammatory component.



We have evidence that bleeding is much more common in a joint when the joint has been previously damaged. I think that ... micro-bleeding is probably happening the whole time in joints and muscles, which is the site of main pathology in haemophilia.

But the patient ... can't actually work out whether the minor ache in his knee is due to his arthritis or is it due to a new bleed. Some of these episodes of bleeding will reach a greater threshold, where the bleeding is obviously very significant, but ... our suspicion is that a lot of episodes of bleeding are subclinical and attributed by the patient to the inflammation that he experiences day to day because of all the previous joint damage. Certainly if you go to an operation on somebody's joint ... you can see that the lining of the joint looks like mushroom risotto, for want of a better word, and that it is very bloody.

So one would expect that these joints have been damaged by bleeding early in life ... [T]he synovium, the lining of the joint, becomes much more friable and, like fronds of sea weed, waves in the cavity of the joint and, naturally enough, that can be a focus for very, very tiny episodes of bleeding.

Obviously, if the patient then has trauma – about half of our patients would come in and say, 'I have a bleed. I know why. I banged my elbow coming down the stairs.' About half of them would say, 'I woke up this morning, I have a bleed and I don't know why.' So these things are by no means as well understood as you might think.<sup>48</sup>

**2.32** The bleeding patterns in haemophilia are complex because they are variable. Although it is reported that patients get around of 30-40 bleeds a year, an absolute characteristic is that whole weeks might pass with no problems and there might then be a run of several bleeds over a few weeks. A particular precipitating factor, especially in children, is a concurrent infection, such as an ear infection, with bleeding more likely to happen in that situation.<sup>49</sup>

**2.33** In the case of mild haemophilia, factor levels may vary from time to time. Factor VIII is an acute phase protein, a protein the levels of which fluctuate, even in healthy patients, in response to tissue injury. This variability is seen more often in mildly affected patients, depending both on how the test is done and on the general health of the patient. For example, patients who have developed arthritis in older age, and therefore have ongoing inflammation, may show an increase in background Factor VIII from 20 to 30 iu/dl. Classification might change permanently if a patient with mild haemophilia develops an inhibitor to factor therapy: that would convert the individual into a more severely affected patient.<sup>50</sup> Illness of any kind might cause a transient increase since inflammation or infection may increase the general activity of several acute phase proteins. A patient's normal Factor VIII level of 20 iu/dl might transiently go up to 30 if he gets pneumonia, for example. In addition, Factor VIII assays are not necessarily the easiest test to carry out and different laboratories testing the same sample might produce different results.<sup>51</sup> The figures for Factor VIII levels in any particular case can give an impression of precision which is not achieved in clinical practice.

---

<sup>48</sup> Dr Winter – Day 15, pages 66–67

<sup>49</sup> Dr Winter – Day 15, page 63

<sup>50</sup> Ibid, pages 63–64

<sup>51</sup> Ibid, page 59

**2.34** Fluctuation in factor level is less likely in people with severe haemophilia. In a significant percentage of patients there is the deletion of a gene responsible for Factor VIII production so that they cannot make any Factor VIII at all and their Factor VIII level will not increase as an acute phase protein because, even if they have an illness such as pneumonia, the liver cannot make any Factor VIII under any circumstances.<sup>52</sup>

**2.35** Dr Colvin explained some common situations:

Children with severe haemophilia usually present, in the first 18 months of life, particularly at the time when they begin to get up and run around or crawl around and bump into things. So the little child with severe haemophilia gets bruises on the shins and may develop haemarthrosis, particularly in the knees and ankles, or when they are trying to put toy soldiers into their mouths, they may cut the mouth and get bleeding from the mouth.

So many children with severe haemophilia who don't have a family history may find – or their parents may find – that they are accused of non-accidental injury, which of course is extremely upsetting for someone who later proves to have a significant blood disorder. But when you are dealing with children with mild or moderate haemophilia ... spontaneous bleeding or bleeding after minor injury is not quite so common, so that you may need quite a significant injury in order to cause bleeding. For example a dental extraction, a classical injury which would cause trouble, or if there is a more important injury, where ... there is a twisted ankle or a twisted knee that may lead to bleeding or at the time of a major contusion like falling off your bicycle or having an operation.

So the person with mild to moderate haemophilia may remain undiagnosed for quite a long time, and being diagnosed at the age of 5 or 6 or 7 years is pretty routine and I have seen patients being diagnosed with mild haemophilia in their 60s and 70s. So it just depends on the level of trauma to which you are subjected. But ... to be diagnosed with haemophilia perhaps after dental extraction at the age of 7 is absolutely typical of the condition.<sup>53</sup>

**2.36** It was suggested to Dr Colvin that people with severe haemophilia may experience bleeding without a trigger. He said:

That's true, although the majority of bleeding in severe haemophilia takes place into the joints and muscles, which are the moving parts. However, it is the case that people with haemophilia, particularly severe haemophilia, may have spontaneous [bleeding] – intracranial haemorrhage is the best example – where there is clearly no discernible trigger. Maybe somebody might have bumped their head, but there is no doubt that some people with haemophilia, particularly severe haemophilia, have truly spontaneous bleeding. Of course, it is still possible that there might have been some minor defect in the circulation within the brain that pre-disposes to this spontaneous bleeding. So the word 'spontaneous' is certainly valid in everyday speech; whether it is completely valid at a scientific level is less clear.<sup>54</sup>

---

<sup>52</sup> Ibid, page 60

<sup>53</sup> Dr Colvin – Day 2, pages 78–79

<sup>54</sup> Ibid, pages 83–84

**2.37** Dr Winter's views on the prevalence of sub-clinical bleeding have been noted at paragraph 2.33. Professor Christopher Ludlam, Director of the Edinburgh Haemophilia Centre, commented on bleeding into the brain in particular:

It is likely that ... we all have a small amount of bleeding in our brains from time to time. We all have good – or most of us have good clotting systems and it stops very quickly and heals up. The problem in haemophilia is that once bleeding starts, it takes a long time to stop. You do not necessarily get a greater flow of blood but it just goes on and on and on and on, and if that happens in the brain, then it often has catastrophic consequences.<sup>55</sup>

**2.38** Mild haemophilia does not imply mild bleeding. Once a person with mild or moderate haemophilia begins to bleed after an event such as a tonsillectomy, he will go on bleeding until something is done. A tonsillectomy could be life threatening because a large amount of material is removed from the throat and the airway is critical: death from bleeding could very easily take place.<sup>56</sup>

**2.39** Because the severity of haemophilia in an individual may not correlate with the frequency of treatment with blood products, it is not possible definitively to associate the severity of haemophilia with the risk of infection from blood products. Perhaps the most one can say is that there is a broad relationship between risk from replacement therapy and the individual's history of bleeding that required replacement therapy.

### *Impact of haemophilia*

**2.40** The balance of risk and benefit in the use of blood, blood components and blood products in general medical and surgical practice may often be relatively uncomplicated. In extreme cases, without a transfusion the patient may die in the course of treatment for the condition requiring medical intervention. Lifelong treatment for an incurable condition, which haemophilia generally is (short of liver transplantation), raises more complex questions. The forms of therapy available for managing the condition change over time, and with those changes come changes in the benefits and in the risks associated with them. Choice of therapeutic materials may become an issue, and any risk/benefit analysis is inevitably complicated by that. The patient's response to therapy may also change. Throughout, however, there is one factor in the balance of risk and benefit that is relatively stable: the risk of progressive illness and death that is inherent in blood coagulation disorders. It is clear that those risks, reflected in morbidity and mortality rates, influenced patients, the Haemophilia Society and haemophilia clinicians. It is important to take note of these risks as the history of treatment and increasing knowledge of risk developed.

**2.41** The extent to which patients' lives and life expectancy were compromised before clotting factor concentrates became available was noted in the Preliminary Report and reference was made to reported studies.<sup>57</sup> According to the studies referenced, life expectancy was increased by the use of factor replacement therapy until a position was reached, in 1977–79, when median life expectancy in moderately affected haemophilia patients was estimated to exceed by several years that of the general male population. Median life expectancy for severely affected haemophiliacs (defined as <2% Factor VIII

---

<sup>55</sup> Professor Ludlum – Day 18, pages 22–23

<sup>56</sup> Dr Colvin – Day 2, page 88

<sup>57</sup> Preliminary Report, paragraphs 3.46–3.49, noting that the Birch Report was a study from Illinois.

at this stage) remained a little below the median for the general population. The oral evidence led at the Inquiry was more direct and emphasised the adverse consequences for patients of bleeding episodes over time.

**2.42** In his written submission to the Archer Inquiry,<sup>58</sup> Dr Winter wrote about life for the haemophilia patient before effective treatment was available:

Without treatment we know that life expectancy is very limited. The Birch report in the 1930s disclosed that only 20% of patients with severe Haemophilia could expect to live beyond twenty years. A Finnish study in 1960 showed that the average life expectancy for patients with severe Haemophilia was twenty five years. The commonest cause of death was internal bleeding, particularly into the brain or gastro intestinal tract. Although Haemophilia appears to have been around for a very long time, no treatment was available until the early 1960s because factor VIII circulates in the blood in only tiny amounts and no way had been found of concentrating factor VIII from blood.<sup>59</sup>

**2.43** Dr Winter commented in oral evidence on the natural history of haemophilia:

I think it may be relevant to say that if you ... want evidence of what happens when somebody with severe haemophilia doesn't get treated, you don't only need to look back to these retrospective studies, which were a long time ago and not many of them, you can go to one of the developing countries because the cost of concentrate is so significant, there are many developing countries where, as in Pakistan, they have got very nice hospitals, experienced doctors, good nurses, they are a nuclear power, but they have no concentrate. In the centre in Islamabad, where we visited twice, there are upward of 250 children with severe haemophilia, of which one of them lived beyond the age of 18.

So that remains the natural history of haemophilia. Without treatment, as happened to members of the Royal Family, the likely thing by far is that you will have some life-ending event of serious and spontaneous internal haemorrhage before the age of 20 or so years. That is the natural history of severe haemophilia.

....

You can look at the old footage of the Tsarevich being carried round Moscow at the age of 8 and he is completely crippled and can't walk, and in Pakistan hardly any of the children we were doing clinics with, hardly any of them – certainly none of them had normal joints and most of them were bedbound.<sup>60</sup>

**2.44** Untreated, haemophilia has always been, and remains, a serious, debilitating and potentially fatal disease. It is clearly this factor that has, throughout the reference period, driven the search for therapeutic materials and methods intended to reduce exposure to risk of bleeding or to treat the patient for bleeds when they occur, which has for much of that time involved the risk of transmission of viral infections.

<sup>58</sup> The Archer Inquiry was an independent, non-statutory Inquiry on 'NHS Supplied Contaminated Blood and Blood Products' chaired by Lord Archer of Sandwell which reported in 2009.

<sup>59</sup> Dr Winter's submission to the Archer Inquiry [PEN.015.0283]

<sup>60</sup> Day 15, pages 56–57

### *Treatment of haemophilia and risks*

**2.45** By the commencement of the reference period, the main preparations used in the treatment of haemophilia were early forms of factor concentrates and cryoprecipitate. The history of production and use of these materials in Scotland is discussed in Chapter 20, *Haemophilia Therapy – The Period up to the Early 1980s* and Chapter 21, *Haemophilia Therapy – Use of Blood Products*.

### **Cryoprecipitate**

**2.46** Cryoprecipitate was the first effective treatment for bleeding that was readily available throughout Scotland.<sup>61</sup> It was prepared, mainly at RTCs in the opening years of the reference period, from individual blood donations.<sup>62</sup> In use, it was a high-volume product. Typically, doses used in treatment required a number of units to be administered at the same time. In Glasgow and the West of Scotland, an ‘empirical daily dosage scheme’ was adopted from the mid-1960s: 10 packs were used for minor bleeding episodes and 20 packs for major episodes, with further infusions as required. A patient treated at the Glasgow Centre in accordance with the empirical dosage scheme might have 20 bleeds in the course of a year, each requiring treatment for four days with 20 packs of cryoprecipitate per day. In the course of the year the patient would have been exposed to 1600 units (20 x 4 x 20) derived from up to 1600 donors.<sup>63</sup>

**2.47** At the levels of usage implied, for patients requiring frequent treatment, cryoprecipitate exposed the recipient to a large number of donors. It was soon recognised that cryoprecipitate might be associated with transmission of virus infection. In 1966, Vincent del Duca and R. Bennet Eppes reported the transmission of hepatitis following use of cryoprecipitate.<sup>64</sup> Two Glasgow patients were reported in 1969 to have had jaundice after infusion.<sup>65</sup> They also had received blood and FFP and the report was tentative in respect of any relationship between infusion and infection. Dr Judith Pool<sup>66</sup> responded to del Duca’s 1966 report of transmission:

We are not aware of this complication after the administration of more than 3000 cryoprecipitates in our own institution, but know of no reason why such preparations should be any more free of transmissible hepatitis than other single donor units given in large numbers.<sup>67</sup>

**2.48** Dr Pool’s response acknowledged the risk inherent in multiple treatments with cryoprecipitate. While each unit of cryoprecipitate had a single donor origin, the accumulation of units for any one treatment and of repeated treatments over time exposed the recipient to increasing risk. At the level of use suggested by the empirical dosage scheme in Glasgow and the West of Scotland, the risk of transmission in the course of a year was as great as would have arisen from use of the large pool concentrates eventually produced in Edinburgh.

<sup>61</sup> Cryoprecipitate is the solid residue which remains after the thawing of frozen plasma. It contains most of the Factor VIII from FFP.

<sup>62</sup> Paragraph 3.27 of the Preliminary Report is inaccurate in stating that units of the product were prepared from many litres of plasma.

<sup>63</sup> As noted in paragraph 2.64 below, Dr Winter said that some patients had treatment 30-50 times a year or even more. Evidently, such patients would have been exposed to yet more units (and donors) than in the example given above.

<sup>64</sup> Del Duca and Eppes, ‘Hepatitis Transmitted by Antihæmophilic Globulin’ *New England Journal of Medicine*, 1966; 275:965 [PEN.018.1455]

<sup>65</sup> Forbes *et al*, ‘Cryoprecipitate Therapy in Haemophilia’ *Scottish Medical Journal* 1969, 1: 1 – 9 [LIT.001.4018]

<sup>66</sup> Dr Pool was a physiologist at Stanford University who, in 1964, discovered cryoprecipitate.

<sup>67</sup> Judith Pool, Letter to the Editor in Response to Del Duca and Eppes (q.v.) *New England Journal of Medicine*, 1966; 275: 966 at 1456 [PEN.018.1455] at 1456

**2.49** The administration of cryoprecipitate involved some problems. It was very laborious to prepare, taking two people up to an hour to prepare a dose from about 20 frozen bags, which had to be removed from deep freeze, thawed in a water bath and then reconstituted. Given the nature of the production processes involved, the Factor VIII activity in each bag was not measured and was not known, and clinicians could not scientifically calculate the dose required for the patient. It was difficult to inject and particularly difficult to administer to children.<sup>68</sup>

**2.50** Cryoprecipitate could also have quite significant side effects.<sup>69</sup> Some patients who had multiple previous transfusions, which included most haemophilia patients receiving treatment, might react against protein impurities in the cryoprecipitate and that could make the administration of the cryoprecipitate quite an unpleasant experience for the patient. Over the period of an hour the patient might shake and shiver, run a fever, have muscle aches and feel generally unwell.<sup>70</sup>

**2.51** The difficulties in administering cryoprecipitate and the practical problems sometimes associated with access to treatment in hospital out-patient departments are discussed in Chapter 21, *Haemophilia Therapy – Use of Blood Products*. Dr Winter emphasised that it was a very harrowing experience for the patient. He had never, in all his years of haemophilia practice, heard a patient say, 'I went to casualty with a bleed and everything went well'. He said that never happened. Not only was cryoprecipitate not a very good medical treatment for the patients, having to go to hospital to have that treatment was 'a dreadful experience'.<sup>71</sup>

**2.52** The incentive to use concentrates when they became readily available was clear. The introduction of concentrates, and increase in their supply in the mid-1970s, heralded a major revolution in haemophilia care. Before then, schooling in particular had been so variable an experience for children with haemophilia that there was a dedicated boarding school in Hampshire, the Lord Mayor Treloar School, for patients with haemophilia. When concentrates became available, boarding provision was no longer required.<sup>72</sup> Concentrates were much easier to use than cryoprecipitate and in particular, unlike cryoprecipitate, they did not need to be stored deep-frozen.

### Factor concentrates

**2.53** Early Factor VIII concentrate, known as Cohn Fraction 1, was prepared in Edinburgh from the 1950s, using plasma from about a dozen donations. Cohn Fraction 1 was reported to be associated with the transmission of hepatitis in the 1960s.<sup>73</sup>

**2.54** As far as the patient was concerned, risk was a function of the number of units infused, in the case of cryoprecipitate and early small-pool concentrates. In the course of the reference period, progressive technological development increased the volume of plasma used to produce a single batch of factor concentrates to a point where many thousands of donations were pooled together by some manufacturers. Before effective virucidal treatment of blood products became available, that inevitably increased the number of recipients exposed to risk from a single batch of product. However, there was

<sup>68</sup> See Professor Ludlam's descriptions of use of cryoprecipitate – Day 18, pages 32–38

<sup>69</sup> Dr Winter – Day 15, Page 79

<sup>70</sup> Ibid Pages 81–82

<sup>71</sup> Ibid Pages 79–81

<sup>72</sup> Ibid Page 73

<sup>73</sup> Marder and Shulman, 'Major Surgery in Classic Hemophilia Using Fraction I' *American Journal of Medicine*, 1966; 41:56-75 [PEN.018.1432]

an incentive to use the newer products in light of the advances they brought in clinical management of the patient.

**2.55** In the case of later concentrates, risk was primarily a function of the number of units used in their production. At about the beginning of the reference period, batches of fractionated product produced at the Royal Infirmary of Edinburgh Royal Infirmary had already involved hundreds of donation units and, with the move to Liberton, 1000 units was the initial batch quantity. Very few infusions of concentrate were required to raise the risk of virus transmission to levels approaching 100%.

### *Changes in patient management*

**2.56** Factor concentrates opened the door to home therapy as clinicians could issue concentrate that was small in volume and could be kept in a domestic refrigerator. The concept of comprehensive care evolved. Usually from the age of about three, depending on the state of the child's veins and the competence of the parents, the family would be taught how to inject and the patient would go on home therapy for the rest of his life. The patient would then attend clinic every two to three months, depending on the severity of the disorder, for a comprehensive clinical review.<sup>74</sup> The breakthrough brought a 'golden interval' that lasted from about 1973 until the years of viral contamination problems began some five or six years later. Dr Winter said that haemophilia patients were having better attendance rates at school, getting decent jobs and receiving early treatment at home for their bleeds. There were fewer joint problems.<sup>75</sup>

**2.57** In its initial phase, home therapy, like earlier hospital treatment, was used in response to need when the patient had or anticipated a bleed. Some adult haemophilia patients reported an early and brief phase of a few minutes when they had an 'aura' that indicated that not all was well. That would be followed very soon by obvious clinical signs of the bleed, wherever in the body it might be. For joint bleeding, the major clinical indicator would be pain or swelling. Patients were taught that, because the joint was very hot due to the blood in it, they should rub the back of the hand over the affected joint, such as the knee, and compare the good joint with the bad. If the bad knee was a lot hotter, that was a very good sign of an acute episode of bleeding. If the patient were a child, he might be in distress, in particular if the parent passively tried to move the joint, by straightening the knee and the ankle. The child would resist because it was painful, as well as it being hot. In day-to-day home life it was usually obvious that the child did have a bleed, if it was into a joint or a muscle.<sup>76</sup>

**2.58** For many years cerebral bleeding was the leading cause of death in haemophilia patients. It has not been eliminated even today but its incidence is very much lower than it was 30 years ago. Identifying major risks was a significant focus for teaching families before a patient went on home therapy. Instruction included the identification of times when it was of the utmost importance that the centre should be contacted immediately, day or night, for assistance. Those included cases in which a child had a significant head injury, lost consciousness or started to vomit after a head injury. Another major area of concern was bleeding into the mouth. If any of these things were to happen, patients and parents were taught to get in touch right away because the centre would wish to administer clotting factor concentrate very quickly and to assess the child clinically.<sup>77</sup>

---

<sup>74</sup> Dr Winter – Day 15, Pages 72–73

<sup>75</sup> Ibid Page 73

<sup>76</sup> Ibid pages 75–76

<sup>77</sup> Ibid pages 76–77

**2.59** In theory, home treatment in response to a bleed might not have been expected to increase the risk of viral infection: the availability of home treatment did not increase the risk of a bleed. Patients did not, however, always seek treatment at hospital before the advent of home therapy. Having regard to Dr Winter's evidence, there was an incentive to put up with the pain and inconvenience of a minor bleed rather than go to hospital. It would be reasonable to infer that there would be an increase in use of concentrate because of the convenience afforded by home treatment and, therefore, an increase in viral infection risk overall.

**2.60** The next stage in the development of practice was the introduction of prophylaxis in the 1980s. A practice pioneered by Swedish physicians, it followed the observation that, if a child with severe haemophilia was given Factor VIII or Factor IX regularly (three times a week in this study), then, although their factor levels were not normalised, a baseline zero per cent level of Factor VIII would be changed into a baseline of five per cent. Although the patient would still bleed on even minor trauma, he would not bleed spontaneously. Prophylaxis became widespread practice in Europe.<sup>78</sup>

**2.61** Superficially, it might seem reasonable to infer that increasing use of factor concentrates, with home treatment and with prophylaxis, was accompanied by increasing risk of viral infection. However, there was evidence, referred to in Chapter 21, *Haemophilia Therapy – Use of Blood Products*, that early treatment helped prevent bleeds from developing and that had a beneficial effect on total consumption of factor concentrates.

**2.62** Commercial concentrate production, on which English haemophilia practice in particular was heavily dependent, had by the mid-1970s come to involve the processing of very large plasma pools. Before effective virus inactivation, the risk inherent in the product itself had increased. Dr Winter said:

That was my understanding, that by the time concentrate production was well underway by the mid 1970s, the pool size would be at least 20,000 and sometimes higher.

....

The mathematics is actually quite straightforward. There are studies showing that the incidence of the virus that we now know as Hepatitis C in US donor plasma in the 1970s was of the order of 1 per cent. So if you were giving somebody with haemophilia a treatment that came from 20,000 donors, and one in 100 of them had Hepatitis C, each time the patient had a treatment they were getting a couple of hundred, at least, different Hepatitis C infections, and of course this treatment was being given to them maybe 30 to 50 times a year, or even more often than that.

So our understanding, as haemophilia doctors, is that it was absolutely inevitable that if you had Factor VIII concentrate in the 1970s, particularly from US donor plasma, it was absolutely inevitable that you were getting a number of different Hepatitis C infections, and clinically quite an interesting observation that has been made is Hepatitis C comes in different genotypes, six different genotypes – I say quite often, there have been quite a few experiences in my centre and in a number of other centres that we have treated a patient with a

---

<sup>78</sup> Ibid pages 73–74



known genotype, say genotype number 1, and we have cleared that genotype and retested him to be then told by the viral laboratory we have now found another genotype. So our understanding based on this mathematics is that these patients were multiply infected with Hepatitis C, as we now call it.<sup>79</sup>

**2.64** There was less extensive use of imported concentrate in Scotland generally. Imported, commercially-produced Factor VIII was used, however, especially in Edinburgh and Glasgow, from time to time, and specialised imported products were used more widely.<sup>80</sup> The use of domestic Scottish products was believed to carry less risk because the pool size was smaller and the prevalence of infection in the donor population was thought to be lower than in the USA. The differences were not sufficient to eliminate risk in Scotland, however, and in time it came to be understood that the general position remained the same as elsewhere: the move to concentrates increased the risk of transmission of viral infection. Regular prophylactic rather than reactive treatment may have increased exposure and risk further, whether Scottish or imported products were used, at least as far as Hepatitis C was concerned.

**2.65** By the mid-1970s, many UK patients with haemophilia had liver function blood test results which, with the benefit of hindsight, were suggestive of a hepatitis-like pattern. The patients were, by and large, very well. It was possible to demonstrate that maybe 5%, perhaps slightly higher than that, had circulating levels of Hepatitis B; a small number could be demonstrated to have had Hepatitis A, so-called infectious hepatitis; and about 20% could be shown to have antibodies against Hepatitis B (and had therefore been exposed to Hepatitis B). However, for the majority of the other patients who had a hepatitis-like picture on their liver function blood tests, all the standard Hepatitis A and Hepatitis B markers were negative. Most were infected with 'non-A, non-B Hepatitis' as a result of the use of factor concentrates, which only unusually gave clinical symptoms. That was not understood at the time.<sup>81</sup>

### *Risks of transmission: HCV*

**2.66** The risks of transmission of HCV by administration of therapy for coagulation disorders in Scotland were largely eliminated by the introduction for clinical use of effective virus inactivated concentrates (Factor IX in October 1985 and Factor VIII in April 1987).<sup>82</sup> Until those dates, all patients in treatment were exposed to risk of infection.

### *Risks of transmission: HIV*

**2.67** As with HCV, the risks of transmission of HIV were substantially eliminated by the introduction of effective virus inactivation of factor concentrates (December 1984/January 1985).<sup>83</sup> Patients were exposed to risk of infection throughout the early 1980s, though that did not become apparent until 1984. It is now clear from the phylogenetic analysis of retained samples that very few HIV-infected individuals donated blood during the few critical years before effective viral inactivation was introduced.<sup>84</sup>

<sup>79</sup> Dr Winter – Day 15, pages 83–84

<sup>80</sup> SNBTS paper 'Resources Required for Adequate Treatment of Scottish Haemophiliacs' [SNB.001.4943] at 4944

<sup>81</sup> Day 15, pages 86–87

<sup>82</sup> See Chapters 22 and 23.

<sup>83</sup> See Chapter 24, *Viral Inactivation of Blood Products for Haemophilia Therapy*, paragraphs 24.8–24.9 and Chapter 3, *Statistics*, paragraph 3.43

<sup>84</sup> The Edinburgh Cohort of eighteen patients who were found to have acquired HIV infection in 1984 were associated with two (possibly three) donors. See Chapter 10, *Knowledge of the Geographical Spread and Prevalence of HIV/AIDS 2*, paragraphs 10.121–10.122. Phylogenetic analysis, which enables the definition of genetic relationship among samples from several sources, was vital to this discovery and is discussed in that chapter.

### Other people exposed to risk

**2.68** As noted in the Preliminary Report, other people were exposed to the risk of transmission of viral infection in a National Health Service context, specifically clinical and laboratory staff and other hospital workers and researchers.<sup>85</sup> They were exposed to all of the consequences of infection to which those presenting as patients were exposed. These people became patients as a result of participation in treatment and other operations.

**2.69** In Edinburgh, the risk was illustrated in the transmission of 'infectious jaundice' (in this case Hepatitis B) in the Medical Renal Unit at the Royal Infirmary and the Nuffield Transplantation Surgical Unit at the Western General Hospital between June 1969 and May 1970. There had been two previous cases but, in this short period, 18 cases of infection occurred in dialysis patients and six in people who had had contact with dialysis patients. Four of the contacts were members of staff and two were relatives of patients. In the same period four of the 18 patients had died. One member of staff had died and an additional member of staff, a clerk in the haematology department at the Western General Hospital, had also died.<sup>86</sup> Though not within the Terms of Reference, these examples show that the classes at risk from time to time were wider than those who came into NHS care as patients in the first instance.

### Summary

**2.70** Successive developments in clinical practice reduced risks to patients, although, on the whole, they did not change patients' needs for treatment. As with all innovations aimed at patient safety, they removed or reduced the risk, or some of the risk, that was known to be inherent in previous practice. Other risks remained. All red cell therapy, for example, continued to carry a risk of transmission of HCV, until routine screening of blood for antibodies to Hepatitis C was introduced in the UK on 1 September 1991.

**2.71** Throughout the reference period there was significant use of human blood and blood components, FFP and cryoprecipitate in surgical and medical practice. Patients receiving transfusions have been among those exposed to the risk of transmission of virus infection. Estimates of the numbers of patients who may have been infected are discussed in Chapter 3, *Statistics*, and a summary has been noted in paragraph 2.1 above. Taken together, transfusion patients represent the largest cohort of NHS patients relevant for the purposes of this Report.

---

<sup>85</sup> Preliminary Report, paragraph 3.2

<sup>86</sup> SHHD background note on infections [SGH.002.3818]



## CHAPTER 3

### STATISTICS

#### Introduction

#### 3.1 Term of Reference 4 required the Inquiry:

To investigate the systems for recording and monitoring the numbers of NHS patients in Scotland treated with blood and blood products, with particular reference to the numbers exposed to risk of infection with the Hepatitis C virus and HIV and the numbers contracting either or both such infections as a consequence of such treatment.

**3.2** The National Health Service (NHS) patients who were treated with or received blood and blood products and were put at risk of infection with both HIV and the Hepatitis C virus (HCV), or HCV alone have been described in Chapter 2, *Patients at Risk* paragraph 2.1. This chapter attempts to estimate the numbers of patients infected with one or other or both viruses. For the purposes of this chapter, the patients are divided into four groups:

- i. Patients with bleeding disorders who were infected with HCV as a result of treatment with blood products.
- ii. Patients who were infected with HCV as a result of blood transfusion.
- iii. Patients with bleeding disorders who were infected with HIV as a result of treatment with blood products.
- iv. Patients who were infected with HIV as a result of blood transfusion.

Surgical and medical patients transfused with blood and blood components are the largest group of NHS patients exposed to infection by HCV.

**3.3** Within the group of patients with blood coagulation disorders, some sub-groups, including female carriers of the disorders now recorded in the statistical registers, have become numerically significant in the past decade. Very few of these were known, and fewer still received blood products in the 1970s and 1980s. The numbers of those patients infected or potentially infected with HCV or HIV are very small indeed. They do not affect the overall picture and are not discussed separately in this chapter.<sup>1</sup>

**3.4** The search for reliable data for the numbers of patients treated by the NHS in Scotland with blood, blood components or blood products and thereby exposed to risks of transmission of HCV and HIV, and of the numbers who were infected, has proved for the most part to be extremely difficult. Contemporary records, whether of patients exposed to risk or of the incidence of infection, were either not maintained at all, or have become over time incomplete and unreliable. For much of the period it would not have been possible to maintain contemporaneous records of transmission of infection, given the dates when the viruses responsible for the diseases were first identified. This is particularly the case in respect of patients infected with HCV as a result of transfusion. The picture is clearer in the case of HIV infection where reports of infection arose over a

---

<sup>1</sup> The witness 'Christine' is a carrier of Haemophilia A and contracted HCV from a transfusion of Factor VIII prior to surgery in 1981. See Chapter 6, *An Examination of the Effects of Infection with Hepatitis C on the Patients and their Families, Including Treatment*.

relatively short and well-defined period of time. These records were recent and appear to have been reasonably reliable. Investigation of transmission was possible in many such cases.

**3.5** However, even in the case of HIV, reports of the numbers of patients infected with the virus, or suffering from AIDS, in the UK generally and Scotland in particular have not always been consistent or comprehensive. Further, it became apparent during the Inquiry's investigations that information has not been disseminated equally among professional groups directly involved in patient care, other related professional groups, patient groups and the general public, with the result that there are inconsistencies among the sources of information that have been difficult, or even impossible, to resolve.

**3.6** As a result of work carried out after the oral hearings, by the Scottish Haemophilia Directors and Dr Charles Hay and colleagues at the National Haemophilia Database, it is now possible to be confident of the number of patients with blood disorders who acquired HIV infection from therapy administered in Scotland. It has not been possible without some qualification to arrive at precise figures for the numbers of patients actually infected in any of the other three groups. Recorded, hard data contribute to the overall picture, but there are no comprehensive NHS records of unquestionable accuracy for either disease in any category of patients, extending over the whole of the period under review.

**3.7** A short answer to Term of Reference 4 would be:

- In the case of each infection there was a period when the agent of transmission was not identified, and no diagnostic test for infection was available, so an effective recording of comprehensive data would therefore have been impossible.
- During the period in question there were no satisfactory regulatory or other central administrative systems for recording and monitoring the numbers of NHS patients in Scotland treated with blood and blood products, or the numbers exposed to the risk of infection with HCV or HIV, or the numbers contracting either or both such infections as a consequence of such treatment.
- Such provision as was devised for reporting and recording relevant data was not enforced and was ineffective.

**3.8** However, notwithstanding the lack of systematic recording and monitoring of patients, it was recognised by the Inquiry that it might be possible for a retrospective analysis to be carried out, either by extraction and analysis of the material found, or using this basic data for statistical analysis and projection. The investigation has therefore been extended to include more complex study in order to determine whether relevant information can be deduced from available data using statistical modelling techniques.

### **Systems for reporting and recording infection**

**3.9** Infection of the liver with hepatotropic viruses has generally been seen as an issue only since the Second World War, partly because blood transfusion (in the broadest sense) has been practised widely only since then. It is only relatively recently, since the 1960s, that the impact on the human population of 'viral hepatitis' has been perceived at all.<sup>2</sup> From 1932,

---

<sup>2</sup> Professor Zuckerman pressed for notification of hepatitis in 1966 as essential for the measurement of the scale of post transfusion hepatitis in the UK: 'Correspondence – Blood Transfusion and Infectious Hepatitis', *British Medical Journal*, 5 November 1966: 1136 [LIT.001.0247]

there was a requirement to notify cases of 'infective jaundice' but 'infective jaundice' was defined exclusively as 'spirochaetosis ictero-haemorrhagica', indicating an 'icteric' or symptomatic condition.<sup>3</sup> In 1968, that limited definition was removed, and the notifiable disease became 'infective jaundice', without further definition.<sup>4</sup> One aim of this change was to assist Medical Officers of Health to obtain more precise information about the prevalence of hepatitis and the circumstances in which it was spread.<sup>5</sup> Growing awareness of the prevalence of hepatitis (in the broadest sense of disease causing inflammation of the liver) in the UK, led to provision for notification of cases of 'viral hepatitis', which became reportable as an infectious disease under the Public Health (Infectious Diseases) (Scotland) Regulations 1975, which came into force on 2 April 1975.

**3.10** Retrospective studies from America and modelling studies from France, in addition to data and studies from the health protection agencies, suggest that, in Western countries generally and in Scotland in particular, the rate of growth of NANB Hepatitis/HCV infection accelerated through the 1970s and 1980s, largely related to intravenous drug use.<sup>6</sup> The rate of growth slowed thereafter, but the numbers infected continue to grow, and are expected to increase well beyond 2020.<sup>7</sup> Until the second half of the 1980s NANB Hepatitis infection was generally thought not to be a potentially serious condition.<sup>8</sup> So far as present purposes are concerned, this goes some way to explaining the lack of data on the incidence and prevalence of the disease, both generally and among haemophilia and other NHS patients. Furthermore, until discovery of the HCV virus in 1988 and subsequent epidemiological studies in the 1990s, NANB Hepatitis was thought probably to be due to more than one agent, and could not be identified by any serological test available. The background facts were not conducive to the development and implementation of an effective reporting strategy.

### *The Public Health (Infectious Diseases) (Scotland) Regulations 1975*

**3.11** Under the 1975 regulations a medical practitioner, on becoming aware that a patient was suffering from a notifiable disease, had a legal obligation to inform the chief administrative medical officer for the area health board 'forthwith' by means of a prescribed certificate.<sup>9</sup> The regulations required only bare details to be given and did not address the possible or likely means by which the disease had been contracted.<sup>10</sup> The chief administrative medical officer for each health board had an obligation, at the end of each week or as soon as practicable thereafter, to send to the Common Services Agency for the Scottish Health Service (the CSA) a return of the number of cases of each notifiable disease intimated to them during that week.<sup>11</sup> In addition, they had an obligation to report immediately to the Chief Medical Officer any serious outbreak of any infectious disease which, to their knowledge, had occurred in their area.<sup>12</sup>

<sup>3</sup> Public Health (Infectious Diseases) Regulations (Scotland) 1932, SR&O 1932/1047

<sup>4</sup> Public Health (Infectious Diseases) (Scotland) Amendment Regulations 1968, SI 1968/1493

<sup>5</sup> Health and Welfare Services Circular No.26/1968: *Notification of Infective Jaundice and Measles*, 27 September 1968 [SGH.002.3268]

<sup>6</sup> Dr Gillon – Day 6, page 20

<sup>7</sup> Hutchinson *et al*, 'Modelling the Current and Future Disease Burden of Hepatitis C among Injecting Drug Users in Scotland', *Hepatology*, September 2005 [LIT.001.4373]

<sup>8</sup> See Chapter 15, *Knowledge of Viral Hepatitis 2 – 1975–1985*

<sup>9</sup> Public Health (Infectious Diseases) (Scotland) Regulations 1975, SI 1975/308, Regulation 3

<sup>10</sup> *Ibid* Schedule 2

<sup>11</sup> *Ibid* Regulation 4

<sup>12</sup> *Ibid* Regulation 7

**3.12** The system was not effective. The regulations, which were unfortunately introduced just before the several distinct forms of viral hepatitis and their clinical manifestations began to be understood, did not promote epidemiological understanding of hepatitis. The existence of an NANB Hepatitis virus or viruses (in time, principally Hepatitis C) had only recently been postulated (in 1974) when the regulations came into force in 1975. Professor David Goldberg's group at Health Protection Scotland (HPS), (which collects and analyses statistical and epidemiological data relating to blood-borne viruses, sexually-transmitted infections and other diseases and infections), and its predecessor the Scottish Centre for Infection and Environmental Health (SCIEH), concluded that such data as were returned and registered were not reliable.<sup>13</sup> The reports required of medical practitioners did not contain adequate information on the prevalence of infection.<sup>14</sup> Professor Goldberg explained further that, following the 1991 introduction of reliable testing and screening for HCV, it soon became clear that the numbers reported by clinicians bore no relationship to the actual data HPS recovered from laboratories testing samples for evidence of infection. They found that data recorded by virology laboratories were over 90% complete and accurate, undermining the reliability of the different and inconsistent data held on the register. Use of the data reported under the regulations would have hindered HPS in developing its understanding of the epidemiology of HCV infection.<sup>15</sup>

**3.13** The regulations could never have been effective in securing full reporting of the incidence of viral hepatitis. There were several problems with the regulatory regime. 'Viral hepatitis' is not a specific disease. It can be caused by a number of hepatitis viruses.<sup>16</sup> Until well into the reference period not enough was known about the forms of viral hepatitis to enable effective reporting requirements to be developed and enforced. Professor Goldberg said that, in reality, clinicians rarely reported the clinical entity, viral hepatitis, to health boards.<sup>17</sup> Interpretation of the regulations as amended from time to time appears to have given rise to difficulties.

**3.14** NANB Hepatitis/Hepatitis C infection could not be diagnosed without a definitive test for the virus or its antibody. Until 1989–90 there was no diagnostic blood test available generally, to demonstrate prior exposure to HCV. In the UK routine testing was not introduced until September 1991. When the regulations came into force in 1988, overt clinical jaundice was thought to be characteristic of viral hepatitis.<sup>18</sup> In time it came to be recognised, however, that most patients who contracted NANB Hepatitis/HCV did not develop jaundice and that transmission of infection was largely a silent event which would not have alerted clinicians to the obligation to report.

**3.15** Nevertheless, viral hepatitis remained in the scheduled list of notifiable infectious diseases under the Public Health (Notification of Infectious Diseases) (Scotland) Regulations 1988.<sup>19</sup> These Regulations consolidated, with amendments, the 1975 Regulations relating to the notification and prevention of infectious disease.

<sup>13</sup> HPS have been responsible for retaining this information since 2007, having taken over this role from the Information Services Division (ISD)

<sup>14</sup> Professor Goldberg – Day 6, pages 103–104

<sup>15</sup> Ibid page 142

<sup>16</sup> Ibid page 103

<sup>17</sup> Ibid

<sup>18</sup> See Preliminary Report, paragraphs 6.8 to 6.11

<sup>19</sup> SI 1988/1550, Public Health (Notification of Infectious Diseases) (Scotland) Regulations 1988. The Regulations were made under the Infectious Disease (Notification) Act 1889 (c.72) and the Public Health (Scotland) Act 1945 (c.15)

## European law

**3.16** As regards blood products, Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community Code relating to medicinal products for human use, included an obligation on Member States to take all appropriate measures to 'encourage' doctors and other healthcare professionals to report to a competent authority suspected adverse reactions.<sup>20</sup> The Directive also obliged Member States to establish a pharmacovigilance system whereby those who were authorised to market a medicinal product were required to report to the competent authority all suspected serious adverse reactions to the product.<sup>21</sup> Directive 2001/83/EC did not apply to whole blood, plasma or blood cells.<sup>22</sup>

**3.17** As regards whole blood and blood components (ie red cells, white cells, platelets and plasma), Directive 2002/98/EC introduced an obligation on Member States to ensure that any serious adverse events or reactions relating to the quality or safety of blood or blood components were notified to a competent authority.<sup>23</sup> The Directive was implemented in the UK by the Blood Safety and Quality Regulations 2005,<sup>24</sup> which required 'blood establishments'<sup>25</sup> and hospital blood banks to notify the Secretary of State of any serious adverse events or reactions relating to the quality or safety of blood and blood components.<sup>26</sup>

**3.18** Before the Blood Safety and Quality Regulations 2005 came into force, there were no effective regulatory obligations on clinicians or others to report NANB Hepatitis/HCV or HIV infection from blood transfusion. The 2005 Regulations improved the regulatory regime, but came into force after the events that are relevant to this report.

**3.19** The 2005 Regulations reflected growing knowledge of the characteristics of transmissible diseases and of the difficulty of tracing infected patients who had received transfusions many years previously, when there may have been differing standards, for example, between peripheral hospital blood banks and transfusion centres. While transfusion centres had been inspected for many years by the Medicines Inspectorate, hospital blood banks had not. The regulations stipulated for the first time that hospital blood banks and transfusion centres should be brought fully within the Medicines and Healthcare Regulatory Authority (MHRA) framework, and the role of the MHRA was strengthened accordingly. The provisions recognised a gap in the traceability of previous donations and therefore of the patients who received them. Traceability, with a proper 'trail', became entrenched in the new regime and an obligation was placed on clinicians, blood banks and the transfusion service to report formally to the MHRA when there was a serious adverse event in transfusion, such as transmission of virus infection.<sup>27</sup>

<sup>20</sup> Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use, Article 101 [http://ec.europa.eu/health/files/eudralex/vol-1/dir\\_2001\\_83\\_consol\\_2012/dir\\_2001\\_83\\_consol\\_2012\\_en.pdf](http://ec.europa.eu/health/files/eudralex/vol-1/dir_2001_83_consol_2012/dir_2001_83_consol_2012_en.pdf)

<sup>21</sup> Ibid Article 103

<sup>22</sup> Ibid Article 3 paragraph 6

<sup>23</sup> Directive 2002/98/EC of the European Parliament and Council of 27 January 2003 setting standards of quality and safety for the collection, testing, processing, storage and distribution of human blood and blood components, Article 15. <http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2003:033:0030:0040:EN:PDF>

<sup>24</sup> SI 2005/50, Blood Safety and Quality Regulations 2005, which came into force on 8 February 2005

<sup>25</sup> Defined in the Regulations as any person who carries out any of the following activities: 'the collection and testing of blood or blood components' or 'the processing, storage and distribution of blood and blood components when they are intended to be used for transfusion' (Regulations 1(3) and 3(2))

<sup>26</sup> 2005 Regulations, regulations 7 and 9

<sup>27</sup> Dr Gillon – Day 6, pages 11–12



## *Public Health etc. (Scotland) Act 2008*

### Hepatitis C

**3.20** Since 2005, and following public consultation, the Public Health etc. (Scotland) Act 2008 added further requirements, effective from 1 January 2010.<sup>28</sup> The Act involved significant reform and modernisation of the public health/health protection regime in Scotland. Testing laboratories are now required to report to health boards information about infection of individuals testing positive for hepatitis viruses.<sup>29</sup> For Hepatitis B and Hepatitis A, that is important because there is a vaccine available for these infections and close contacts can be identified and offered vaccination. In the case of Hepatitis C the public health importance of reporting is less clear. There was, and is, no vaccine available. For that reason the close contacts of individuals who were infected with Hepatitis C are generally not contacted.<sup>30</sup> However, there are now increasingly effective treatments available for HCV which may be offered to those found to be infected, which will generate demand for more effective tracing of people possibly infected.

**3.21** In the 2008 Act, Hepatitis A, B, C and E viruses are scheduled as 'notifiable organisms', and the generic term 'viral hepatitis' has been removed from the list of notifiable diseases.<sup>31</sup> The Act requires the director of a diagnostic laboratory which has identified a notifiable organism to notify, within 10 days, the health board in whose area the diagnostic laboratory is situated, as well as the CSA (presumably, in practice, Health Protection Scotland), of certain information.<sup>32</sup> As in the previous legislation, only bare details require to be notified and there is no duty to include the possible or likely means by which the organism was transmitted.<sup>33</sup> Fundamentally, notification depends on there being a listed organism identifiable by laboratory testing. Where diagnosis of disease depends on a laboratory test, linking surveillance of diseases to the laboratory testing process is likely to be a much more satisfactory procedure than that under the previous notifiable diseases regime. HCV infection is not a notifiable disease reportable by medical practitioners in terms of section 13 of the Act.

### HIV/AIDS

**3.22** HIV never became a reportable disease under the regulations at any stage.<sup>34</sup> The AIDS (Control) Act 1987 required each health board to make periodic reports to the Secretary of State of information including the numbers diagnosed with AIDS, the numbers with AIDS who had died and the numbers of positive HIV antibody test results. The reports by health boards did not involve identification of individual patients and would have been based on the board's internal statistical records.<sup>35</sup>

**3.23** In 2006 the Scottish Executive consulted on public health legislation in Scotland. The analysis of responses to that consultation confirmed strong support for the repeal of the AIDS (Control) Act<sup>36</sup> as well as a majority view in favour of including STIs (of which

<sup>28</sup> [http://www.legislation.gov.uk/asp/2008/5/pdfs/asp\\_200885\\_en.pdf](http://www.legislation.gov.uk/asp/2008/5/pdfs/asp_200885_en.pdf) The Bill leading to the 2008 Act was introduced in the Scottish Parliament on 25 October 2007 and its legislative history and relevant documents are available at the Parliament's website: <http://www.scottish.parliament.uk/parliamentarybusiness/Bills/16454.aspx>

<sup>29</sup> Public Health, etc. (Scotland) Act 2008, S 16

<sup>30</sup> Professor Goldberg – Day 6, page 104

<sup>31</sup> 2008 Act, section 12 and Schedule 1, Part 2

<sup>32</sup> 2008 Act, S 16

<sup>33</sup> 2008 Act, S 16(6)

<sup>34</sup> Dr Gillon – Day 6, pages 63–64

<sup>35</sup> AIDS (Control) Act 1987, S 1 [http://www.legislation.gov.uk/ukpga/1987/33/pdfs/ukpga\\_19870033\\_en.pdf](http://www.legislation.gov.uk/ukpga/1987/33/pdfs/ukpga_19870033_en.pdf)

<sup>36</sup> <http://www.scotland.gov.uk/Publications/2007/03/30093343/0#> at Chapter 4, paragraph 1.5

HIV is an example) in the new notification system.<sup>37</sup> The arguments against a notification requirement for HIV or any other STIs appear to have been based on considerations of confidentiality and concern that it would have an overall negative effect on their surveillance. The point is not referred to in the Policy Memorandum to the subsequent Public Health (Scotland) Bill nor was it specifically explored during the Health and Sport Committee hearings, although there was some related discussion.<sup>38</sup>

**3.24** Part 2 of the Schedule to the Bill as introduced included on the list of notifiable organisms to be reported by diagnostic laboratories, 'any other clinically significant pathogen found in blood'. In its Stage 1 Report on the Bill, the Health and Sport Committee expressed its concern that this form of words could give rise to problems if directors of laboratories were, for example, to decide that HIV should be reported. In particular, it would compromise reassurances being given to people with STIs that confidentiality would be maintained. The words in question were removed by way of amendment during the passage of the Bill. The 1987 Act, in so far as it extended to Scotland, was repealed by the 2008 Act with effect from 1 January 2010. Under the 2008 Act, HIV/AIDS remained not listed either as a notifiable disease or as an organism.

**3.25** The regime established by the 2008 Act is relatively untried. Some parts of it are novel and it will take time to develop experience of it. For example, the scope of the requirement to notify 'Health Risk States' in particular is novel and may become clearer in time. The Inquiry has not investigated the operation of the current legislation, and it would be inappropriate to comment on it further.

**3.26** As matters stood during the material period up to 1991, the provisions for notification were not effective as a means of informing relevant medical authorities of the prevalence of infection with any relevant disease. For the purposes of the Inquiry it has been necessary to use other sources of information to attempt to paint a picture of the position as it emerged.

### **Patients with bleeding disorders infected with Hepatitis C as a result of treatment with blood products**

**3.27** The first group of patients to be considered is referred to in paragraph 3.2, item i, and consists of patients with bleeding disorders, primarily haemophilia, who were exposed to infection with Hepatitis C through their treatment with blood products. Determining the number of patients exposed to HCV as a result of their treatment by the NHS in Scotland is not straightforward because several sources of data are available, each reporting slightly different numbers. It has been possible to compare these and, to a great extent, reconcile the differences.

#### *Databases of patients with bleeding disorders*

**3.28** From the early 1950s a UK haemophilia register of anonymised data was established and maintained in Oxford in the form of a card index. The register was initially funded by the Medical Research Council.<sup>39</sup> It was taken over by the United Kingdom Haemophilia Centre Directors' (later 'Doctors') Organisation, (the UKHCDO) in about 1968. At the outset,

<sup>37</sup> [www.scotland.gov.uk/Publications/2007/03/30093343/0#](http://www.scotland.gov.uk/Publications/2007/03/30093343/0#) at Chapter 5, paragraph 2.4

<sup>38</sup> <http://archive.scottish.parliament.uk/s3/committees/hs/or-08/he08-0402.htm#Col529> at column 551 – 'Sexually transmitted diseases have been left off the list – I gather that that is because the Government does not want to inhibit people coming forward for treatment ...'

<sup>39</sup> Professor Ludlam – Day 14, page 53

there were widely-held reservations among haemophilia clinicians about the registration of information about patients. These reservations often related to confidentiality. The issue came to a head at a meeting of the UKHCDO in November 1979. It was resolved that the project should continue.<sup>40</sup> The database comprises information collected from all UK haemophilia centres. In practice, Scottish Haemophilia Directors returned anonymised data to Oxford as part of the national database and that arrangement has continued.

**3.29** In the meantime, it was proposed that the Scottish Home and Health Department (SHHD) should take over the similar register of patients with bleeding disorders that had been maintained for Scotland. There were objections, however, concerning the propriety of a central register containing the names and addresses of patients. Some patients had been concerned that there might be leakage of information, and it was agreed at a joint meeting of the SNBTS and Haemophilia Directors on 24 January 1977, that this desire for confidentiality should be respected. The cards were distributed to the Regional Haemophilia Directors to be held locally.<sup>41</sup>

**3.30** It appears that thereafter data were held by Haemophilia Centre Directors and Regional Transfusion Directors in Scotland on locally devised systems which were not necessarily compatible as between transfusion practitioners and haemophilia clinicians.<sup>42</sup> It is likely that the Scottish Haemophilia Centres had held local databases of patients prior to 1977 and continued with these without modification in the new regime.

**3.31** Thus, in the 1970s there came to be two parallel databases of patients: informal local indices at each hospital where blood disorder patients were treated and a national, increasingly anonymised, database maintained by the UKHCDO to which each treatment centre sent information. This state of affairs was formalised at UK level at the end of 1979. Locally, Haemophilia Directors and other clinicians continued to hold data relating to their own patients.

**3.32** There were, and remain, limitations on the accuracy of the UKHCDO data. Capturing data concerning all of the patients proved to be a slow business at least until 1980. Quite apart from the resistance to disclosing information, already noted, patients often exercised a choice to be managed at local hospitals even where there was not a dedicated haemophilia facility. Some needed persuasion to accept the inconvenience of going to a bigger centre, which might involve travelling considerable distances, even though care might be better there.<sup>43</sup> As explained by the UKHCDO, the rapid increase in numbers of registered patients in the first decade after the database was established, suggested that early registration data may be incomplete.<sup>44</sup>

**3.33** The problem relating to the earlier years was illustrated by Dr Hay with reference to Glasgow. Between 1970 and 1980, the Glasgow registrations for haemophilia at the UKHCDO, unadjusted for duplicate registrations, are as set out in Table 3.1.<sup>45</sup>

<sup>40</sup> Minutes of the Tenth Meeting of the UK Haemophilia Centre Directors held in Oxford on Tuesday and Wednesday, 20th and 21st November, 1979 [LOT.003.4058] at 4071

<sup>41</sup> Note of Meeting of Directors of the Scottish National Blood Transfusion Service and Haemophilia Directors on 24 January 1977 [SNB.001.5033]

<sup>42</sup> For example, in the west of Scotland in 1977 donor information was kept on coded computer tapes, with the master file held in BTS headquarters. That reflected, for the time, a fairly advanced use of technology. The minute of the meeting does not disclose whether others followed a similar course. Until the early 1980s blood transfusion records and blood bank records in hospitals tended generally to be in paper form. Paper records were more vulnerable to loss, destruction or accidental discard.

<sup>43</sup> Dr Hay – Day 8, pages 10–11

<sup>44</sup> Ibid, pages 18–19

<sup>45</sup> Preliminary Report: Appendix 1 – UKHCDO Data [PEN.013.1433]

**Table 3.1: Count of Glasgow patients at five-yearly intervals**

		Haemophilia A	Haemophilia B	Totals
1970	Royal Infirmary	71	7	78
	Royal Hospital for Sick Children	3	0	3
				81
1975	Royal Infirmary	102	15	117
	Royal Hospital for Sick Children	8	0	8
				125
1980	Royal Infirmary	196	52	248
	Royal Hospital for Sick Children	55	14	69
				317

**3.34** The increase in each case was far in excess of the birth-rate or any other factor indicating real growth over the period. This was a period when mortality was beginning to be offset by the benefits of concentrate therapy, and that may to some extent have increased the numbers of patients remaining on the register. However, few data were submitted during the early part of the period. Haemophilia care was fragmented in the west of Scotland at this time. Many patients were managed at smaller hospitals around the south west of Scotland at the beginning of the period but, with the advent of increasingly effective treatment, they gradually gravitated towards the centre. The Glasgow pattern is highly unlikely to have been unique, and the lack of reliability of early data must have been common.

**3.35** It appears reasonable to avoid speculation as to probable numbers and to treat the 1970 registrations as wholly unreliable in estimating numbers of patients treated and therefore exposed to some level of risk. It also appears reasonable to accept that the number of 1975 registrations would require to be modified to reflect the probability that the process of gathering patients into the reporting system was continuing and had not completely captured all relevant patients. The numbers recorded in the UKHCDO database from 1980 (as adjusted) are reasonably firm.

**3.36** A continuing problem relates to the 'hub and spoke' care model which was developed and which has resulted in some patients being registered and managed at more than one centre.<sup>46</sup> The data required to be adjusted to exclude duplications. Investigation by the UKHCDO subsequent to the publication of the Preliminary Report uncovered inaccuracies in the data provided to, and published by, the Inquiry. The Inquiry is grateful to the UKHCDO for the work carried out to check the database, internally and against extant original records, and to provide adjusted data. The database, which has improved over time and now provides a wealth of relevant data, has become the primary source of published information on exposure to risk among this class of NHS patients, and their treatment thereafter.

### *UKHCDO and Scottish Haemophilia Directors' data on patients with bleeding disorders*

**3.37** The primary sources of published up-to-date data are the UKHCDO Bleeding Disorder Statistics for April 2010 to March 2011, and April 2011 to March 2012. The adjusted numbers of patients with clotting factor deficiencies in Scotland known to the

<sup>46</sup> UKHCDO report *National Haemophilia Database: Bleeding disorder statistics for the Penrose Inquiry, April 2012* [PEN.019.0927] at 0956

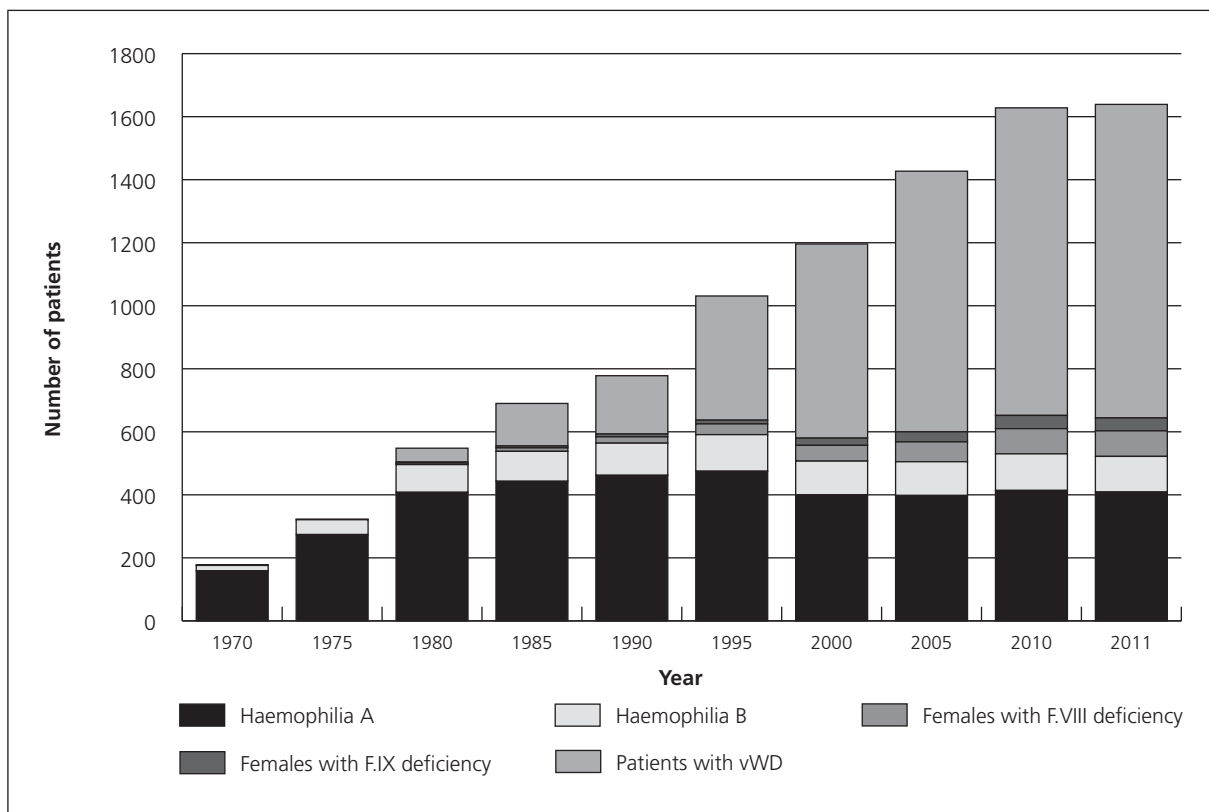
UKHCDO and cross-checked with Scottish Haemophilia Centres, at April 2012 (subject to the reservations about the accuracy of data before 1980 already noted) are as set out in Table 3.2.<sup>47</sup>

**Table 3.2: Count of registered patients: All Scottish centres**

	Haemophilia A	Haemophilia B	Females with F.VIII deficiency	Females with F.IX deficiency	vWD	Total
1970	159	17	0	0	2	178
1975	274	47	0	0	2	323
1980	408	88	5	3	44	548
1985	443	95	11	6	135	690
1990	462	102	20	9	185	778
1995	475	116	34	12	394	1031
2000	400	107	50	23	616	1196
2005	398	107	63	32	827	1427
2010	414	116	80	42	976	1628
2011	409	113	81	41	995	1639

**3.38** The pattern of individuals registered with each condition is illustrated in Figure 3.1.

**Figure 3.1: Individuals with bleeding disorders registered in Scotland**



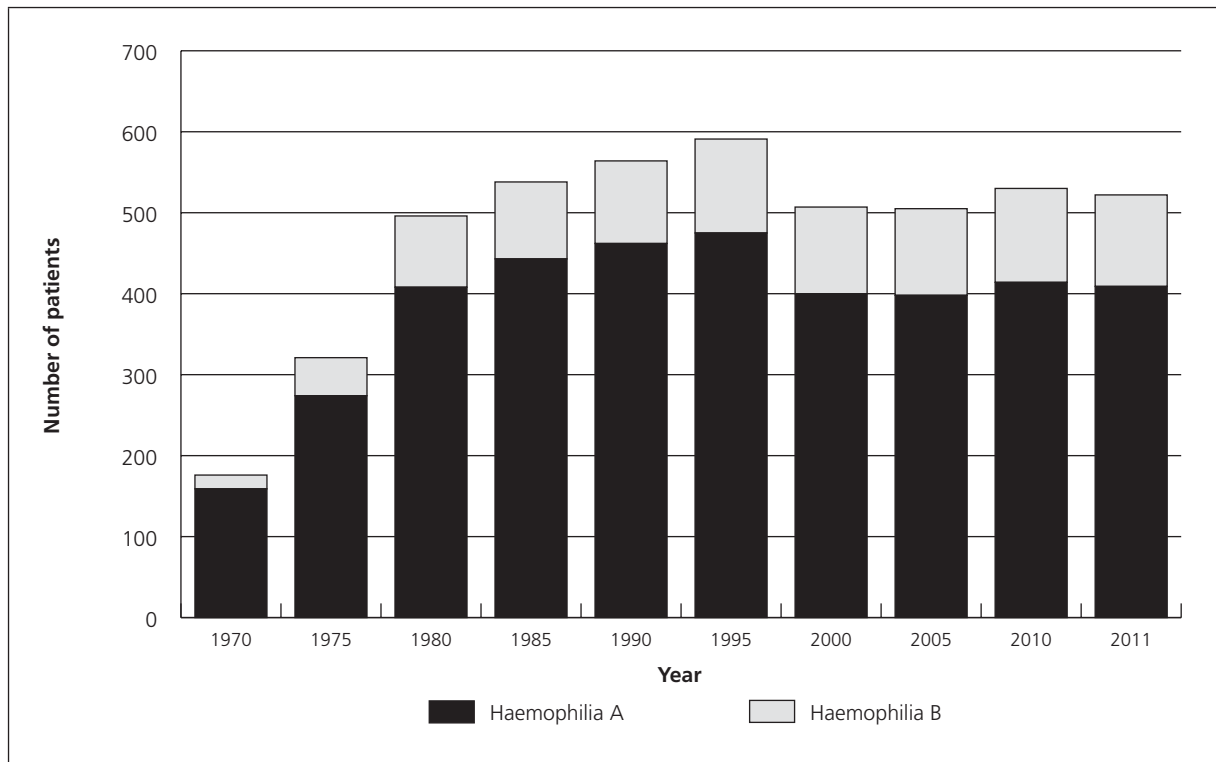
<sup>47</sup> The data are extracted from the UKHCDO report *National Haemophilia Database: Bleeding disorder statistics for the Penrose Inquiry, 2012*, Table 2 [PEN.019.0927] beginning at 0956

**3.39** Setting aside early inaccuracies, the numbers of Haemophilia A and Haemophilia B patients registered are reasonably consistent over the period from 1980. The trends in registered female and von Willebrand's disease (vWD)<sup>48</sup> patients cannot be explained in terms of natural growth in prevalence of the diseases. Three factors may have contributed:

- Increasing sophistication in the diagnosis of mild forms of the diseases.
- Greater diligence in reporting to UKHCDO.
- A growing tendency, in operating the hub and spoke model, for peripheral haemophilia centres and other, non-specialist, hospital units to refer patients with these less serious conditions to haemophilia centres in the major cities.

Isolating the numbers for individuals with Haemophilia A and B, the pattern is illustrated in Figure 3.2.

**Figure 3.2: Individuals with Haemophilia A and Haemophilia B registered in Scotland**



**3.40** These data are accepted as accurate for the purposes of this report. The data for patients with Haemophilia A and Haemophilia B provide a reasonable view of the majority of patients potentially exposed to risk in and after 1980, since registration would have followed attendance at a haemophilia centre, whether the patient was treated or not. The numbers cannot be treated as completely accurate, since it is likely that some patients (particularly mildly and moderately affected patients) still preferred to receive the required treatment locally, rather than at what may have been a remote haematology clinic. Consequently, such patients were not referred to a haemophilia centre, and were not registered with UKHCDO.

<sup>48</sup> Von Willebrand's disease is an inherited blood disorder with symptoms of spontaneous bleeding similar to haemophilia, although significantly affecting women as well as men (unlike haemophilia).

**3.41** The UKHCDO Bleeding Disorder Statistics for April 2010 to March 2011<sup>49</sup> show the total numbers of UK patients currently on the register for that year, and provide a basis for comparison of the Scottish data in Table 3.2 with the position in the rest of the UK, as set out in Table 3.3.<sup>50</sup>

**Table 3.3: Count of registered patients: All Scottish centres and all other centres – 2011**

	Haemophilia A	Haemophilia B	Females with F.VIII deficiency	Females with F.IX deficiency	vWD M + F	Total
All centres	5367	1133	1116	345	9112	17,073
Scotland	409	113	81	41	995	1639
Centres other than Scotland	4958	1020	1035	304	8117	15,434
Scotland/ all centres %	7.62	9.97	7.26	11.88	10.92	9.6
Scotland/ rest of UK %	8.25	11.08	7.83	13.49	12.6	10.62

**3.42** It is not possible to make a similar comparison for earlier years, since the Scottish data before 2011 have been fully revised (for the purpose of informing this Inquiry) to avoid duplication, while the figures for the rest of the UK have not. The figures available for the UK as a whole are set out in Table 3.4.

**Table 3.4: Count of registered patients: All UK centres**

	Haemophilia A	Haemophilia B	von Willebrand's disease	Total
1987	5195	982	2215	8392
1990	5339	1055	2688	9082
1995	5413	1133	4105	10,651
2000	5385	1165	5955	12,505
2005	6012	1276	7718	15,006
2009	6480	1372	9265	17,117

**3.43** The lack of fit of the von Willebrand's data with the data for Haemophilia A and B is as clear for the UK as it is for Scotland. The trends in growth of registered von Willebrand's disease appear generally to reflect the sensitivity of the results to variations in reporting and other factors referred to above. There is no other rational explanation for the apparent explosion in growth of the disease in Scotland, or in the UK as a whole. It is known that, historically, the disease was under-diagnosed. It is now recognised to be the most common bleeding disorder, but it is usually a mild disorder. Most patients were, and still are, more likely to be managed locally and outside the specialist haemophilia service.

<sup>49</sup> UKHCDO (2011) *UK National Haemophilia Database Bleeding Disorder Statistics for April 2010 to March 2011*. Available: <http://www.ukhcdo.org/docs/AnnualReports/2011/UKHCDO%20Bleeding%20Disorder%20Statistics%20for%202010-2011.pdf> Last Accessed 3 February 2015

<sup>50</sup> Data for 2011–2012 are available in the UKHCDO Annual Report for that year. However, the data for Scottish registrations relate at latest to 2010–2011. Differences are small and are unlikely to alter significantly the ratios of Scottish to UK patients.

In that case they may not be reported to the National Haemophilia Database at all.<sup>51</sup> These data continue to be revised. For present purposes they are accepted as an accurate reflection of the information available to the UKHCDO and the Scottish Haemophilia Directors.

### *Numbers of bleeding disorder patients infected with Hepatitis C*

#### UKHCDO – Initial research

**3.44** All patients with coagulation disorders were exposed to risk if they required treatment with blood, blood components or blood products, before the introduction of routine screening of blood donations for HCV and effective virus inactivation. Cryoprecipitate was commonly associated with transmission of HCV infection. Factor concentrates were almost universally associated with transmission of HCV. This was the case whether the concentrates were produced by commercial companies or by the NHS and whether a patient received a single treatment or multiple treatments.<sup>52</sup> An SNBTS Factor IX concentrate, effectively heat-treated to inactivate the virus, was released in October 1985. By 1987 effective virus inactivation had been introduced for PFC's Factor VIII concentrate, and manufacture of concentrates by the older processes had stopped. In each case, until effective heat treatment was introduced it is likely that almost all haemophilia patients who received treatment in the 1970s and most of the 1980s with factor concentrates made from the large pools of plasma, contracted Hepatitis C.

**3.45** Data of patients' use of factor concentrates were held in the National Haemophilia Database, and the UKHCDO provided an estimate of the number of patients exposed to Hepatitis C on the basis of their exposure to concentrate administered in a Scottish Haemophilia Centre. A UKHCDO statistics report was produced in April 2012 following additional work by the organisation and by the individual haemophilia centres in Scotland to enter additional data into the database, to correct inaccuracies in data previously entered and to cross-check all of the data entered against the UKHCDO's paper archive and against the information held by the Scottish centres.<sup>53</sup> It was acknowledged that there were weaknesses in the exercise. Quite apart from inherent problems leading to duplication of entries, the data were only as good as the submissions on which they were based. Further, in his introduction to the updated report of April 2012, Dr Hay stated:

Inevitably, given the time that has elapsed since the period of interest, there remain gaps and many centres no longer have records stretching that far back and have not been able to cross-check everything. Nevertheless, we believe that the data presented is now as complete and as accurate as we are able to make it.<sup>54</sup>

**3.46** The UKHCDO extracted data from the National Haemophilia Database as adjusted, which indicated that 296 living patients and 216 deceased patients treated at Scottish centres had been exposed to HCV, giving a total of 512.<sup>55</sup> Within that total, research

<sup>51</sup> Dr Hay – Day 8, page 22

<sup>52</sup> Ibid pages 33–35; *Methodology for collation of Scottish HCV & NANB data for Penrose Inquiry*, Dr Campbell Tait, 23 February 2011 [PEN.013.0016] at 0019 and 0020, paragraph 4; Dr Tait – Day 14, page 84; literature referred to in paragraph 7.4, footnote 3 of the Preliminary Report.

<sup>53</sup> The further work undertaken by the UKHCDO in conjunction with the Scottish Haemophilia Centres is more fully set out in Dr Hay's introduction to the updated UKHCDO report, UKHCDO report *National Haemophilia Database: Bleeding disorder statistics for the Penrose Inquiry*, 2012 [PEN.019.0927] at 0933

<sup>54</sup> Ibid [PEN.019.0927] at 0934

<sup>55</sup> Ibid [PEN.019.0927] at 0985, Table 8. There is an error in the summation of the figures. The figure for Inverness patients who were alive in 2011 should be 26.



uncovered a number of duplications. Excluding these, the adjusted totals provided by the UKHCDO were 254 living patients and 193 deceased patients, a total of 447. That was the position at April 2012 when the UKHCDO produced its updated report.<sup>56</sup> Table 7 in the report provided a diagnostic breakdown of patients known to the UKHCDO as at 2011, both alive and dead, who were thought to have been infected with Hepatitis C by virtue of exposure to clotting factor concentrates, prior to effective virus inactivation (1987). The data are summarised below in Table 3.5.

**Table 3.5: Estimate of the number of patients exposed to Hepatitis C based on historical clotting factor concentrate exposure from a Scottish Haemophilia centre: April 2012 Survey**

Diagnosis	Alive	Dead
Haemophilia A	165	158
Haemophilia A with liver transplant	1	3
Acquired Haemophilia A	2	3
Haemophilia B	58	19
Females with VIII deficiency	7	0
Females with IX deficiency	4	0
von Willebrand's disease	16	10
Temporary coagulation defect, now normal	1	0
Totals	254	193
Total number exposed	447	

**3.47** These numbers reflected the adjustments to UKHCDO raw data required to exclude double counting where patients were treated at more than one centre and returned by each.<sup>57</sup> The total number of deaths from all causes in the population, 193, has been cross-checked with the Office of National Statistics. The number of liver-related deaths appears to be 21.<sup>58</sup>

**3.48** The figures tabulated are based on known concentrate exposure, believed to be solid data. The strengths of the exercise are:

- The data were collected contemporaneously rather than retrospectively and so the documentary evidence on which they were based was as complete as it was ever going to be. In some cases the original local documentation had been destroyed and the National Haemophilia Database was the only available evidence.
- The Database was compiled from data for each patient submitted by the managing centre.
- The UKHCDO had data on patients who died before the advent of testing and data on patients subsequently lost to follow-up for which there was now no information available directly from the centres.<sup>59</sup>

<sup>56</sup> Ibid [PEN.019.0927]

<sup>57</sup> Ibid [PEN.019.0927] at 0981

<sup>58</sup> Ibid [PEN.019.0927] at 0986, Table 9

<sup>59</sup> Dr Hay's letter dated 16 January 2013, page 5 [PEN.019.1319] at 1323

**3.49** Dr Hay commented that the estimate of 447 patients exposed to Hepatitis C on the basis of concentrate therapy was probably an under-estimate of the total population at risk. It did not include provision for the number of patients likely to have been exposed through treatment with blood, blood components or cryoprecipitate, rather than concentrates.<sup>60</sup> In oral evidence, Dr Hay expanded on this:

The other thing you need to recognise about these figures is that they are likely to be conservative because they are based on our records of concentrate exposure and some patients may only have been treated with blood components, plasma or cryoprecipitate, and we feel that our data on that exposure may be incomplete ...

So we have assumed that everyone who has had concentrate will have been exposed to Hepatitis C if they were treated during the period of risk. But they may in fact have contracted Hepatitis C before their first exposure to concentrate from treatment with blood components, particularly if they have a severe bleeding disorder and require regular treatment.<sup>61</sup>

**3.50** The results were not presented as definitive.

### Scottish Haemophilia Centre Directors

**3.51** The Scottish Haemophilia Centre Directors provided the Inquiry with separate estimates of the number of patients registered with Scottish Haemophilia Centres who were infected with the Hepatitis C virus as a result of their treatment with blood products (coagulation factor concentrate, cryoprecipitate or fresh frozen plasma) in February 2011 and March 2013. Dr Campbell Tait, Director of the Haemophilia Centre at Glasgow Royal Infirmary, explained that in February 2011 the Scottish Directors used UKHCDO data relating to patients at risk of having contracted Hepatitis C as a result of their treatment between 1970 and 1988,<sup>62</sup> and HCV status data from patient records held at Scottish Haemophilia Centres.<sup>63</sup> The Scottish Haemophilia Directors excluded from the UKHCDO data any patient whose first treatment was outwith Scotland, any patient known to have tested negative for Hepatitis C post-1991 (76 patients) and any patient whose sole treatment at a Scottish Haemophilia Centre during the relevant period was with non-plasma based products (for example synthetic agents such as Desamino-D-arginine-vasopressin (DDAVP)). The Directors then added a small number of patients known by Scottish Haemophilia Centres to be HCV positive, most likely from treatment in Scotland, but who did not appear on the list from the UKHCDO.

**3.52** In summary, comparison of the outcomes of the Scottish Haemophilia Centre Directors' study in February 2011<sup>64</sup> and the April 2012 UKHCDO survey appeared to show material differences in the numbers of HCV-infected patients with Haemophilia A or B and patients with von Willebrand's disease. This information is set out in Table 3.6.

<sup>60</sup> UKHCDO report *National Haemophilia Database: Bleeding disorder statistics for the Penrose Inquiry*, 2012, page 51 [PEN.019.0927] at 0983. The Inquiry understands that the UKHCDO statistics report categorises cryoprecipitate as a 'blood component' rather than as 'concentrate'.

<sup>61</sup> Dr Hay – Day 8, pages 41–42

<sup>62</sup> *Methodology for collation of Scottish HCV & NANB data for Penrose Inquiry*, Dr Campbell Tait, 23 February 2011 [PEN.013.0016] (this methodology superseded an earlier methodology, [PEN.001.0057].)

<sup>63</sup> The start date of 1970 is a few years before the introduction and widespread use of factor concentrate in Scotland. Having said that, there may well have been patients with haemophilia who were infected with Hepatitis C in the 1960s as a result of treatment with cryoprecipitate or other blood products (made from much smaller pools of plasma than factor concentrate in the 1970s and 1980s). These patients will not be included in the estimates provided by the Scottish Haemophilia Directors.

<sup>64</sup> *Methodology for collation of Scottish HCV & NANB data for Penrose Inquiry*, Dr Campbell Tait, 23 February 2011 [PEN.013.0016] at page 0018

**Table 3.6: Comparison of the Scottish Haemophilia Centre Directors' study and the UKHCDO survey**

Diagnosis	UKHCDO survey: April 2012	Scottish Directors' study: February 2011
Haemophilia A	332	303
Haemophilia B	77	68
von Willebrand's disease	26	62
Other coagulation disorders	12	26
Total	447	459

**3.53** Dr Tait commented on weaknesses in the Scottish Directors' study at that stage:

Determining whether patients remaining on the list, who have never had an HCV antibody test undertaken, had NANB or HCV is very difficult. Some of the patients are dead and have no remaining blood sample that could be tested for HCV. Otherwise clarification will require detailed review of historical medical case notes (which in many centres no longer exist). It is possible that some of these patients have undiagnosed HCV .... Therefore it is the intention of the Scottish Haemophilia Centres to, where possible, trace these 'unknowns' and suggest HCV testing where appropriate.

Some of these patients only had a very few treatments in Scotland, and were probably visitors who if they did have HCV would likely have contracted it outwith Scotland – but we have insufficient information to be certain.

Therefore the final list supplied to [the Inquiry] represents the estimated maximum number of bleeding disorder patients who contracted HCV from treatment in Scotland.<sup>65</sup> The accuracy of the data is limited by the assumptions made. There are small numbers of patients who received PFC Factor VIII before July 1987 who are HCV negative and the numbers of patients infected as a result of cryoprecipitate therapy only, are likely to be overstated.<sup>66</sup>

**3.54** HCV negative patients would comprise patients exposed to the virus but were not infected, and patients who were infected but had cleared the virus. In their methodology statement, the Scottish Haemophilia Directors indicated that they had assumed that all patients treated with coagulation factor concentrates or cryoprecipitate prior to July 1987 contracted Hepatitis C, unless they had subsequently been tested negative.<sup>67</sup> On that basis, up to 62 von Willebrand's patients may have contracted HCV in Scotland. The UKHCDO estimated that 26 von Willebrand's patients treated at Scottish Haemophilia Centres contracted HCV infection.<sup>68</sup>

<sup>65</sup> Elsewhere, Dr Tait described the estimate of 459 patients who contracted HCV as a result of treatment in Scotland as a 'cautious overestimate': *Methodology for collation of Scottish HCV & NANB data for Penrose Inquiry*, Dr Campbell Tait, 23 February 2011 [PEN.013.0016] at 0018, paragraph 1

<sup>66</sup> Ibid [PEN.013.0016], at 0017 and 0018, paragraphs 10–12

<sup>67</sup> Ibid at [PEN.013.0016]

<sup>68</sup> UKHCDO report *National Haemophilia Database: Bleeding disorder statistics for the Penrose Inquiry, 2012* [PEN.019.0927] page 52.

**3.55** In addition to estimating the maximum number of NHS coagulation disorder patients infected with Hepatitis C, the Scottish Haemophilia Directors provided an estimate of the minimum number infected as a result of treatment in Scotland. In their February 2011 study that minimum number was 314, on the basis that 314: 'represents the numbers that we know who are or have been Hepatitis C antibody positive, plus a small number who were never tested but we have evidence that they clinically suffered an episode of non-A non-B hepatitis'.<sup>69</sup> That estimate was therefore based on hard data.

**3.56** The totals advised by the UKHCDO and the Scottish Haemophilia Directors at this stage were broadly consistent with the advice received by Lord Ross' Expert Group<sup>70</sup> that approximately 500 haemophilia patients were likely to have become infected with Hepatitis C as a result of treatment in Scotland with blood products.<sup>71</sup> However, the initial exercises not only produced figures that differed numerically; more significantly it identified differences in the nature of the data available and the assumptions used. Dr Hay of the UKHCDO and Dr Tait, representing the Scottish Haemophilia Directors, were asked to reconsider their evidence. They did so and each produced further information.<sup>72</sup>

**3.57** Dr Tait's statement of 8 January 2013, revealed differences in underlying data among the various estimates provided. The UKHCDO based the estimate of likely HCV-infected patients (447) on the assumption that the virus was transmitted on the patient's first exposure to clotting factor concentrates. The UKHCDO database did not include information on patients' known HCV status, positive or negative. In his evidence, Professor Goldberg had explained that HPS was aware of 351 individuals who had received blood factor concentrates and who had been diagnosed as Hepatitis C antibody positive.<sup>73</sup> These data related solely to bleeding disorder patients in Scotland who had tested positive for anti-HCV and who were likely to have acquired infection through blood product exposure. The HPS data did not distinguish patients according to the country in which it was likely they were infected, and did not take account of any patients who had died before antibody testing became available in about 1990. A recent review of the Scottish Haemophilia Directors' data had shown that among the cohort of 351 infected patients identified in Scotland there were 46 who were thought to have contracted HCV from prior treatment outwith Scotland. The Scottish Haemophilia Directors' own exercise had revealed 15 patients not included in the UKHCDO list; accordingly the UKHCDO figure could be adjusted to 462, which was similar to the Directors' figure of 459.

**3.58** Having reviewed the data in 2013, Dr Tait advised on the range:

- A minimum number of 300 to 305 bleeding disorder patients known to have contracted HCV (as assessed by HCV antibody positivity) through haemostatic treatment in Scotland.

<sup>69</sup> Dr Tait – Day 14, page 83 and *Methodology for collation of Scottish HCV & NANB data for Penrose Inquiry*, Dr Campbell Tait, 23 February 2011 [PEN.013.0016] at 0017, paragraph 8

<sup>70</sup> See paragraph 3.173

<sup>71</sup> Final Report of Lord Ross' Expert Group, March 2003; paragraph 4.8. <http://www.scotland.gov.uk/Publications/2003/03/16844/20519>. This advice appears to have been received from the UK Haemophilia Directors (letter dated 24 July 2002 from Dr Brian McClelland to Mr Bob Stock, Special Advisor [SGH.005.7201] at 7202). While it is not clear how that figure was arrived at, it may have been based on the approximate number of patients with bleeding disorders in Scotland who received treatment with concentrate during the relevant period.

<sup>72</sup> Dr Hay's letter dated 16 January 2013: [PEN.019.1319] Dr Tait's response to further questions on statistics, 8 January 2013: [PEN.019.1306]

<sup>73</sup> Professor Goldberg – Day 6, pages 116–119. See also Professor Goldberg's statement on statistics relating to haemophilia patients infected with HCV dated 1 February 2011 [PEN.001.0206], questions 1 and 2 at 0206 and accompanying tables at 0207. A breakdown of (a) the health board area where each patient resides or, if not known, where the positive sample was taken, (b) the reported blood disorder and (c) the year of the earliest specimen positive for HCV antibody is shown at [PEN.001.0206] at 0207.

- An estimated upper figure of 459 to 462, based on the Scottish Haemophilia Directors' estimate of 459 patients and the UKHCDO figure of 447 increased by 15 patients not on the UKHCDO list who were known to the Scottish Directors to be anti-HCV positive, most likely due to treatment in Scotland.<sup>74</sup>

**3.59** On 26 March 2013 the Inquiry received an updated version of the Scottish Haemophilia Directors' calculations as prepared for publication.<sup>75</sup> The Inquiry is grateful for the additional work carried out. In its final form, the paper reported that 455 patients with bleeding disorders were estimated to have been infected with HCV by coagulation factor provided by NHS Scotland before 1989. Of these, 440 were agreed with the updated UKHCDO database and 15 further patients were known to Scottish Haemophilia centres but did not appear in the list prepared by UKHCDO.

**3.60** In order to chart outcomes after infection, Khan and colleagues reported on a second cohort of 302 patients, of whom 255 were included in the revised total of 455 patients infected in Scotland and 47 were infected elsewhere but followed up in Scotland.<sup>76</sup> Of the 302 patients, 293 had Polymerase Chain Reaction (PCR) testing performed and of that 293, 51 patients (17.4%) cleared the infection naturally. Of the group of 293 patients who were tested, 243 were PCR positive at some stage. One of those 243 patients was documented as being positive on one occasion and tested negative thereafter despite having no treatment, giving a total of 51 patients with natural clearance. Further, of those 243 patients, 103 had by February 2012 completed combination anti-viral treatment with ribavarin and alpha-interferon or pegylated interferon. The overall sustained viral response for combination therapy was 38.8%.<sup>77</sup> Fourteen of the 302 (4.6%) had a diagnosis of hepatocellular cancer, and 10 of those patients had died at February 2012. By the same date, 11 patients had undergone liver transplantation (seven for liver failure and four for liver cancer) and seven of them were still alive.<sup>78</sup>

#### UKHCDO – Further research

**3.61** Following the 2012 report (and as anticipated in it), the UKHCDO began a more detailed and systematic HCV look-back study, partly stimulated by the Inquiry. In collaboration with each haemophilia centre, including those in Scotland, data were collected from haemophilia centres on individual patients' Hepatitis C test results. In a letter dated 16 January 2013,<sup>79</sup> Dr Hay explained that at January 2013, and with the UKHCDO HCV look-back still incomplete, a very preliminary overall estimate of the numbers infected with HCV should first include the 447 patients (alive and dead) exposed to infection by concentrate, as set out in the earlier exercise. Dr Tait's review then noted that there were 15 patients known by the Scottish Haemophilia Directors to be HCV positive, most likely due to treatment in Scotland, who were not included in the UKHCDO list of 447 patients. Adjusting for those increased the UKHCDO figure to 462. The amended and additional data provided by the UKHCDO was not available when the Scottish Haemophilia Directors updated their estimates as set out in the paper by Khan and colleagues.

<sup>74</sup> Dr Tait's response to further questions on statistics, January 2013 [PEN.019.1306] at 1307

<sup>75</sup> Khan *et al*, 'Assessment of hepatitis C infection and outcomes in the Scottish haemophilia population', *Haemophilia*, 2013; 19:870–875 [PEN.019.1336] This version contained minor adjustments to figures previously provided, together with new information about treatment and follow-up.

<sup>76</sup> *Ibid* [PEN.019.1336] at 1341

<sup>77</sup> *Ibid* [PEN.019.1336] at 1343

<sup>78</sup> *Ibid* [PEN.019.1336] at 1342

<sup>79</sup> Dr Hay's letter dated 16 January 2013 [PEN.019.1319]

**3.62** Dr Hay provided a further table showing a diagnostic breakdown of 85 Scottish patients exposed only to blood components (plasma, cryoprecipitate and blood or platelet concentrates) and not exposed to (factor) concentrates during the period of risk.<sup>80</sup> Not all of the patients in this group would have become infected with HCV.

**Table 3.7: Estimate of the number of patients in each diagnostic group exposed to Hepatitis C based on historical plasma exposure from a Scottish Haemophilia centre (January 2013; based on first 20% data only)**

	Alive	Dead
Haemophilia A	18	9
Haemophilia B	1	2
Females with Factor VIII deficiency	4	0
Females with Factor IX deficiency	3	0
von Willebrand's disease	33	6
Factor VII deficiency	1	0
Factor IX deficiency	1	0
Factor XII (Hageman) defect	1	0
Factor XIII deficiency	1	0
Fibrinogen deficiency	1	0
Platelet defects (misc)	2	0
Unclassified	0	1
Temporary coagulation defect, now normal	1	0
Total	67	18

**3.63** On the basis of data available in the look-back exercise as a whole, Dr Hay estimated that patients selected in this way would have an 18.6% probability of HCV infection. This would add a further 16 patients to the UKHCDO number. Of that group of 16, chronic HCV infection would be expected in 10-12.<sup>81</sup> Whilst this approach permitted him to estimate the proportion of that group exposed to HCV, it did not permit him to identify individual patients likely to have been infected.<sup>82</sup> This look-back study was ongoing at the time and Scottish centres had by then submitted only 20% of the data requested. More accurate data might therefore become available on completion of the exercise.<sup>83</sup>

**3.64** As noted already, it is highly likely that almost all of the patients exposed to risk in the course of their treatment with factor concentrates before effective heat treatment was introduced, will in fact have had Hepatitis C virus transmitted to them at some time. However, current understanding of the natural history of infection with HCV indicates that a percentage of patients will either not have developed an HCV infection or will have cleared the virus spontaneously. Where that is due to a protective immunity or to the individual's other genetic characteristics, the same outcome will follow a subsequent infection.<sup>84</sup> Estimates vary, as indicated by the evidence noted so far.

<sup>80</sup> Ibid [PEN.019.1319] at 1326

<sup>81</sup> Ibid [PEN.019.1319] at 1324

<sup>82</sup> Ibid [PEN.019.1319] at 1326

<sup>83</sup> Ibid [PEN.019.1319] at 1324

<sup>84</sup> See Chapter 13, *Knowledge of Viral Hepatitis Now*, paragraph 13.17

### *Discussion of the reported estimates*

**3.65** It is still not possible to achieve a satisfactory reconciliation of all available sources of data. The additional evidence of Dr Hay and of Dr Tait is accepted as providing the best estimates that can be made on the sources of information available. They provide a measure of reconciliation of the upper figures and therefore an indication of the likely extent of the problem. However, each has stated that the exercises now reported are continuing. The UKHCDO continues to refine its exercise. The Scottish Haemophilia Directors group continues to seek out and assess patients who have or may have received coagulation treatments prior to 1989–91 and who remain untested for HCV. It is a slow ongoing process.

**3.66** In the circumstances it is important to avoid underestimating the prevalence of HCV infection among blood disorder patients. While some percentage of those at risk may have avoided infection and others will have cleared infection spontaneously, these numbers cannot be known with any certainty. It seems safer to proceed on the basis that all of those at risk were infected. The UKHCDO estimate (as adjusted in conjunction with the additional data provided by Dr Tait) of 462 patients infected by concentrates is accepted on that basis. The number infected by blood components and plasma products is speculative at this stage. It is possible to estimate a number arithmetically, but any exercise is based on the selection of assumptions required for the calculation. The data gathered to date (20% of the data sought) are not a random sample and cannot be assumed to represent the whole class. So far, it appears that 16 patients can be added to the 462. It is not known what the remaining 80% of data will reveal and no provision is therefore made for any additional numbers of patients which may be generated.

### *Patients with bleeding disorders known to have been infected with Hepatitis C*

#### **Health Protection Scotland**

**3.67** Agencies other than UKHCDO recorded lower numbers of patients said to have been infected with HCV. As previously observed, Professor Goldberg gave evidence that HPS is aware of 351 individuals who had received blood factor concentrates and been diagnosed as Hepatitis C antibody positive.<sup>85</sup> For each of these individuals there was no information to indicate that blood factor concentrates had been received outside Scotland.

**3.68** Dr Tait suggested that the HPS data could be reconciled with the Scottish Haemophilia Directors' data. A review carried out in February 2012 by Dr Henry Watson of the Directors' 2007 review of HCV and its treatment in Scotland had identified, within the cohort of HCV-positive bleeding disorder patients, 46 persons who were thought to have contracted HCV from prior treatment outwith Scotland.<sup>86</sup> Adjusted for these patients, the HPS figure was reduced to 305, a close similarity to the Scottish Haemophilia Directors' figure for bleeding disorder patients known to be HCV positive from treatment in Scotland.<sup>87</sup>

**3.69** That is accepted. Yet it indicates that the HPS database presently captures, and is able to capture, only part of the relevant data. It provides clear evidence of the numbers found to be infected on testing at virology laboratories reporting to HPS. Of necessity that cannot cover patients who were never tested while they were alive. As shown in Table 3.5, UKHCDO data suggest that, by April 2012, 193 Scottish blood disorder patients exposed

<sup>85</sup> Paragraph 3.57

<sup>86</sup> Dr Tait's Response to further questions on statistics, 8 January 2013 [PEN.019.1306]

<sup>87</sup> Paragraph 3.55

to clotting factor concentrates before 1988 had died. Some might have been collected by retrospective testing of stored samples, but that would be of assistance only if there had been a systematic study of stored samples. There is no evidence of that having happened. Finally, as Professor Goldberg indicated, clinical information available to HPS is very limited in respect of the underlying diagnoses of those tested.<sup>88</sup>

### The Skipton Fund

**3.70** The Skipton Fund<sup>89</sup> advised that 231 patients with bleeding disorders living in Scotland who had received treatment with blood products and who were alive as at August 2003 had received payments from the Fund.

**3.71** HPS and Skipton data might suggest that the actual numbers infected may have been lower than the estimates already mentioned. However, some patients may well have been infected by the virus but cleared it prior to the availability of testing. Others may have died without infection with Hepatitis C being diagnosed. Some may survive without signs or symptoms of infection having been noted or brought to the attention of those keeping the relevant records.

**3.72** In the case of the Skipton Fund, it cannot be assumed that every person entitled to make a claim did so, and there is some concern about the reliability of a very small number of the claims admitted.<sup>90</sup> It would not be appropriate to adjust downwards the numbers of patients infected, as inferred from exposure to risk, on the basis of these recorded data.

**3.73** The Skipton data are consistent with the UKHCDO data on living patients: given the limits on accuracy in the exercise as a whole, the difference between 231 and 254 living patients is not significant.

### Hepatitis C – secondary transmission

**3.74** As discussed elsewhere in this Report, secondary transmission of Hepatitis C occurs relatively rarely from mother to baby and, even less commonly, as a result of sexual transmission.

**3.75** As regards possible secondary transmission of HCV from patients with bleeding disorders to their partners, Dr Tait said:

Where appropriate, during counselling, HCV infected haemophilia patients were informed about the suspected low risk of sexual transmission and that partners could be tested. This testing could be undertaken by the partner's GP, by the Haemophilia Centre or by the Infectious Disease Units in Glasgow and Aberdeen. In reality, only a small number of partners attended the Haemophilia Centres for testing (approximately 40 between Edinburgh and Glasgow), and I understand from colleagues that only 1 partner was found to be positive. Since the Haemophilia Centre staff had no direct contact with other partners, nor necessarily knew their identity, we have no information on their HCV status.<sup>91</sup>

<sup>88</sup> Professor Goldberg – Day 6, pages 99–100; Professor Goldberg's statement on statistics relating to haemophilia patients infected with HCV dated 1 February 2011 [PEN.001.0206] at 0211

<sup>89</sup> See paragraph 3.140

<sup>90</sup> See paragraph 3.146

<sup>91</sup> *Methodology for collation of Scottish HCV & NANB data for Penrose Inquiry*, Dr Campbell Tait, 23 February 2011 [PEN.013.0016] at 0018, paragraph 13



**3.76** Beyond noting that a minority of patients who contracted Hepatitis C as a result of infected blood or blood products may in turn have inadvertently infected others, it is not possible for the Inquiry to make an estimate of the number of individuals who may have contracted Hepatitis C as a result of secondary infection. It seems reasonable, however, to conclude that the number will have been very small and given the margins of error inherent in the overall estimation of patients at risk, would not make any material difference to assessing the scale of infection.<sup>92</sup>

### *Conclusions on HCV infection among patients with bleeding disorders*

**3.77** The most reliable estimates of the number of patients with bleeding disorders who were exposed to risk of infection with Hepatitis C as a result of their treatment in Scotland are those provided by the UKHCDO in collaboration with the Scottish Haemophilia Directors. Together, they have the best relevant data. Given their expertise in this area and the detailed investigation they have made of their respective records, their evidence is accepted as sufficiently reliable to support conclusions on numbers overall. Taking on board this ongoing work and using the data from the UKHCDO's ongoing look-back exercise, so far the best estimate appears to be about 478.

### *Hepatitis C as a cause of death among patients with bleeding disorders*

**3.78.** The Inquiry attempted to establish how many patients with bleeding disorders had died as a result of infection with HCV. The Inquiry was assisted by evidence from the Scottish Haemophilia Directors, the UKHCDO and Professor Goldberg of HPS.

**3.79** Dr Campbell Tait, on behalf of the Scottish Haemophilia Directors, stated:

To date we have not been able to establish with certainty the current status (alive or deceased) for many patients on the list. This work is ongoing and may well be updated following the cross-referencing exercise with the HPS database. We also have no readily available information on causes of death, but again efforts will be made to establish this detail. Thus at present we can only determine that of 314 cases known to be HCV positive or likely to have had NANB hepatitis, 88 are known to be no longer alive, and of these 88 liver disease was a major contributor to death in 29 out of the 65 for which we currently have 'cause of death' details.<sup>93</sup>

**3.80** Dr Tait confirmed that for the 65 patients for whom cause of death details were available, the data were provided largely by HPS from the information noted on death certificates, albeit some data may also have been provided by the UKHCDO.<sup>94</sup> To date, Dr Tait and colleagues have not been able to undertake further work on the causes of death of coagulation disorder patients infected with HCV.<sup>95</sup>

<sup>92</sup> The witness 'Laura' was a case of secondary infection – the only case disclosed by the evidence. See Chapter 6, *An Examination of the Effects of Infection with Hepatitis C on the Patients and their Families, Including Treatment*.

<sup>93</sup> *Methodology for collation of Scottish HCV & NANB data for Penrose Inquiry*, Dr Campbell Tait, 23 February 2011 [PEN.013.0016], at 0020, paragraph 5

<sup>94</sup> Day 14, Pages 130–131

<sup>95</sup> Dr Tait's response to further questions on statistics, 8 January 2013 [PEN.019.1306]

**3.81** Dr Tait discussed a separate exercise undertaken by the Scottish Haemophilia Directors to document key features relating to HCV infection in patients looked after in the Scottish centres. Dr Tait explained: 'The patients included were predominantly infected in Scotland but include small numbers of HCV-infected patients who had moved to Scotland and were being cared for in a Scottish centre.'<sup>96</sup> The results of that exercise were set out in an Abstract which noted that, overall, 248 of 291 patients infected with Hepatitis C (85%) were still alive as at summer 2007. Death had occurred in 11 out of 33 patients (33%) who were co-infected with HIV, against 32 out of 260 patients (12%) who were infected with Hepatitis C only.<sup>97</sup>

**3.82** The updated statistics report provided by the UKHCDO included data on the cause of death of the 193 patients who had been exposed to Hepatitis C as a result of their treatment with factor concentrate and who, as at 2011, were known to be dead. The report explained:

The number and causes of death data are derived from reports from centres and reports from the Office of National Statistics. We provide them with details of all (25,000+) patients registered with the database and they flag them up when they die and send us death certification data.<sup>98</sup>

**3.83** The UKHCDO advised that of the 193 patients exposed to Hepatitis C as a result of their treatment with factor concentrate who were known to have died as at 2011, 21 patients had a liver-related cause of death.<sup>99</sup>

**3.84** Professor Goldberg gave evidence that, as at December 2009, of the 351 patients with blood disorders recorded by HPS as having contracted Hepatitis C as a result of treatment with a blood factor, 78 patients were known to have died.<sup>100</sup> Of these 78 individuals, 15 had a primary liver-related cause of death recorded on their death certificate and 15 had a secondary liver-related cause of death recorded. Professor Goldberg added the caveat that 'it is not possible to conclude, from this information alone, if Hepatitis C materially contributed to death in these instances'.<sup>101</sup> As will be seen in the discussion of deaths among transfusion patients at paragraph 3.260, Professor Goldberg did not regard death certificates as a reliable means of identifying those whose cause of death related to infection with Hepatitis C.

**3.85** As can be seen from the discussion above, it has not been possible to arrive at an exact number of deaths resulting from HCV infection among patients with bleeding disorders. The current status of some patients is unknown, and even where a patient is known to have died, determining the role of HCV from the information on the death certificate involves some guesswork. The following figures emerged from the various investigations reported to the Inquiry:

<sup>96</sup> *Methodology for collation of Scottish HCV & NANB data for Penrose Inquiry*, Dr Campbell Tait, 23 February 2011 [PEN.013.0016] at 0020, *Scottish Haemophilia Directors 2007 review of HCV and its treatment in Scotland*. This list of patients is different to the list of 459 patients discussed above, who the Scottish Haemophilia Directors considered may have been infected with HCV as a result of their treatment in Scotland.

<sup>97</sup> Khan *et al* 'Outcomes of hepatitis C infection in a large haemophilia population' [PEN.013.0008].

<sup>98</sup> UKHCDO report *National Haemophilia Database: Bleeding disorder statistics for the Penrose Inquiry*, 2012, page 55 [PEN.019.0927] at 0987

<sup>99</sup> *Ibid*, table 9, pages 54–55 [PEN.019.0927] at 0986–7

<sup>100</sup> Professor Goldberg's statement on statistics relating to haemophilia patients infected with HCV, dated 1 February 2011 [PEN.001.0206], question 5 and page 0208. While 273 individuals were 'not known to have died', that does not mean that any of these individuals had not in fact died. Some of these individuals may have died but their deaths were not notified to HPS.

<sup>101</sup> Professor Goldberg's statement on statistics relating to haemophilia patients infected with HCV [PEN.001.0206], question 5

Source	Population in study	Deaths with liver-related cause
Scottish Haemophilia Directors (reported by Dr Tait)	314 cases known to be HCV +ve or likely to have NANBH	29
UKHCDO	193 patients known to be HCV +ve and known to have died at 2011	21
HPS (reported by Professor Goldberg)	351 cases recorded as HCV +ve	30

### Patients exposed to risk of transmission of Hepatitis C as a result of blood transfusion

**3.86** The second group to be considered is referred to in paragraph 3.2, item ii, and consists of patients who were exposed to infection with Hepatitis C through transfusion with blood or blood components.

**3.87** There are several particular issues relating to transmission of HCV by transfusion around:

- the number of patients exposed to risk of infection;
- the number of individuals infected with HCV;
- the number of those infected who have been seriously affected by disease;
- the mortality from liver disease among those infected; and
- the numbers of infected individuals who might still be alive.

**3.88** Finding the answers to some of the questions that arise remains problematic. For example, the Inquiry has gathered evidence of the adverse consequence of infection for specific individuals, reflected in the narrative of patients' experiences, which demonstrates that in some cases the progression of disease has been associated with severe morbidity. These patients essentially make up a large but self-selected group of individuals prepared to provide evidence to the Inquiry. It cannot be assumed that they are representative of a wider population of patients, and inferences about total numbers affected to a similar extent cannot be valid. At most a general inference that significant numbers of patients are probably severely affected would be justified.

**3.89** It is not known how many patients in Scotland contracted Hepatitis C as a result of blood transfusion, following the increasing use of transfusion between the end of the Second World War and the introduction of the screening of donors for Hepatitis C in September 1991. There are several reasons for that. The size of the total population at risk is not known – that is the numbers of patients receiving transfusions of whole blood, or blood components which might have transmitted the virus, in the course of surgical or medical treatment, over the period when there was in fact a risk of transmission of infection. That period started before the reference period of the Inquiry. Material risk was probably low in the early 1970s. It grew thereafter with the increased prevalence of HCV infection in the general population, and by inference to some extent in the donor population. That increase can be estimated statistically, but is essentially unquantifiable. This major building block in any statistical analysis of the extent of HCV infection in transfusion recipients is at best incomplete.

**3.90** Inevitably, much of the evidence received has related to retrospective studies. In general terms, regardless of the infection concerned, the length of time over which the interval of retrospection extends may be a factor affecting the availability and reliability of the data available for study. There may be insufficient biological material (usually stored serum) from possibly infected individuals available to researchers for study. The virulence of the agent affects the reliability of studies. Very serious, often fatal, diseases may have left few survivors by the time the retrospective analysis is attempted. The age and co-morbidity of the infected individuals at the time of transmission also affects the population available for study. The longer the time that has elapsed since the putative transmission event, the more likely it is that the recipient has died. The cause of death may be related to the infection transmitted, or a cause other than the infection itself.<sup>102</sup> Older individuals affected by other unconnected but serious illnesses, may have died before the retrospective study is carried out, unaffected by the infection transmitted or where the contribution of that infection had not been identified.

**3.91** The infection may be distributed within a very large, heterogeneous, population. It may be impractical to test individuals from all cohorts within the population and extrapolation from one particular group to the population as a whole may lead to serious inaccuracies. Similarly, attempts to identify the incidence and prevalence of an infection from symptoms, may be vitiated when only a small proportion of those infected display recognisable symptoms within weeks, months or even years of acquiring the infection. The study of Hepatitis C in NHS patients provides a particular example of these difficulties.

**3.92** In contrast to patients with coagulation defects, most of whom benefit from regular monitoring and treatment as part of the management of their primary disease, the follow-up of patients receiving blood transfusion in the course of medical or surgical procedures has been less structured and less comprehensive. In addition, the vast majority of patients who have contracted Hepatitis C through transfusion are likely to have done so at a time before the virus was identified. By the time tests became available to diagnose the disease, many of those patients will have died untested for the virus (mostly as a result of age-related conditions or as a result of the condition which necessitated the transfusion). Of those patients who contracted Hepatitis C through transfusion and who were still alive when diagnostic tests became available, many have not been tested for Hepatitis C. Most of these patients will have been unaware that they may have been infected with the virus at the time of transfusion, since only a small minority of patients experience significant symptoms when first infected. For the majority of patients who are infected, symptoms readily related to the infection are unlikely to appear until decades later.<sup>103</sup> On the other hand, a proportion of those exposed to the virus either do not become infected or, if infected, spontaneously clear the virus and in either case would test negative for the virus. They would not go on to develop any Hepatitis C disease manifestations.

**3.93** Of those patients who develop symptoms and who test positive for Hepatitis C, a transfusion (possibly many years ago) may not be identified by the patient or the patient's clinician as the likely source of infection. In those cases where transfusion is identified as a possible route of transmission, matters may be complicated by the presence of other

---

<sup>102</sup> Dr Gillon – Day 6, page 22

<sup>103</sup> Professor Goldberg and Dr Schnier stated, 'HCV infection, in over 95% of instances, is a silent event, with the consequences of long standing infection only becoming apparent decades after its acquisition'. *Estimation of the Number of Individuals Infected as a Consequence of Blood Transfusion in Scotland 1970–1991* – Goldberg and Schnier [PEN.018.1561], paragraph 4.1.

possible routes of transmission which cannot be excluded, such as intravenous drug use, which is by far the most common route of transmission overall in Scotland and in the rest of the UK.

**3.94** Despite these considerable difficulties, the Inquiry has attempted to investigate the number of patients who may have contracted HCV as a result of blood transfusion in Scotland. Several sources of evidence have been drawn to the attention of the Inquiry. There were radical changes in reporting structures in 1995 and 1996 which complicate discussion of the sources and of the data contributed. It is appropriate, however, to note that the problem facing the Inquiry is not new: look-back studies were initiated to find and inform those who had been infected, out of a sense of responsibility for their welfare. The investigation of the numbers affected arose incidentally in that context, and it is to the conduct and outcome of those studies that it is necessary first to turn.

### *The look-back studies*

**3.95** Targeted HCV look-back studies, first in the Edinburgh and south east region of the SNBTS and later throughout the UK, are discussed generally in Chapter 35, *An Investigation into the Steps Taken to Identify the Individuals who were Infected (Look-back)*. In 'targeted look-back' the donation histories of individuals found to be infected when screened for a specific pathogen are followed with a view to tracing possible recipients of blood, blood components or products prepared from previous donations by those individuals, in order to ascertain whether any of the recipients may have contracted the virus. For the purposes of this chapter, the outcome of the national HCV look-back discussed in Chapter 35 at paragraphs 35.182 to 35.193 is relevant.

**3.96** The national look-back was initiated in 1995 and ran until 1998, using data available following the introduction of anti-HCV screening in September 1991. Prospective donors who tested positive comprised individuals who had not been dissuaded from offering blood by self-exclusion literature, which they may have ignored or not known of, or which they may have thought irrelevant to them. For present purposes, those found to be anti-HCV positive can be assumed to have been apparently healthy individuals. The results of the first few months of testing in England and Scotland, showed anti-HCV prevalence values among the blood donors tested, of 0.066% and 0.088% respectively.

**3.97** In the case of return donors found to be HCV positive, prior donations were traced and, where available, stored samples were tested for infection. The destinations of infected donations were then traced, and those used for clinical purposes identified. The hospitals to which blood or blood components – red cells or platelets, for example – were issued were contacted through formal routes, informed of the facts and asked for details of the status of the individual component. They were asked in particular whether a patient had received it and, if so, whether the recipient patient could be identified.<sup>104</sup>

**3.98** On 31 January 2006 the Health Minister of the Scottish Executive provided the results of the look-back exercise to the Health Committee of the Scottish Parliament.<sup>105</sup> The results, taken from the final report of the look-back exercise, are summarised in Tables 3.8 and 3.9.

<sup>104</sup> Dr Gillon – Day 6, pages 75–76

<sup>105</sup> See Letter from National Medical & Scientific Director, SNBTS, to Dr Aileen Keel, Scottish Office, dated 28 April 1998 [SGF.001.2174] and Scottish Hepatitis C Lookback Results – 9 April 1998 [SGH.002.8669]; the note to paragraph 7 of Letters from Minister for Health and Community Care [PEN.002.0801] at 0804; and more generally, paragraphs 9.309 to 9.313 of the Preliminary Report.

**Table 3.8: Results of Scottish Hepatitis C look-back**

Hepatitis C positive donors who had given blood before 1991	360
Donations by those donors	1658
Components prepared from those donations	2026
Of which – Traced	1356
Not traceable	670
Number of recipients identified by hospitals	880
Potentially eligible for counselling and testing	266
Of which – Counselling and tested positive	133
Counselling and tested negative	70
Other – Declined; not appropriate for testing; results not reported back to SNBTS	63
Deceased	536
Not traceable	78

**3.99** The number identified in the Scottish look-back report may have substantially understated the full extent of the problem. Screening and enquiry after the commencement of HCV testing in September 1991 identified infected blood donors who had given donations before 1991. Previous donors who were infected with HCV but did not present again after the introduction of HCV testing in September 1991 could not be identified, nor could their prior infective donations. Among recipients of blood from donors in this category there may have been individuals who developed the clinical manifestations of HCV infection and were treated by the NHS, before or after September 1991. The look-back exercise did not target those individuals.

**3.100** As shown in Table 3.8, in total the group identified had given 1658 donations which were available for clinical use. The data recorded showed that an average of 1.2 components were prepared from each donation. The destinations of 1356 of the total of 2026 components were traced. The destinations of the remaining 670 were not traced, and therefore whether they were applied in treating patients, or discarded, could not be determined. Only 880 recipients of the 1356 components traced were identified. Five hundred and thirty-six of these recipients (60%) were already dead by 1995 and could not, therefore, be tested.<sup>106</sup> Of the remaining recipients, some were not traceable, some were unwilling to be tested, some patients were very elderly, very ill or had a low life expectancy, or were incapable of consenting to testing, and some results were not returned for recording. In the end, in Scotland, 133 individuals were counselled and tested positive, 70 were counselled and tested negative, and the remainder fell out of the scope of the project. Only 203 of the 880 recipients contributed relevant data.<sup>107</sup>

**3.101** Data recovered and held by the HPA on the National Hepatitis C Register in respect of 103 of these patients show known dates of exposure as set out in Table 3.9.<sup>108</sup>

<sup>106</sup> Dr Gillon gave evidence that various studies had been carried out in different parts of the world which showed that in the late 1980s and early 1990s, about one half of patients who received a transfusion died within a few years, often as a result of the underlying condition which necessitated a transfusion, or through old age: Day 6, page 29

<sup>107</sup> Dr Gillon – Day 6, pages 26–30

<sup>108</sup> Dr Gillon's statement on statistics relating to transfusion-transmitted HCV [PEN.001.0043] pages 3–4

**Table 3.9: Known dates of exposure to HCV**

1977	1
1983	3
1984	4
1985	8
1986	11
1987	9
1988	14
1989	19
1990	15
1991	19
Total	103

**3.102** The range of values over the period probably reflects the reality that for earlier periods more patients would have died or have disappeared without having been identified.<sup>109</sup> Furthermore, it is likely that the proportion of donors found to be HCV positive in 1991 who would also have been donors in the early 1980s, is smaller than in the later years of the decade. Forty nine of those 103 patients were known to be alive at January 2011. In Dr John Gillon's view, Hepatitis C caused or materially contributed to the deaths of eight of the 54 patients known to have died. In one case no cause of death is known.<sup>110</sup> Of the 53 for whom death certificates were available, Hepatitis C was recorded on 14 only, though all 53 were known to have been infected.<sup>111</sup> Dr Gillon explained:

I should also add that these data are so far not analysed by HPA and haven't been published. So this was kindly made available to us by Dr Helen Harris for the purposes of the Inquiry. The interpretation which I have given is a personal interpretation, and may not reflect what they finally decide when they analyse these things formally through HPA and publish the data ....

I really categorised people into those who had clear evidence that their final demise was fairly directly attributable to hepatic disease. In other words they have liver failure or a complication such as sepsis, or they had hepatocellular carcinoma. Again, there may be a primary cause of death such as bronchial pneumonia, but hepatocellular carcinoma ... that is clearly attributable to the Hepatitis C.

So my reading is that eight of these 53 had a final illness where Hepatitis C was the significant factor.

....

I think that by and large at this sort of length of follow-up, which is 20 years plus now, that's broadly in line with what's in the published literature.<sup>112</sup>

<sup>109</sup> Dr Gillon – Day 6, page 49

<sup>110</sup> Dr Gillon's statement on statistics relating to transfusion-transmitted HCV [PEN.001.0043] at 0047

<sup>111</sup> Dr Gillon – Day 6, pages 54–55

<sup>112</sup> Ibid, pages 56–58

**3.103** In response to a request by the Inquiry, the SNBTS produced a paper on look-back<sup>113</sup> which sought to explain the relative ineffectiveness of the procedure in relation to HCV. The paper highlighted:

- In contrast to HIV, HCV was present in the population for several decades before a test was implemented;
- HCV typically remained silent following infection in most individuals for many years. HIV may progress rapidly;
- the epidemiology of HCV infection was less well understood than that of HIV, and measures to exclude at-risk donors in the period before development of a test were less effective, though exclusion measures related to HIV infection presumably reduced the numbers of donors with HCV;
- the greater the period elapsed between transfusion and the look-back exercise, the more likely it is that the patient will have died from a cause other than Hepatitis C;
- the increasing use of component therapy put more recipients at risk from a single donation;
- blood bank and hospital records were seldom available from the pre-computer era, and it was almost impossible to trace the fate of donations from before the early 1980s. After the early 1980s many blood banks relied on paper records which could not be searched systematically. It was therefore frequently impossible to establish whether, or to whom, a blood component was transfused; and
- the highly efficient patient tracking systems available today are a relatively recent development.<sup>114</sup>

**3.104** In oral evidence, Dr Gillon expanded on the difficulties with the Hepatitis C look-back exercise.<sup>115</sup>

- Early donor card records were not searchable.<sup>116</sup>
- It was not possible for the SNBTS to identify all prior donations by an infected donor.
- It was not until 1983 or 1985 (depending on the region involved) that a computer system was in place by which each donation could be linked to each donor and, importantly, to each recipient.
- Even where previous donations by an infected donor could be identified, there were difficulties in tracing the recipients of each donation.
- Different transfusion centres and hospitals had different record keeping systems.
- There were difficulties in cross-referencing donation numbers with recipients and vice versa.
- Medical records were lost or destroyed.
- Over time, recipients may have married (and changed their surname) or moved address.

<sup>113</sup> SNBTS – LOOKBACK – *Procedures to identify, trace and offer counselling and testing to patients who received blood components from donors subsequently found to be positive in tests for HIV and HCV* [PEN.017.2220]

<sup>114</sup> Ibid [PEN.017.2220] at 2229

<sup>115</sup> Dr Gillon – Day 6, pages 17–26

<sup>116</sup> Ibid pages 23–24



While the look-back exercise was undoubtedly worthwhile, in Dr Gillon's view, as a means of trying to identify, counsel, test and treat those patients at risk of having contracted Hepatitis C as a result of blood transfusion, it was not a reliable guide to the number of patients likely to have become infected with Hepatitis C through transfusion.

**3.105** Dr Gillon's evidence is accepted. The HCV look-back exercise cannot be relied on as providing an accurate measure of the number of NHS patients exposed to the risk of transfusion-transmitted Hepatitis C virus. Nor does it provide, of itself, a basis for estimating total exposure.

### SNBTS donor data: reporting of transfusion-transmitted infection

**3.106** During the reference period, clinicians were encouraged to report to the blood transfusion service any adverse reactions arising from the transfusion of blood and blood products, including the transmission of infection.<sup>117</sup> However, as previously discussed at paragraph 3.11, there was no effective legal obligation on clinicians to report, nor was there any legal obligation on the transfusion service to report to the Secretary of State or any other central authority, any adverse reactions of which they were aware. It is unlikely that surgeons or other clinicians who were not in a professional relationship with the SNBTS would have read the relevant guidance.<sup>118</sup>

**3.107** A Scotland-wide Hepatitis C diagnosis database, now maintained by HPS, was set up in 1996. The SNBTS and HPS now share basic data on HCV infection. The data are held by the National Microbiology Reference Unit for HPS.<sup>119</sup>

**3.108** The UK transfusion services set up a voluntary informal reporting system in 1996, the Serious Hazards of Transmission (SHOT) system, under which a central body collects and analyses anonymised information on adverse events and reactions in blood transfusion, from all healthcare organisations involved in the transfusion of blood and blood components in the UK and makes recommendations to improve patients' safety.<sup>120</sup> Since then Dr Brian Dow has collated all look-back cases and reports from Scotland and forwarded them to SHOT, providing a database from 1998.<sup>121</sup>

### HPS Hepatitis C Diagnosis Database

**3.109** Anonymised data acquired from Hepatitis C testing laboratories in Scotland is recorded by HPS in the Hepatitis C Diagnosis Database.<sup>122</sup> The primary objectives of the database are (1) to determine the total number of persons diagnosed with HCV infection in Scotland (from whatever source), by reference to year, NHS board, age, gender, risk group and referral source and (2) to monitor trends in diagnosed HCV infection in the Scottish population.<sup>123</sup>

**3.110** Professor Goldberg explained that virology laboratories (in hospitals throughout Scotland) hold information obtained from the Hepatitis C test request form that accompanies a blood sample to the laboratory.<sup>124</sup> Unlike the test request form for HIV,

<sup>117</sup> Recommendations to that effect were contained in various versions of *Notes on Transfusion*. (See for example the 1974 edition [DHF.001.2039] at 2062 and the 1984 edition [DHF.003.0394] at 0413.)

<sup>118</sup> Dr Gillon – Day 6, page 11

<sup>119</sup> Infection Surveillance Report No 11 – 1998–2009 [PEN.001.0053]

<sup>120</sup> Dr Gillon – Day 6, page 34; [www.shotuk.org](http://www.shotuk.org)

<sup>121</sup> *Ibid* page 34

<sup>122</sup> Professor Goldberg – Day 6, page 99

<sup>123</sup> See the HPS website: <http://www.hps.scot.nhs.uk/surveillance/SystemsDetail.aspx?id=33>

<sup>124</sup> Professor Goldberg – Day 6, pages 99–100

there is no standardised Hepatitis C test request form for use throughout Scotland.<sup>125</sup> All forms contain a space for 'additional information' or 'clinical information'. It is by interrogating the test request forms sent to the laboratory that HPS is able to access the information they need for their health surveillance and epidemiological purposes.<sup>126</sup> In his written statement Professor Goldberg said that: 'Hepatitis C information available to HPS ... is not as comprehensive or accurate' as in the case of HIV, due to the use of forms of varying design.<sup>127</sup> It is apparent that there are two deficiencies in the existing arrangements: the lack of consistency in form design and lack of consistency in returning relevant information. Professor Goldberg said that 'sometimes' clinicians provide the laboratory with relevant information in the space for 'additional information' or 'clinical information'.

**3.111** HPS took over data collection from the SNBTS, and the numbers generated by the database are discussed below at paragraphs 3.131–3.139.

### *The numerical evidence: known or recorded cases of transfusion-transmitted HCV*

#### **SNBTS donor data**

**3.112** In the period between 1 September 1991 and 31 December 2009, for which detailed data are available, the SNBTS conducted anti-HCV testing on 546,843 donations from new donors and 4,663,441 donations from repeat donors.<sup>128</sup> It was found that 450 new donors and 417 repeat donors were infected with HCV (that is to say were anti-HCV positive), a total of 867. Though the aggregate numbers were found to be similar, the prevalence rates differed widely. On average over the period the rate of positive donations from repeat donors was 8.94 per 100,000. The rate for new donors was 82.29 per 100,000. The rate overall was 16.64 positive donations per 100,000. The numerical distribution of infected donations over the period is reflected in Figure 3.3. The relative rates per 100,000 donations are shown in Figure 3.4.

**3.113** The data for 1991 are not comparable with the data for the rest of the period, since four months only are reflected in the numbers. For the whole of 1991, SNBTS National Statistics records 332,731 donations (approximately three times the total for the part year). The total for 1992 was 332,825. For the full years from 1992 onwards, a downward trend in positive results has been apparent. It is highly likely that a proportion of the return donors found to be anti-HCV positive in 1992 would have tested positive in the first eight months of 1991. Many donate annually. It is also likely that some donors in that eight-month period who did not return in 1992 would have tested positive. While it might be speculated that the result would be to shift the peak of infected donations back one year, it is impossible to say what the peak values would have been. Individuals' donation patterns vary widely, though the return donor population as a whole is reasonably stable. The trend is reliable only from 1992 onwards.<sup>129</sup>

<sup>125</sup> Professor Goldberg's statement on statistics relating to haemophilia patients infected with HCV dated 1 February 2011 [PEN.001.0206] at 0211

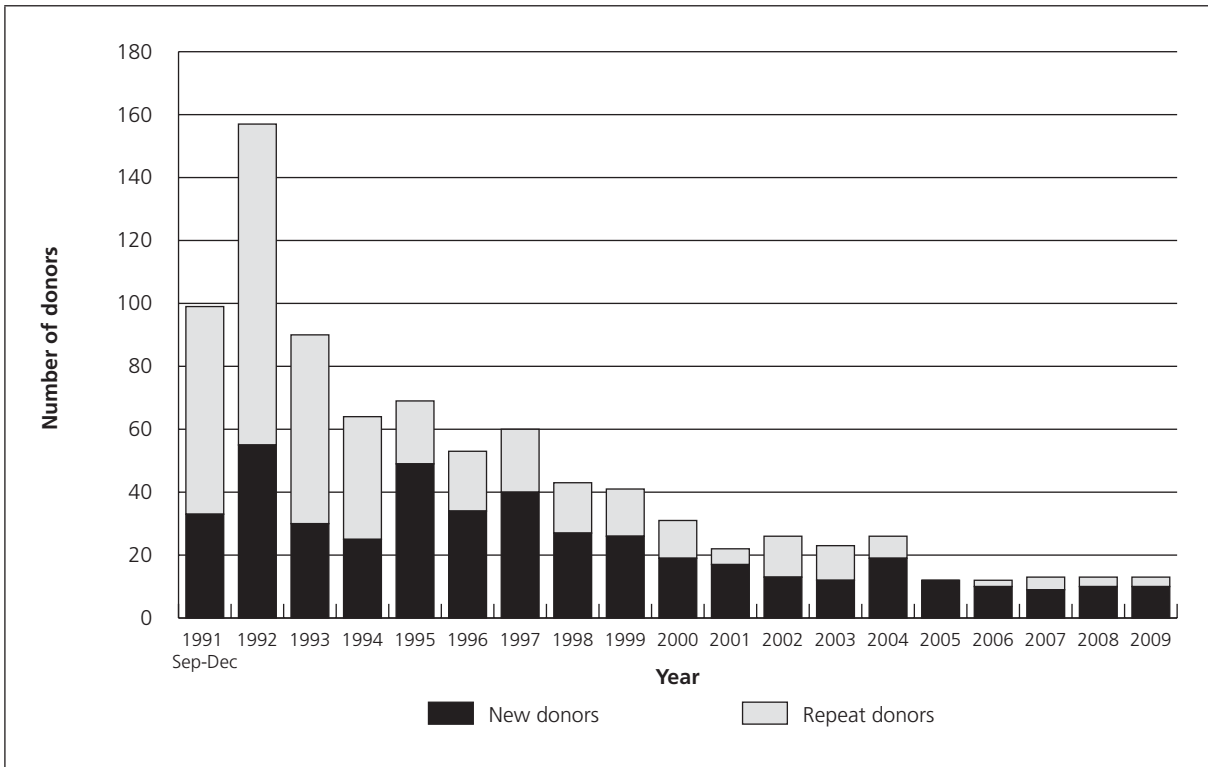
<sup>126</sup> Professor Goldberg – Day 6, page 100

<sup>127</sup> Professor Goldberg's statement on statistics relating to haemophilia patients infected with HCV dated 1 February 2011 [PEN.001.0206] at 0212 and Day 6, pages 146–147.

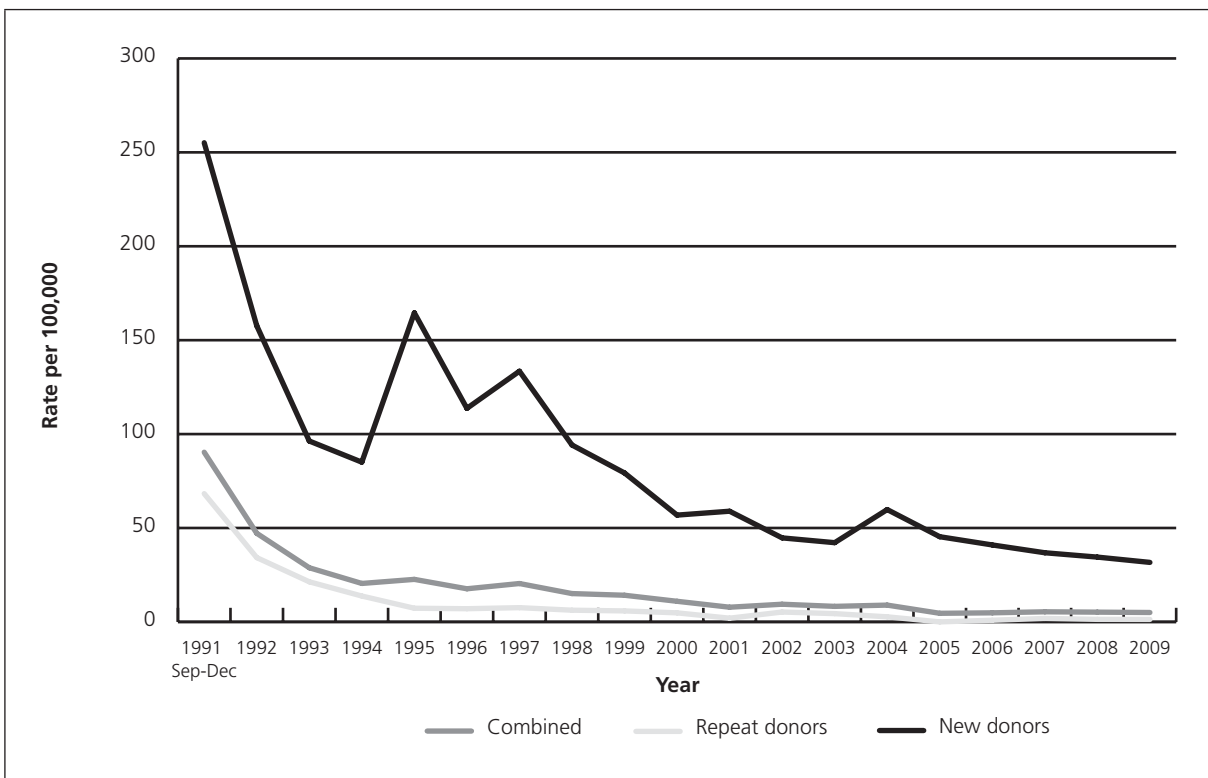
<sup>128</sup> *Infection Surveillance Report No. 11 1998–2009*, SNBTS National Microbiology Reference Unit, data as at 12 July 2010 [PEN.001.0053]

<sup>129</sup> The trend has continued. See: Health Protection Agency (2011) *Hepatitis C in the UK*. Available: [http://webarchive.nationalarchives.gov.uk/20140714084352/http://www.hpa.org.uk/webc/HPAwebFile/HPAweb\\_C/1309969906418](http://webarchive.nationalarchives.gov.uk/20140714084352/http://www.hpa.org.uk/webc/HPAwebFile/HPAweb_C/1309969906418) Last accessed 3 February 2015

**Figure 3.3: HCV-infected blood donations: Scotland**



**Figure 3.4: HCV-infected blood donations: Scotland: Rate per 100,000**



**3.114** As would be expected, in the case of return donors, the numerical trend reflects the relatively high initial effectiveness of a new screening test on a largely stable donor population. Dr Gillon identified two further possible contributory factors to the trend: a change in population prevalence of infection, and better donor selection.<sup>130</sup> Of the total of 867 HCV-positive blood donors, 59 (6.8%) stated that blood transfusion was the only risk factor for exposure to infection.<sup>131</sup> That number might include individuals who were transfused outside Scotland. Their cases have not been investigated individually.<sup>132</sup> Initial enquiries known to Dr Gillon established a date of transfusion in nine of 59 cases.

**3.115** The reliability of these reports of an association with transfusion is open to question and it is unclear what inferences can be drawn from the information generated. The following factors demonstrate this lack of clarity:

- The 59 individuals were people who, on receiving counselling, indicated that they thought they had received a blood transfusion in circumstances that suggested that the transfusion might be responsible for their infection. There was no objective verification of their statements.
- The information depended entirely upon reporting by the individual.<sup>133</sup>
- The reporting may have understated their experience of transfusion, as in the case of patients who had forgotten that it had happened, or who may have been transfused under anaesthetic, or who may not have understood the procedure carried out to be a transfusion.
- A clinician responsible for an injection of platelets might not always have informed the patient that he or she had been transfused. For example, in one study in Italy of patients who had well-documented transfusion-transmitted HCV infection, none of the patients knew they had been transfused.<sup>134</sup>
- The responsibility of transfusion may have been overstated by patients who concealed, innocently or otherwise, previous conduct exposing them to risk, such as intravenous drug use, body piercing or tattoos.<sup>135</sup>
- The process will not have identified individuals who were transfused in Scotland but diagnosed as infected in England or Wales or abroad.<sup>136</sup>

**3.116** The differences in prevalence values between return and new donors are significant. The relatively high, and in percentage terms sustained, levels of HCV-positive donations from new donors supports the view that donor demographics and donor selection practices contributed to a relatively low prevalence of HCV-positivity among the established donor population as compared to the general population (represented by the new donors). On the other hand, the impact on total prevalence of HCV-positive donations was low because throughout the period the pattern was dominated by donations from return donors.

<sup>130</sup> Dr Gillon – Day 6, page 67

<sup>131</sup> Dr Gillon's statement on statistics relating to transfusion-transmitted HCV [PEN.001.0043]

<sup>132</sup> Dr Gillon – Day 6, page 73

<sup>133</sup> *Ibid* page 37

<sup>134</sup> Casiraghi *et al*, 'Long term outcome (35 years) of Hepatitis C after acquisition of infection through mini transfusions of blood given at birth', *Hepatology*, 2004; 39:90-96 [LIT.001.4027]

<sup>135</sup> Dr Gillon – Day 6, pages 38–39

<sup>136</sup> *Ibid* page 74

### Patients reported to SNBTS by clinicians as possible cases of transfusion-transmitted (TT) HCV

**3.117** The next group of patients identified by the SNBTS comprised individuals reported to the SNBTS by clinicians, for the most part hepatologists and gastroenterologists, who had treated a patient infected with Hepatitis C where the information available suggested that the likely mode of infection had been transfusion. These cases were investigated individually. It was not always possible to establish a diagnosis of transfusion-transmitted Hepatitis C with certainty. Archives of frozen plasma or serum samples mostly dated back only as far as 1986 and it was often not possible to trace the implicated donors for testing.<sup>137</sup>

**3.118** This exercise was carried out by SNBTS retrospectively to attempt to answer the Inquiry's questions about the incidence of transfusion-transmitted HCV infection, and was dependent on finding and researching individual patients' records in transfusion centres.<sup>138</sup> After that it became a question of judgement. Dr Gillon said:

[T]he information is open to interpretation. It can be difficult to know whether to say, "Well, we accept this as a case of transfusion transmission. This one probably is but we really don't have enough documentary evidence to say with certainty".

On a number of occasions we can rule it out. We can say the blood that this person received was tested, all the donations were negative, all of the donors have come back and tested negative subsequently. We can be confident that transfusion did not transmit that infection. There are some cases where you can feel that the information that we have is a bit skimpy and therefore you would hesitate to say that this is likely to be a transfusion transmission. But we know there are other ways of picking up transmissible viruses in hospital environments, as we will see in some of the data from the renal units, for instance. Therefore, unless we can identify a donor and establish that link with certainty, there is always a bit of interpretation that's necessary here. I have tried to be inclusive here. In other words, not to wish to minimise the figures in any way, but there is this caveat that, we can never be certain unless we make the link.<sup>139</sup>

**3.119** After investigation of the reports, the numbers accepted as 'known' cases of transfusion-transmitted HCV, as detected by these means, were:

- Glasgow and west of Scotland 6
- Edinburgh and east of Scotland 15
- Dundee (east of Scotland) 4
- Aberdeen (north east Scotland) 3
- Inverness (north of Scotland) 0

<sup>137</sup> Ibid page 32

<sup>138</sup> Ibid pages 33–34

<sup>139</sup> Ibid pages 34–35

**3.120** It is apparent that the numbers for the two major centres are not proportionate to the respective populations of the regions. Dr Gillon thought that the total number of 28 underestimated by a considerable margin the residual number of undetected TT HCV cases.<sup>140</sup> Historically, the SNBTS tended to see reports from haematologists, for instance, who were dealing regularly with patients requiring multiple transfusions. There was fairly close and constant interaction with them. Similarly, in units which used a lot of blood, like cardiac surgery, renal units and other units with whom the SNBTS had clinical links, clinicians were more alert to the possibility of transfusion-transmission than a surgeon at a district general hospital who was much less likely to think of the possibility.<sup>141</sup>

**3.121** Actual dates of transmission have not been established in these cases. For all but one patient, probable dates lie between 1979 and March 1991. One patient received multiple transfusions between 1970 and 1983 and identification of the infective donation was impossible.<sup>142</sup>

**3.122** As regards this group of known infected patients, one cannot equate the number of cases of transfusion-transmitted Hepatitis C reported by clinicians, with the prevalence of transmission. As already noted, only about 20% of individuals who contract Hepatitis C will experience an initial acute period of illness (eg jaundice) and may be aware that they have contracted a disease. The corollary is that the vast majority of patients who contract Hepatitis C, and their clinicians, will be unaware at the time that infection with the virus has occurred. While a patient may, many years or decades later, develop symptoms and be tested for Hepatitis C, only in some cases will the patient and treating clinician attribute that to a prior transfusion and only in a minority of these cases will this be reported to the SNBTS. Many more cases will remain undetected or unreported for a number of reasons, including the death of many patients before symptoms from hepatitis developed, the patient or clinician not attributing infection to a transfusion occurring many years previously or the clinician not reporting the matter to the SNBTS. While 28 cases in this category were accepted by the SNBTS as being 'known' cases of infection, Dr Gillon stated: 'I think there is no doubt that a total of 28 is way off what is the reservoir of such cases in the population. We don't know by how much of course.'<sup>143</sup>

### *Summary of SNBTS known or recorded cases*

**3.123** On SNBTS evidence, the total number of patients infected by transfusion and identified in these various exercises was therefore 220 (133 patients identified by the look-back exercise plus 59 donors who were thought to have been infected by a prior transfusion, plus 28 patients reported to the SNBTS by clinicians). Dr Gillon thought that the total numbers identified by his studies were probably minimum numbers for infections in Scotland.<sup>144</sup>

**3.124** Dr Gillon acknowledged that there was a theoretical possibility of overlap among the three groups of patients, but it was unlikely to have occurred. He knew of no HCV positive donor in the SNBTS group who was subsequently identified as a patient in the targeted look-back. The documentation and procedures used in the targeted look-back differed from the other groups. Patients from the third group were individually researched.

<sup>140</sup> Dr Gillon's further statement on statistics [PEN.013.1557] at 1558 and Day 6, Page 40

<sup>141</sup> Dr Gillon – Day 6, pages 41–42

<sup>142</sup> Dr Gillon's statement on statistics relating to transfusion-transmitted HCV [PEN.001.0043] at 0046

<sup>143</sup> Dr Gillon – Day 6, page 40

<sup>144</sup> Ibid page 77

There was a risk that a patient identified within the third group might subsequently have been identified by the targeted look-back without a connection having been made. The anonymising of data recorded by the HPA, and the numbers of cases recorded by the HPA, made it impossible to rule out the possibility, but the risk was unlikely and the numerical impact of such an event would be small.<sup>145</sup>

**3.125** It would not be appropriate to conclude on the basis of the SNBTS donor data that only 59 HCV positive blood donors had been infected by blood transfusion. In particular, donors who stopped donating prior to the introduction of Hepatitis C screening in September 1991 would not be included. Similarly, neither the 133 patients identified by the look-back exercise nor the 28 reported by clinicians provides a reliable guide to the total who may have become infected. Nor is it possible to develop from these numbers an estimate of the total number of patients who may have been infected by transfusion. None of the individual figures provides a basis for inference of that total. Individually, the cohorts are too small to support a more general conclusion. In total they represent an aggregate only of small numbers in specific groups: they are not random samples from which a more general picture can be inferred.

### Renal and other units

**3.126** Following the development of tests for HCV antibodies, certain patients were screened for HCV on a regular basis by local virology laboratories. The patient groups included people with haemophilia, bone-marrow transplant recipients, and renal dialysis patients. Some positive data were derived from this work. Transfusion transmitted HCV was confirmed from the patients' treatment records.

**3.127** Renal dialysis patients considered to be known positives for TT HCV were identified separately. The renal unit in the west of Scotland had monitored the patients because of the well-known risk of hepatitis transmission in renal units.<sup>146</sup> Initial interest had been in Hepatitis B, which had a high prevalence in patients on chronic dialysis, for reasons that were poorly understood at the time. In addition, patients with chronic renal failure are usually anaemic, and those with severe anaemia as part of their condition require regular transfusions. Therefore, many of them would have had numerous transfusions and most of those would probably have predated the time when the sample archive was started in the west of Scotland in 1986. The patients in this group were reported by the renal units in the west of Scotland as possibly having been infected with transfusion-transmitted Hepatitis C when they started routine testing for HCV antibody.<sup>147</sup> These patients may have been infected through blood transfusion, but the large number of transfusions administered, and substantial risk of nosocomial infection from other sources, made it impossible to say if and when they had been infected by transfusion-transmission.<sup>148</sup>

**3.128** In addition, a very small number of patients had, prior to the national look-back exercise, been identified by the West of Scotland Blood Transfusion Service as HCV positive. These patients numbered 18 and were primarily people with leukaemia who had received multiple transfusions over many years, leading to bone marrow transplantation. The dates of the transfusions were between 1982 and April 1991; identification of the infective donations was considered impossible because of the number of transfusions involved.

<sup>145</sup> Dr Gillon's further statement on statistics [PEN.013.1557] at 1558 and Day 6, page 40

<sup>146</sup> Dr Gillon – Day 6, pages 42–43

<sup>147</sup> Ibid pages 43–44 and Dr Gillon's further statement on statistics [PEN.013.1557] at 1559

<sup>148</sup> Dr Gillon's statement on statistics relating to transfusion-transmitted HCV [PEN.001.0043] and Day 6, Pages 44–45

**3.129** Dr Gillon said:

In such a case, really the only way you can find if there is a donor who transmitted would be to have archive samples which you can go back and test. We have certainly in Edinburgh done occasional look-backs where we have tested between 100 and 200 samples, which is a very big exercise. Occasionally it does provide results. But some of these patients will have had hundreds of individual units of transfusion and many of them will have had these transfusions before the archive samples started, which would make it impossible.<sup>149</sup>

**Conclusion on the SNBTS data**

**3.130** On the basis of these SNBTS data, it is possible to conclude only that 238 known patients (220 + 18) were infected by transfusion-transmitted Hepatitis C, but that they are very likely to be parts only of larger cohorts of patients.

**Health Protection Scotland data**

**3.131** As noted above, HPS took over data collection from SNBTS. The changes introduced by the Public Health etc. (Scotland) Act 2008 with effect from 1 January 2010, appear to give regulatory effect to the practice of HPS in obtaining information directly from HCV diagnostic laboratories. Professor Goldberg said, however, that HPS 'got better information by going direct to the hepatitis testing laboratories' on a voluntary basis, and that the 'voluntary approach' enabled HPS 'to get the information that we actually needed'.<sup>150</sup>

**3.132** The SNBTS data were passed to HPS' National Microbiology Reference Unit.<sup>151</sup> The remit of HPS is primarily related to preventing future infection and disease. As noted above, HPS established its Hepatitis C diagnostic database in 1996. By then blood transfusion and blood products were not serious issues in the context of preventing further transmission of HCV (since by that time blood donations were screened for HCV and blood products were subjected to processes that were effective in inactivating any Hepatitis C virus in the product). Currently 1000 to 1500 people are thought to become infected with Hepatitis C in Scotland every year, and behaviour exposing people to risk is the focus of much of the energies of HPS, but this does not relate to blood transfusion.<sup>152</sup>

**3.133** As already noted at paragraph 3.20, information is acquired from Hepatitis C testing laboratories in Scotland. The various request forms document demographic information and identifying information. In deriving the information they need for surveillance and epidemiological purposes, HPS then includes other pieces of information that are obtained through surveys of various population groups and also clinical information obtained through a national clinical database.<sup>153</sup>

**3.134** The data available to HPS and recorded in the HCV database indicated that 304 individuals may have been infected with HCV by blood transfusion. In these cases, transfusion could only be regarded as a possible and not a definite or confirmed route of acquisition.<sup>154</sup> In arriving at the figure of 304 cases, 51 individuals were excluded because

<sup>149</sup> Day 6, pages 46–47

<sup>150</sup> Professor Goldberg – Day 6, pages 103–104

<sup>151</sup> Dr Gillon – Day 6, page 15

<sup>152</sup> Professor Goldberg – Day 6, pages 111–112

<sup>153</sup> Ibid pages 99–100

<sup>154</sup> Ibid pages 98–99



they recorded intravenous drug use as well as having received blood transfusions. Between 80% and 90% of drug injectors at most centres were infected with Hepatitis C and it is thought that the 51 individuals were much more likely to have been infected by that means than by blood transfusion.<sup>155</sup> A further 49 had also been previously excluded because the information provided indicated very strongly that they received their infected transfusions abroad.<sup>156</sup> That did not conclusively prove that the remaining 304 were transfused in Scotland, only that they might have been transfused in this country.<sup>157</sup>

**3.135** The data are acceptable as accurate reflections of the information available, given the criteria applied, but they do not define the scope of the problem of transfusion-transmitted HCV infection. Professor Goldberg said:

I think that, because there is so much uncertainty about these cases ... what we are doing here is just taking some information that has been recorded on a request form. We did not seek additional information. We didn't clarify whether indeed the information provided was accurate. So that was why the word "possible" was provided here.

If I had to put money on it, I would say that less than 50 per cent of the 304 contracted their HCV through blood transfusion.<sup>158</sup>

**3.136** That was his personal assessment, but he was not sure that there were sufficient data to make a judgement, and his ultimate position was that 'don't know' was probably the correct answer.<sup>159</sup> It is appropriate to accept that view of the position. The identification of 304 individuals as possibly infected by transfusion-transmission already involves a number of assumptions. Breaking the number down further, without a rational basis, seems problematic.

**3.137** However, while acknowledging that the lack of confirmation associated with blood transfusion was a weakness in the system, Professor Goldberg stated that he was 'pretty confident' that the information that Scotland had on Hepatitis C was 'as good as, if not better than, anywhere else in the world'. He added:

I think there are weaknesses in our information base with respect to blood transfusion and blood factor, but in general our information about Hepatitis C is pretty good. If you want to compare our diagnostic information, ie numbers of people known to be infected, with the information available in England, then we are in a far superior position in terms of the completeness of our data and indeed its accuracy.<sup>160</sup>

### *Conclusion on the HPS data*

**3.138** Like the SNBTS data, the HPS data relate to patients who had been identified as HCV positive and for whom it was likely that infection had been transfusion transmitted. The data do not reflect directly the possible or probable level of infection from transfusion in the whole population of patients exposed to risk from infected blood or components.

---

<sup>155</sup> Ibid pages 143–144

<sup>156</sup> Ibid page 144

<sup>157</sup> Ibid pages 144–145

<sup>158</sup> Ibid page 106

<sup>159</sup> Ibid pages 145–146

<sup>160</sup> Ibid pages 110–111

**3.139** Even if all 304 individuals on the HPS database acquired Hepatitis C as a result of blood transfusion, that is highly unlikely to reflect accurately the number of transfusion-transmitted infections in Scotland, largely for the reasons discussed above. In particular, patients will not appear on the HPS Hepatitis C database if they had died (for example from age-related conditions or from the underlying medical condition which necessitated transfusion) prior to the database being set up in 1996. Nor will those patients who contracted Hepatitis C but have never, or have not yet, presented to their GP for examination or treatment. Nor will those patients who have presented but for whom, for whatever reason, their Hepatitis C infection has not been diagnosed or, if diagnosed, has not been attributed to a prior transfusion.

### *The Skipton Fund*

**3.140** The Skipton Fund was established on 25 March 2004 by the Department of Health, to make *ex gratia* payments to people who were infected with Hepatitis C through treatment with NHS blood or blood products prior to September 1991.<sup>161</sup> Payments are made in two stages, the first on proof of infection and the second on proof of progression to serious liver disease. Those living applicants who qualify for a stage 2 payment qualify also for regular payments thereafter. In 2011 the Caxton Foundation was set up to provide charitable benefits to certain individuals who have received blood, blood products or tissue from the NHS and in consequence have been infected with HCV, and to individuals who have had infection transmitted by such a person (the 'primary beneficiaries') and to the partners, carers, children and dependants of primary beneficiaries living or who died before 29 August 2003.

**3.141** As at 25 February 2011, there had been 636 Scottish applications to the Skipton Fund for stage 1 payments, of which 134 patients had also applied for and received stage 2 payments, as shown in Table 3.10 below.<sup>162</sup>

**Table 3.10: Scottish applications to the Skipton Fund at 25 February 2011**

Patients with:	Stage 1	Stage 2
Haemophilia	210	33
Haemophilia with HIV	21	9
Non-bleeding disorder	405	92
Total	636	134

**3.142** At least 24 of the total of 636 had died by 25 February 2011. Fifteen of the stage 1 payments and 15 of the stage 2 payments went to an estate. At that stage there were 405 non-haemophiliac recipients of blood or blood components in Scotland who had been alive or were survived by qualifying beneficiaries as at August 2003 and who received payments from the Skipton Fund. The figure was unlikely to represent the actual number of patients who contracted HCV as a result of treatment with NHS blood or blood products. A minimum of 12 years, in many cases 20 years or more, will have elapsed between the time of infection and the commencement date of the Fund in 2003. Mr

<sup>161</sup> In setting up the Fund the DoH was acting for and on behalf of the UK health administrations, ie the Secretary of State for Health, the Scottish Ministers, the National Assembly for Wales and the Department of Health, Social Services and Public Safety in Northern Ireland. The Fund criteria previously did not allow payments in respect of those who died before 29 August 2003. In January 2011, it was decided to relax that criterion. In England the relaxation was applicable only if such claims were made on or before 31 March 2011. The three month registration window did not apply in Scotland.

<sup>162</sup> E-mail from Nick Fish, Scheme Administrator, dated 25 February 2011 [PEN.019.1358]

Nick Fish, the Scheme Administrator, provided further information on 1 March 2012.<sup>163</sup> By then Skipton had made 670 stage 1 payments in Scotland (34 more than shown in Table 3.10 above). 162 of the individuals, or their estates, had also received stage 2 payments. It is unlikely that there will have been a material increase in the sizes of the haemophilia groups, given the level of monitoring in their case, and it seems reasonable to proceed on the basis that the additional 34 cases could be added to the post-transfusion group which had increased to 439.

**3.143** The accuracy of the Skipton data depends on the accuracy of the medical certificates submitted and the rigour of the assessment procedure carried out.

**3.144** Professor Goldberg commented on the Skipton Fund survival data, in particular as a basis for back-calculating plausible estimates of the number of individuals who must have been infected in the first place. He noted:

[I] asked the Inquiry for details confirming that the individuals considered eligible for Skipton funding had, indeed, acquired their infections through blood transfusion in Scotland but such information was unavailable. It is my understanding that, for some individuals, such information exists but for others, perhaps the majority, judgements were based 'on the balance of probability'. Balance of probability is insufficient information for us to make a judgement as to how likely an individual was infected as a consequence of a blood transfusion, without having access to additional information.<sup>164</sup>

He and his colleagues therefore considered the Skipton data to be insufficiently robust for their purposes.

**3.145** As discussed above, It is clear that HPS' own data and analyses lack the level of certainty that would enable one to say that the reference cohort of infected individuals had 'indeed' acquired their infections through blood transfusion. The Inquiry cannot avoid expressing a view on the ground that certain facts can only be established on a less demanding test. The question is whether the Skipton data can be used, along with other sources (including HPS' evidence), in arriving at a conclusion about the likely level of transfusion-transmitted HCV infection.

**3.146** The Inquiry has identified one case in which a claim was admitted where there is no evidence that the deceased patient acquired his Hepatitis C infection from blood or blood products. There may be more. One cannot proceed on the view that the Skipton data are unquestionably accurate. The information available indicates that applications are decided by the Fund on a balance of probabilities test and if refused, applicants can appeal to an independent Appeal Panel.<sup>165</sup> It appears reasonable to accept the figure of 405 (or 439, if the assumption in paragraph 3.142 is valid) as sufficiently accurate to be taken into account in an overall assessment of the level of transfusion-transmitted infection.

**3.147** However, as previously discussed at paragraph 3.92, some patients may have cleared the virus, some may have died without infection with Hepatitis C being diagnosed, and some may survive without signs or symptoms of infection having been noted or brought to the attention of those keeping the relevant records. In the case of the Skipton Fund, it

<sup>163</sup> Email from Nick Fish, Scheme Administrator, dated 1 March 2012 [PEN.019.0104]

<sup>164</sup> Letter from Professor Goldberg in response to further queries on statistics from Professor Oliver James [PEN.019.0922]

<sup>165</sup> [www.skiptonfund.org](http://www.skiptonfund.org)

cannot be assumed that every person entitled to make a claim did so. In the result, both the number of those who died while infected, and the number of individuals who remain infected, but who have not been registered by the Skipton Fund, are unknown.

**3.148** That number may be significant, and it will be appropriate to return to the Skipton data to consider whether estimates can be made on the basis of the recorded data.

### *Summary of recorded data*

**3.149** In summary, known or recorded cases of transfusion-transmitted Hepatitis C infection represent a minimum number of patients who were infected with Hepatitis C as a result of transfusion and do not reflect the actual number of patients who are likely to have contracted the disease in that way.

**3.150** A wider exercise was required to ascertain whether the available data could, with appropriate analysis and expert advice, provide answers.

### *Statistical modelling*

**3.151** As is illustrated by the earlier discussion of data for actual cases of transmission of infection, attempts by epidemiologists retrospectively to form views on the incidence and prevalence of an infection may be hampered by many factors. The general problems discussed in paragraphs 3.89–3.93 arise also in the context of statistical modelling.

**3.152** With respect to HCV infection, of the two main groups under consideration in this section, the haemophilia population is much more homogeneous. Patients tend to be much younger at the date of infection than transfusion patients. On the whole, haemophilia patients are much more rigorously followed up. In their case it is far easier to get reasonable, if not perfect, estimates of numbers infected with HCV than in the very much larger and more heterogeneous population of surgical and medical patients who have received transfusions in the course of treatment of their primary condition.

**3.153** In addition to these general difficulties, HCV is not a virulent, rapidly progressing disease resulting in severe early clinical manifestations or death. Infection may be diagnosed only after long periods of time since the putative transmission. The retrospective study of transfusion-transmitted HCV from 1991 onwards has been affected by all of these factors. The unreliability of the data on actual cases of infection, and the difficulty in forming general conclusions on the basis of those data, are not unexpected.

**3.154** For these reasons, in the absence of reliable recorded data, statistical modelling techniques were adopted by experts for calculating the numbers of transfusion patients possibly exposed to risk, and the numbers of patients infected. Statistical modelling inevitably depends on a number of assumptions in developing general inferences from the data collected. Dr Gillon said that it was difficult to find good data about prevalence in the donor population, to which to relate reported data on patients.<sup>166</sup> Projections were qualified by the accuracy or inaccuracy of the data available and of the assumptions used to derive them. Transforming the raw data into acceptable numbers proved difficult. All of these difficulties have been readily recognised by the investigators in the following exercises.

---

<sup>166</sup> Dr Gillon – Day 6, pages 10–11

***Dr Soldan, Public Health Laboratory Service (PHLS)***

**3.155** In 2002 Dr Kate Soldan, an epidemiologist based at the Communicable Disease Surveillance Centre, PHLS, and a large team of collaborators, estimated the number of individuals who might have been infected with HCV through blood components administered in England.<sup>167</sup> Dr Soldan later carried out a similar exercise relating to the position in Scotland. The results of her English research were to be published shortly after she carried out her work in relation to Scotland.<sup>168</sup>

**3.156** Dr Soldan constructed a model of the path followed by blood components (red cells, platelets, fresh frozen plasma and cryoprecipitate), which had been prepared from donations collected by eight blood centres in England, and had been traced, from donation to recipient, during the national Hepatitis C look-back programme. The eight centres handled 80% of all blood components entering the programme in England. The number of components, 9222, handled by these centres provided the base data used. Some components were followed through every stage, from delivery to application, and some fell out of the process. The proportion of the components that remained 'observed' at each successive stage in the development of the model was calculated. It was assumed that components that did not complete the observed path would probably have followed the path of those that did, and so they were re-entered into the model at the point at which they fell out of the process. The probability that components with an unidentified fate would follow the observed route was calculated at each stage and used to predict the probable fate of those re-entered components.

---

<sup>167</sup> Early information on the exercise was given to Dr McClelland: *Estimates of Number of Individuals Who May Have Been Infected With HCV by Blood Components* [SGH.005.7201] and documents appended: *Estimated Number of Individuals Infected by Blood Transfusion in Scotland* [SGH.005.7203] and *The Contribution of Transfusion to HCV Infection in England* [SGH.005.7205]

<sup>168</sup> Soldan *et al*, 'Estimates of the contribution of transfusion to HCV infection in England', *Epidemiology and Infection*, 2002; 129:587–591 [PEN.013.1580].

**3.157** The history of the 9222 components is shown below in Table 3.11.

**Table 3.11: Dr Soldan's observed path data**

Total Components	9222	100%
<i>of which:</i>		
Components not traced	2119	23%
Components traced	7103	77%
Components traced	7103	100%
<i>of which:</i>		
Components transfused (4586/7103)	4586	64.6%
Components transfused	4586	100%
<i>of which:</i>		
Components with no known recipient (154/4586)	154	3.36%
Components with identified recipients (4432/4586)	4432	96.64%
Number of identified recipients	4424	100%
<i>of which:</i>		
Recipients known to have died (2711/4424)	2711	61%
Recipients assumed to be alive (1713/4424)	1713	39%
Recipients assumed to be alive	1713	100%
<i>of which:</i>		
Recipients not tested (651/1713)	651	38%
Recipients tested (1062/1713)	1062	62%
Recipients testing positive for HCV (539/1062)	539	50.75%

**3.158** In addition to the 1062 tested recipients of components, from the 80% of centres which handled the 9222 components, test results were available (through the look-back exercise) for 271 other individuals. These patients had received components from one or other of the centres in England, providing the remaining 20% of blood. 50.75% of that number (the percentage testing positive in the observed path: 539 out of 1062) provided 138 additional positive tests, giving an overall total of 677 positive tests from 1333 recipients tested.<sup>169</sup>

**3.159** Applying the observed probabilities to components that fell off the process prior to recipient testing and were re-entered, added 3373 HCV infections:

- 946 where the fate of the component was not traced.
- 107 known to have been transfused but with no recipient identified.
- 1870 known to have been transfused to recipients who had died by the end of 1995.
- 450 who declined testing.

Of these, 1870 (55%) were known to be dead and another 645 (19%) were expected to have died by the end of 1995.<sup>170</sup>

<sup>169</sup> The basis on which the percentage from the defined path was applied to this separate group of results is not clear.

<sup>170</sup> Soldan *et al*, 'Estimates of the contribution of transfusion to HCV infection in England'. *Epidemiology and Infection*, 2002; 129:587–591 [PEN.013.1580] at 1581–2

**3.160** Dr Soldan next estimated the probable number of infections from donations that did not enter the look-back study. The number of donations collected between 1 January 1980 and 1 September 1991 was 25,864,035. An infectivity rate of 0.066% was assumed on the basis of observed data from the first four months of donor testing after 1 September 1991. At that rate, it was estimated that 17,086 anti-HCV positive donations would have resulted. At 1.6 components per donation (reported to be an observed datum in England), 26,647 components from infected donors resulted arithmetically.<sup>171</sup> That number necessarily included all or some of the components that entered the look-back programme, and an adjustment was made to deduct those. Of the 26,647 components, it was assumed that 9756 entered look-back in the material period and that 16,890 did not. That would have predicted an extra 10,905 transfused recipients (16,890 x 64.5%), of whom 6034 were infected (based on the observation that 55% of look-back components resulted in infection). However, that was thought unreliable. It was estimated that 73% of the 9756 components entering the look-back programme were anti-HCV positive and accordingly the estimated number of additional anti-HCV positive components not entering look-back was adjusted to 19,525 (26,647 – (9756 x 0.73)). On the consistent assumption that 64.5% of the components traced were transfused, that was calculated to equate to 12,606 recipients of whom 75% (9455) would be infected, on the basis that only HCV RNA-PCR positive donors transmitted the infection.<sup>172</sup>

**3.161** The aggregate, 13,505 (4050 + 9455), was the number of recipients of blood components estimated to have been infected in England with HCV during the decade prior to the start of anti-HCV testing. Over 8300 (61%) of these patients were either known or expected to have died by the end of 1995.<sup>173</sup> Dr Soldan and colleagues noted that: 'There were, by necessity, many assumptions and extrapolations used, and the results are not therefore expected to be exact.'<sup>174</sup> They stated:

We may have underestimated or overestimated the infections transmitted from 1 January 1980 to 1 September 1991 by using the prevalence of infection at the start of testing without accounting for selective removal of infected donors during the 1980s, or accumulation of prevalence over time. This uncertainty, and others, prohibited including earlier years. If the prevalence of anti-HCV amongst blood donors during the 1970s was assumed to be the same as at the end of 1991, inclusion of the 1970s data would generate approximately 10,000 extra HCV-infected blood recipients.<sup>175</sup>

**3.162** It has not been possible to verify the assumptions made.

**3.163** Professor Goldberg commented:

[W]hat she has done here is she has got some pretty solid data ... and then she has extrapolated the findings to those components for which she doesn't have solid data, and I think that's a reasonable thing to do.<sup>176</sup>

<sup>171</sup>  $17,086 \times 1.6 = 27,338$ . The difference of 691 appears to be related to the reduction required to exclude the components related to the 271 individuals whose test results were added from outwith the main centres.  $691 / 1.6 = 432$ ; and  $271 \times 1.6 = 434$ .

<sup>172</sup> Soldan *et al*, 'Estimates of the contribution of transfusion to HCV infection in England', *Epidemiology and Infection*, 2002; 129:587–591 [PEN.013.1580] at 1582–3

<sup>173</sup> *The Contribution of Transfusion to HCV Infection in England* [SGH.005.7205] at 7206

<sup>174</sup> Soldan *et al*, 'Estimates of the contribution of transfusion to HCV infection in England', *Epidemiology and Infection*, 2002; 129:587–591 [PEN.013.1580] at 1583

<sup>175</sup> *Ibid* [PEN.013.1580] at 1583–1584

<sup>176</sup> Professor Goldberg – Day 6, page 127

**3.164** Professor Goldberg’s evidence is discussed further at paragraph 3.176 below. For the purposes of this Report, it is sufficient to proceed on the basis that the statistical method as applied in England, while open to question in some respects, was not fundamentally undermined by Professor Goldberg, and its results were not seriously disputed on the evidence before the Inquiry.

**3.165** As noted below, the results were used by the Department of Health (DoH), apparently without the need to explain adjustments. On the basis of Dr Soldan’s modelling, the number of HCV infections as a result of blood transfusion in England between 1970 and 1991 can therefore be assumed to have been about 23,500.

### *Department of Health*

**3.166** On 10 January 2011 the DoH published a review of the support available to individuals infected with Hepatitis C and/or HIV by NHS-supplied blood transfusions or blood products, and the dependants of those infected. Annex 2 of the review contained an estimate of the number of Hepatitis C-infected individuals in the UK, who were infected over the period 1970–1991. It was estimated that 28,043 individuals had been infected with Hepatitis C as a result of blood transfusion in the UK during that period.<sup>177</sup> The source for that figure was stated to be the 2002 paper by Soldan and others on the numbers infected in England, ‘corrected to UK’.<sup>178</sup>

**3.167** The population data for the United Kingdom over the period between 1971 and 1991, derived from census returns, are set out in Table 3.12.

**Table 3.12: Population of the UK and constituent countries, 1971–91 (thousands)**

	<b>1971</b>	<b>1981</b>	<b>1991</b>
England	46,411.7	46,820.8	47,875.0
Wales	2740.3	2813.5	2873.0
Scotland	5235.6	5180.2	5083.3
Northern Ireland	1540.4	1543.0	1607.3
Total	55,928.0	56,357.5	57,438.7

**3.168** England had 83% of the total infected population consistently over the period, Wales had 5% and Northern Ireland 2.8%. The Scottish percentage fell from 9.36% to 8.95% and then to 8.85%. For present purposes, it is sufficient to treat Northern Ireland as having 3% and Scotland 9% of the total UK population.

**3.169** The period covered by the DoH estimate was approximately twice as long as the primary period discussed by Dr Soldan in detail (1970–91 as against 1980–91). As already noted, in their published paper the Soldan group commented that if the prevalence of anti-HCV donors during the 1970s was assumed to be the same as at the end of 1991, inclusion of the 1970s data would generate approximately 10,000 extra recipients of HCV-infected blood. Dr Soldan’s 2002 paper therefore suggested that there may have

<sup>177</sup> *Review of the support available to individuals infected with Hepatitis C and/or HIV by NHS-supplied blood transfusions or blood products and their dependants* [PEN.017.1968] at 2007

<sup>178</sup> Soldan *et al*, ‘Estimates of the contribution of transfusion to HCV infection in England’, *Epidemiology and Infection*, 2002; 129:587–591 [PEN.013.1580]



been 23,505 HCV infections as a result of blood transfusion in England between 1970 and 1991.<sup>179</sup>

**3.170** If the United Kingdom blood donor population were assumed to have had the same rate of HCV infection on average throughout the period, the DoH total would be allocated as follows: England 23,276; Wales 1402; Scotland 2524; and Northern Ireland 841. The figure for England is a close approximation of Dr Soldan's estimate of 23,500.

**3.171** Without information about the methodology used by the DoH to adjust for the United Kingdom as a whole, it is not necessarily the case that Dr Soldan's conclusions were accepted nor, if adjusted, to what extent. The most one can establish is that Dr Soldan's conclusions were not challenged by DoH.

**3.172** It seems appropriate to assume that other figures would be reasonable approximations of the data available to the DoH, at least as a starting point. However, the mechanisms by which the DoH values were arrived at are not disclosed, and it is not impossible that they were simply the arithmetical result of extrapolating from Soldan on the basis of population data.

#### *Dr Soldan's Scottish estimates*

**3.173** In 2002 Lord Ross' Expert Group<sup>180</sup> asked Dr Soldan to provide an estimate of the number of patients in Scotland likely to have contracted Hepatitis C as a result of transfusion.<sup>181</sup> Dr Soldan's estimate for Scotland followed the same general methodology as she had developed for the English project.<sup>182</sup> The same statistical model was used and she applied some of the same assumptions, for example in relation to the probability of a blood component being transfused. She also factored in the information available from the Scottish HCV look-back exercise and hence the higher prevalence of HCV among blood donors in Scotland in the first six months of HCV screening (0.088%) when compared with the prevalence among blood donors in England for the first four months' period studied there (0.066%).<sup>183</sup> The exercise was customised by using the numbers of components entering the look-back programme resulting in an identified recipient. It identified recipients who had died, recipients who declined testing, and those who were tested and found to be HCV positive. The exercise was completed using Scottish data and the parameters of the English exercise. Dr Soldan's brief report does not refer specifically to the assumed yield of components per donation. The Scottish datum would have been information that would have had to be provided by the SNBTS. Dr McClelland's letter commenting on Dr Soldan's estimate at the time referred only to 'data from the Scottish HCV look-back programme and also the higher prevalence of HCV in the Scottish donor population' as information provided to customise the exercise.

**3.174** The detailed calculations cannot be replicated in full. However, the results for Scotland, as reflected in Lord Ross' report, were as shown in Table 3.13 below.

<sup>179</sup> ie approximately 10,000 during the 1970s and approximately 13,500 between 1 January 1980 and 1 September 1991.

<sup>180</sup> The Expert Group was set up by the Scottish Executive to consider the financial and other support offered to patients who were infected with Hepatitis C as a result of a blood transfusion or treatment with blood products. It published a preliminary report in November 2002 and a final report in March 2003. Paragraph 4.8 of the Expert Group's final report sets out the figures provided by Dr Soldan. Final Report at <http://www.scotland.gov.uk/Publications/2003/03/16844/20519>

<sup>181</sup> Letter dated 24 July 2002 by Dr Brian McClelland to Mr Bob Stock, Special Adviser [SGH.005.7201], enclosing a copy of Dr Soldan's *Estimated Number of Individuals Infected by Blood Transfusion in Scotland* [SGH.005.7203]

<sup>182</sup> Dr Soldan, *Estimated Number of Individuals Infected by Blood Transfusion in Scotland* [SGH.005.7203]

<sup>183</sup> The exercise had not been completed in 2002 and Dr Soldan can have had only preliminary or estimated data available.

**Table 3.13: Dr Soldan's Scottish estimates**

Number of individuals probably infected with HCV by blood transfusion 1980 to 1991			
	Total	Not known to be dead by 1995	Known/expected to be dead
Identified by HCV look-back programme in Scotland	106	106	0
Received components that entered look-back but did not receive testing in that programme	1243	628	615
Received components issued between 1 January 1980 and 31 August 1991 that did not enter the look-back programme in Scotland	2149	878	1271
Total	3498	1612	1886

**3.175** As noted above, the number identified and tested positive through the national look-back became 133 (Table 3.8), and an adjustment would be required for that change if for no other.<sup>184</sup> Dr Soldan's other data cannot be reconciled with the results of the look-back study. In this exercise the known infections accounted for a mere 3% of the total projected. Dr Soldan commented that many assumptions were used to generate her estimates, some of uncertain validity, and she had serious reservations about the application of her findings to individual cases.

#### *Health Protection Scotland*

**3.176** To assist the Inquiry, Professor David Goldberg and his colleague at Health Protection Scotland (HPS), Dr Christian Schnier, undertook a separate modelling exercise, in collaboration with the SNBTS, to estimate the number of people infected with Hepatitis C as a consequence of blood transfusion in Scotland during the period 1970–91 and the number who were alive as at June 2011.<sup>185</sup> Professor Goldberg explained the differences between his model and Dr Soldan's model as follows:

It should be understood that the model used by Schnier and Goldberg in 2011 for the Penrose inquiry was very different to that used by [Dr Soldan] ... in 2002. Further, the [Goldberg/Schnier] model was built following considerable consultation with Dr McClelland and Dr Gillon of SNBTS. The principal differences between the models is that the Soldan one used "lookback data" to inform its estimates and did not factor in any variation in HCV antibody prevalence among blood donors during 1980–31 August 1991. The Schnier and Goldberg model did not use lookback data to inform its estimates but did use estimates of HCV antibody prevalence among blood donors for each year during 1970–1991 ...

Schnier and Goldberg, in consultation with McClelland and Gillon, made the assumption that the size of the HCV infected IDU [injecting drug users] population in Scotland was directly proportional to the HCV infected donor population.

<sup>184</sup> Letter from National Medical & Scientific Director, SNBTS, to Dr Aileen Keel, Scottish Office, dated 28 April 1998 [SGF.001.2174] and Scottish Hepatitis C Lookback Results – 9 April 1998 [SGH.002.8669]

<sup>185</sup> *Estimation of the Number of Individuals Infected as a Consequence of Blood Transfusion in Scotland 1970–1991* – Goldberg and Schnier [PEN.018.1561]

In addition ... Schnier and Goldberg used a factor to account for the introduction of blood donor deferral in 1984 – a factor not used by Soldan et al.

Two other factors used by Soldan were modified for Scottish purposes; instead of the number of units generated from one blood donation being 1.6 (Soldan), the Scottish estimate, based on local data and expert opinion, was deemed to be 1.25; the proportion of units transfused was estimated to be 56% and not 66% (Soldan).<sup>186</sup>

**3.177** Using their statistical model, Professor Goldberg and Dr Schnier provided an initial estimate of the number of individuals in Scotland infected with Hepatitis C as a result of transfusion between 1970 and 1991.<sup>187</sup> That was followed up by a fuller document in the form of an academic paper.<sup>188</sup> In their paper they set out the various assumptions upon which their model was based.<sup>189</sup> The probability of a transfused blood component being infected with HCV was influenced by factors such as the size of Scotland's Hepatitis C infected population in any particular year and the effectiveness of the SNBTS' deferral policy during the period 1984–91. Direct evidence of the size of the HCV-infected population was not available, either in the Scottish population as a whole or in the population of Scottish blood donor.

**3.178** The available observed data comprised:

- The numbers of blood donations made during the period 1975–91.
- The prevalence of HCV antibody among individuals donating blood during September 1991 – February 1992.

**3.179** Assumptions were required for:

- The number of blood donations made by blood donors during 1970–74.
- The average number of blood components generated by a blood donation.
- The probability of a blood component being transfused.
- The probability of a transfused blood component being infected with HCV.

**3.180** The acceptability of the assumptions is fundamental to the exercise. The World Health Organization's Global Burden of Hepatitis C Working Group in 2004 (referred to in the Goldberg/Schnier paper) emphasised that precise estimation of the incidence of HCV infection was not possible, given available data. Professor Goldberg noted that it was possible only to estimate the numbers of individuals who had acquired infection through blood transfusion (or any other route). A combination of observed data and assumptions based on observation and expert opinion was employed to develop estimates.

**3.181** As in England, the first firm information on the prevalence of HCV antibody in blood donors in Scotland came with the collection of data on anti-HCV among blood donors during the initial months of HCV screening. Prevalence in Scotland over a period

<sup>186</sup> Letter dated 28 February 2012 from Professor Goldberg to Tracey Turnbull, [PEN.019.0896] at 0897, response to question 4

<sup>187</sup> *Estimation of the number of individuals infected as a consequence of blood transfusion in Scotland 1970–1991*, dated 3 and 5 October 2011 [PEN.018.1561]

<sup>188</sup> Schnier and Goldberg, *Estimation of the number of individuals infected and alive as a consequence of blood transfusion in Scotland 1970–1991*, 1 March 2012 [PEN.019.0899]

<sup>189</sup> *Ibid* [PEN.019.0899] at 0900 and 0901

of six months was found to be 0.088%. For present purposes, an important parameter was the proportion of antibody-positive persons who were RNA virus-positive; that is infectious. The first material assumption made by Professor Goldberg and his colleague was that the appropriate proportion was 75% (assumption ii in the report). The other 25% of HCV antibody positive donors would have cleared the infection and would have been HCV RNA-negative, with the result that the prevalence of HCV-positive infectious donors in the donor population in Scotland in 1991 was estimated to be 0.066% (0.088, less 25%).<sup>190</sup> As with other parameters, uncertainty was reflected in their statistical model, which assumed values ranging from 50% to 85%.

**3.182** The basis for Professor Goldberg's assumption was the WHO advice provided by the Global Burden of Hepatitis C Working Group. It had among its key areas of study the natural history of HCV infection, including 'healthy individuals', morbidity and mortality. Other estimates have been made, and a clearance rate of 20% has been referred to.<sup>191</sup> There cannot be a single 'correct' value. Professor Goldberg's adoption of the WHO rate was justifiable in the absence of hard data suggesting a need for variation to account for local factors. It was within, though at the lower end of, the most up-to-date estimates reported by Dr Hay in the UKHCDO updated report of April 2012.<sup>192</sup>

**3.183** From the prevalence of 0.066% estimated for 1991, the next necessary step was to estimate the prevalence of infection in the donor population over the study period, beginning in 1970. There were no relevant observed data for that population. Prior to anti-HCV testing there were no available means of measurement. In developing their estimate of the number of people who acquired HCV infection as a consequence of blood transfusion in Scotland during the period 1970 to 1991, Professor Goldberg and Dr Schnier adopted the results of a study by Hutchinson, Bird and Goldberg, carried out by statistical modelling, which estimated HCV prevalence in injecting drug users (IDUs) between 1970 and 1991, and applied the trend brought out to work back from 0.066% to values for each year (assumption iv).<sup>193</sup>

**3.184** The Hutchinson study was based on local data from Glasgow for the prevalent number of IDUs per calendar year from 1960 to 2000. The data were adjusted for assumptions about age-related use, mortality from non-HCV causes and other factors, to bring out a pattern of the prevalence of HCV infection among current IDUs. The model was then adapted to the whole of Scotland based on available epidemiological data by adjusting for a number of key parameters. The paper was aimed at providing quantitative estimates of the current and future burden of HCV disease in the IDU population in planning a public health response to treatment needs and preventive measures. The characteristics of IDUs affecting HCV disease progression were discussed, and are reflected in the paper.

**3.185** Goldberg and Schnier assumed that the change in HCV prevalence among the blood donor population was proportional to the change in the estimated number of

<sup>190</sup> Ibid [PEN.019.0899] at 0901 and 0902. Note that the derivation of this value of 0.066% is different from Dr Soldan's derivation and use of the same numerical value in her calculations.

<sup>191</sup> See paragraph 3.122. Khan et al found a natural clearance rate of 17.4% among patients with congenital bleeding disorders studies in Scotland: 'Outcomes of hepatitis C infection in a large haemophilia population' [PEN.013.0008] as revised for publication February 2013. They noted that the natural clearance rate (and other factors), closely mirrored the non-haemophilic population. See also Dr Hay – Day 8 pages 41–43 for evidence of his clinical experience of higher rates of clearance.

<sup>192</sup> UKHCDO report *National Haemophilia Database: Bleeding disorder statistics for the Penrose Inquiry, 2012* [PEN.019.0927] at 0983

<sup>193</sup> Hutchinson et al, 'Modelling the current and future disease burden of hepatitis C among injection drug users in Scotland', *Hepatology*, 2005; 42:711 [LIT.001.4373]

HCV-infected IDUs.<sup>194</sup> This was an important assumption. Injecting drug use continues to be both directly and indirectly the principal driver of Scotland's HCV epidemic. There is a direct impact from a donation by an infected injecting, or former injecting, drug user. An indirect impact resulted from a donor who had never used intravenous drugs but acquired HCV infection from an injecting drug user, sexually or through contact with needles or instruments in a healthcare/tattoo/barbershop setting. The Goldberg/Schnier assumption of proportionality reflected the view that approximately 90% of all individuals diagnosed with HCV in Scotland, for whom risk factor information was available, had injected drugs, and that 'an appreciable proportion' of the remainder acquired infection indirectly, by contact with an infected IDU.<sup>195</sup>

**3.186** In addition, the authors noted that in 1984 the SNBTS introduced a deferral policy aimed at reducing the number of donors who were at higher risk of transmitting blood-borne virus infection (ie the leaflets and questionnaires introduced from 1984 to try to exclude donors at a higher risk of transmitting HIV), and they assumed that the deferral policy reduced HCV prevalence in the blood donor population by a constant factor of 66% from 1984 onwards.<sup>196</sup>

**3.187** The progressive development from the 1970s and early 1980s of methods of identifying and deterring high risk donors from giving blood are discussed elsewhere in this Report at Chapter 26, *Donor Selection – Higher Risk Donors*, and Chapter 28, *Donor Selection – AIDS*. At this stage it is appropriate to note only that these steps were taken, and are likely to have reduced the incidence of infection in donations. There is a question related to the quantification of the immediate impact of the policy, and its sustained effect over the period to 1991, to which it will be necessary to return. However, some estimate of the impact of the deferral policy was necessary.

**3.188** Professor Goldberg and his colleagues set out in table 1 of their report<sup>197</sup> an estimate of the prevalence of HCV-positive infectious donors in Scotland as a whole before and after the introduction of donor deferral: that is from 1970 to 1983 and from 1984 to 1991 respectively. The table reflected in the first place the Hutchinson data and the assumption that the change in prevalence among donors was proportional to the estimated change in prevalence among IDUs (paragraph 3.183) and in the second place the assumption that the deferral policy reduced prevalence in the donor population by 66% from 1984. The prevalence in the donor population for each year between 1970 and 1991 which these assumptions generate has been plotted in Figure 3.5.

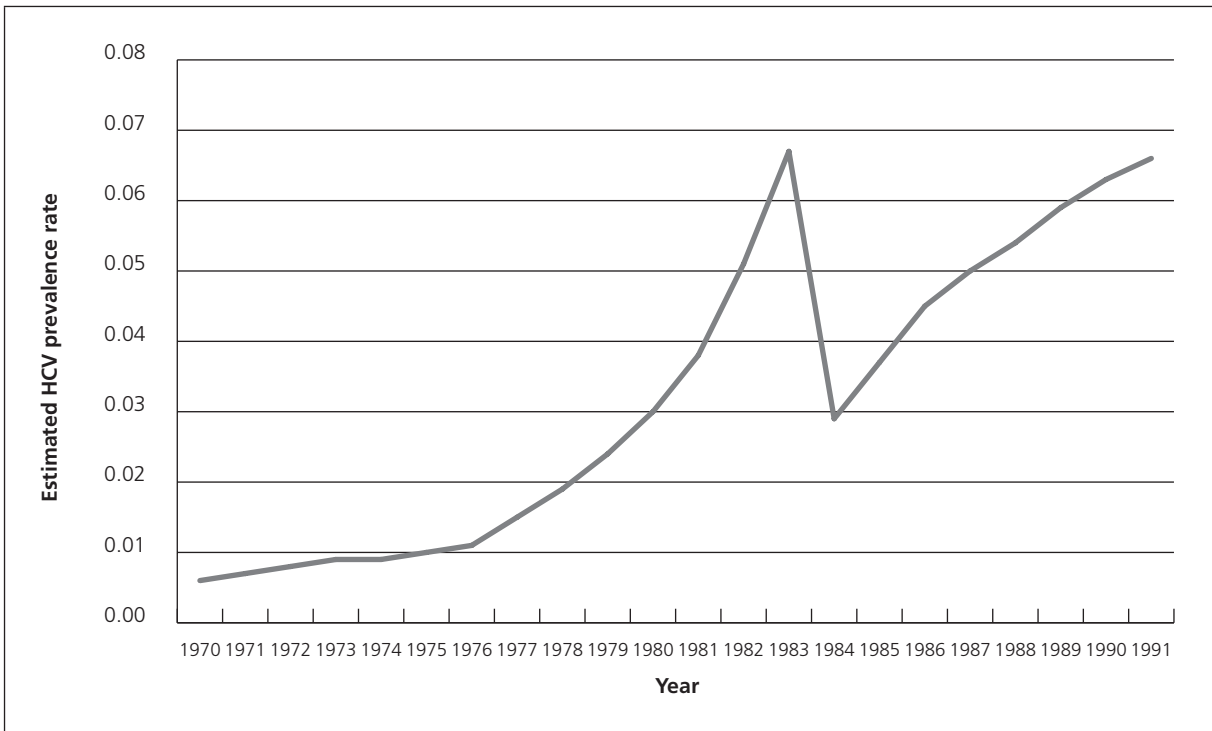
<sup>194</sup> Schnier and Goldberg, *Estimation of the number of individuals infected and alive as a consequence of blood transfusion in Scotland 1970–1991*, 1 March 2012 [PEN.019.0899] at 0902. The estimated number of HCV-infected IDUs in Scotland is shown in appendix 8 of the Goldberg/Schnier paper, [PEN.019.0899] at 0911. The estimated number of IDUs rises from 575 in 1970 to 996 in 1975, 2857 in 1980, 10,689 in 1985 and 18,244 in 1990. These estimates are, in turn, based on the paper by Hutchinson *et al*, 'Modelling the current and future disease burden of hepatitis C among injection drug users in Scotland', *Hepatology*, 2005; 42:711 [LIT.001.4373]

<sup>195</sup> Schnier and Goldberg, *Estimation of the number of individuals infected and alive as a consequence of blood transfusion in Scotland 1970–1991*, 1 March 2012, Assumption iv [PEN.019.0899] at 0900

<sup>196</sup> *Ibid* [PEN.019.0899] at 0902

<sup>197</sup> *Ibid* [PEN.019.0899] at 0902

**Figure 3.5: Effect of Goldberg/Schnier assumptions relating to HCV Prevalence in blood donor population in Scotland**



**3.189** The rapid build-up of prevalence to 0.067% in 1983, reflects directly the assumed correlation of the growth in the number of IDUs and in HCV prevalence in the donor population. From 1984 to 1991, the assumption was that the donor deferral policy consistently reduced the number of infected donations. Professor Goldberg was asked whether a degree of gradation should have been assumed, to allow time for the policy to take effect. He explained that alternatives had been tested, and that it had been concluded that, although the rate selected was intuitive, it was thought optimal.

**3.190** Professor Goldberg's first and seventh assumptions (as listed in the report) were the same as Dr Soldan's: that every recipient of a contaminated unit subsequently developed HCV infection, subject to 'discount' for those who cleared the virus or were never to progress to chronic liver disease, and that the risk of an individual receiving two or more infected units was negligible. In the stochastic model some of the assumptions were modified to express uncertainty.

**3.191** In their stochastic exercise, Professor Goldberg and Dr Schnier estimated that between 1970 and August 1991, a median number of 1533 individuals were infected with Hepatitis C as a result of blood transfusion (the median estimate of 1533 was derived from a lower estimate of 1198 and an upper estimate of 1963).<sup>198</sup> An estimated breakdown per year is provided in table 3 of the paper, which indicates that an estimated median number of 232 individuals were infected with Hepatitis C between 1970 and 1979 and 1026 individuals were infected between 1980 and 1989.<sup>199</sup> In the year prior to HCV screening of donors being introduced (ie 1990), it was estimated that 155 individuals were infected with HCV as a result of transfusion.<sup>200</sup>

<sup>198</sup> Ibid [PEN.019.0899] at 0904

<sup>199</sup> Ibid [PEN.019.0899] at 0904. A footnote to Table 4 states, 'Total statistics are results from simulation and do not equate to the sum of the simulation results by year between 1970 and 1991'.

<sup>200</sup> Ibid [PEN.019.0899] at 0904

**3.192** Based on the assumptions set out in their paper, the authors also estimated that a median number of 296 individuals who were infected with Hepatitis C as a result of transfusion were alive in 2011, of whom 222 were RNA positive (on the assumption that 25% of the 296 cleared the virus and were no longer RNA positive).<sup>201</sup>

**3.193** At least some of the assumptions made by Professor Goldberg and Dr Schnier cannot be verified, and the validity of the figures produced by their statistical model, like the figures produced by other statistical models, is necessarily qualified. If different assumptions and input data are used, different figures are generated.

### *Evidence relating to the statistical models*

**3.194** In discussing Dr Soldan's exercise, Professor Goldberg said that there was a potential bias in the exercise, in particular in applying the same factors to deceased recipients and living recipients who had not been tested, as applied to those who followed the observed path to the end.<sup>202</sup> The difficulty is clearer in the case of the deceased recipients. They were not available for testing. The assumption that the proportion of positive tests derived from testing the living could be applied directly to those who had died is obviously not valid, especially where, as here, the proportion of individuals known or assumed to have died is so high. As Professor Goldberg observed, there must have been reasons why 38% of those assumed to have been alive were not tested.<sup>203</sup>

**3.195** Professor Goldberg said:

But the thing is that the extrapolations appear to be based on the [observed path] and the question is: can you extrapolate? Because there may well be biases in the system which mean that the numbers infected, or the expected numbers infected, may be an underestimate or an overestimate.<sup>204</sup>

**3.196** Commenting principally on Dr Soldan's material, Professor Goldberg said:

I'm not convinced this is the only way to estimate the size of the infected population. I think there are other ways of doing it ... if you use a combination of approaches, then you do reduce uncertainty. But that all takes time and much, of course, is dependent on the information that's available to you. So for Scotland we have information generated through the look-back, but we also have other information about the size of the infected population, ie Scottish population, during the 1980s but also during the 1970s as well. So I would expect to use these data.<sup>205</sup>

And:

[I]f you just use one method, you are opening yourself up a little. I mean, you know, this is actually a very good piece of work undertaken by Kate, who probably knows more about this field than anybody else in the UK. But it does have its limitations and I think we just have to acknowledge these limitations  
....

By and large, when you are doing this sort of work, if you use maybe two or three methods – but much depends of course on the information you have

<sup>201</sup> Ibid [PEN.019.0899] at 0905 to 0909

<sup>202</sup> Professor Goldberg – Day 6, pages 129–130

<sup>203</sup> Ibid, page 130

<sup>204</sup> Ibid, pages 130–131

<sup>205</sup> Ibid, pages 127–128

available to you – I think your confidence in your final outcome is very much greater because if you have considerable differences in your results, you can get an average or you can take what's regarded as the best or whatever.<sup>206</sup>

**3.197** These observations appear to be as relevant to the Goldberg/Schnier model as to Dr Soldan's exercise. Professor Goldberg and Dr Schnier were asked by the Inquiry to re-run their model, omitting the assumption that the donor deferral policy introduced in 1984 reduced the HCV prevalence in the blood donor population constantly by 66%. In response to that request Professor Goldberg advised:

We repeated this modelling exercise to ascertain the impact of (i) a deferral policy with no effect and (ii) a deferral policy, the effect of which increased incrementally between 1983 and 1991. For (i) the number infected until 1991 was estimated to be 1110 (90% credibility interval: 876 to 1413), the number alive as at 2011 was 230 (178 to 294) and the number alive as at 2011 and chronically infected was 173 (128 to 225). For (ii) the estimated number of those infected was 2212 (1657 to 2853), the number alive as at 2011 was 438 (325 to 566) and the number alive and chronically infected as at 2011 was 326 (241 to 435).<sup>207</sup>

**3.198** Professor Goldberg and Dr Schnier were also asked to re-run their model, this time omitting the assumption that the HCV prevalence in the donor population between 1970 and 1990 was directly proportional to the estimated prevalence of HCV in the injecting drug use population. They did so by adopting an approach similar to that of Dr Soldan, and assumed a flat rate based on 1991 data. Professor Goldberg replied:

We modified the model, as requested, using a constant HCV prevalence (0.09% antibody positivity); this generated an estimated infected number of 6784 (5027 to 8776), with the number having survived until 2011 being 1050 (789 to 1364) and the number having survived as at 2011 and being chronically infected, 788 (569 to 1044).<sup>208</sup>

At this stage it is sufficient to note that the changes in assumptions reflected in this paragraph and in paragraph 3.205 below generate very large variations in outcome.

### *HCV infections as a result of blood transfusion between 1970 and 1991: discussion and conclusions on statistical models*

**3.199** As Professor Goldberg accepted, neither of the statistical analyses carried out provided a single, wholly acceptable source of evidence. A sensitivity analysis was not carried out to test the assumptions made in varying conditions.<sup>209</sup> It will be necessary to look at the evidence in the round to determine whether one can make an estimate of the incidence of infection in NHS patients using recorded data and acceptable assumptions.

**3.200** There is one point common to the exercises: the use of relatively low levels of known and objective data of HCV transmission. In Dr Soldan's English paper the known data (derived from the HCV look-back programme in England) accounted for 5% only (677/13,505) of the

<sup>206</sup> Ibid, pages 132–133

<sup>207</sup> Letter from Professor Goldberg in response to further queries on statistics from Professor Oliver James [PEN.019.0922] at 0923, assumption 3

<sup>208</sup> Ibid [PEN.019.0922] at 0924, assumption 4. For completeness, it should be noted that Professor Goldberg added, 'It is my view that the approach used, ie that using the HCV infection IDU estimates, is a novel and scientifically valid one.'

<sup>209</sup> Professor Goldberg – Day 6, pages 134–135



total infections estimated to have been transmitted by transfusion between 1 January 1980 and 1 September 1991. That is a low proportion of known instances of transmission relative to the estimated total. The percentage was higher in the case of patients who survived to 1995, at 13%. The median age of these patients in 1995 was 55 years, significantly lower than the median age of the identified recipients in the group of 3373 added by extrapolation.<sup>210</sup> On any approach, the projections were very heavily dependent on the validity and accuracy of the assumptions made, and that affects the level of confidence in the result. Dr Soldan's paper recognised that.<sup>211</sup> In her Scottish exercise, the known data accounted for 3% of the total infections estimated, which was an even lower proportion.

**3.201** Dr Soldan's application of a constant infectivity rate, derived from the first four months after testing began on 1 September 1991 in England and the initial six months of testing in Scotland, to all donations for the period 1 January 1980 to 1 September 1991, appears to raise a problematic issue.<sup>212</sup> It was one of the features considered by Professor Goldberg to be significant in comparison with his own approach. It assumed that this component of the risk of transmission of infection remained the same throughout the 12 years of the period of study. That is not consistent with a picture in which HCV infection rates were increasing as a result of the practices of intravenous drug users, for example, or, more generally, with the impression that HCV infection in the general population appears to have grown significantly over the 1970s and 1980s.

**3.202** The increase in HCV prevalence in the general population was one of two relevant countervailing trends over that period. The other was the increasing proportion of potential new and returning blood donors, who were dissuaded from donating blood from the commencement of self-deferral policies onwards, by increasing efforts to discourage 'high risk' individuals from presenting at donor sessions to give blood. The deferral of potential blood donors who were at higher risk of blood-borne virus infection, implemented generally in 1984 in the AIDS period, is likely to have had some incidental impact on the risk of transmission of HCV. For that reason alone, the HCV infectivity rate prior to 1984 might have been higher than in the period from 1984 onwards.

**3.203** Another element in the exercise that may have been important was the yield of components per donation assumed in the calculation. The yield in England, based on measurement there, was 1.6 components per donation. In the later Goldberg/Schnier exercise the Scottish yield applied was 1.25 components per donation. There were two possible reasons that may have contributed to the difference. Blood collection in Scotland was plasma-driven in the 1980s and an excess of red cells was inevitable. Dr Gillon speculated that there would have been a higher rate of discard in Scotland, reducing the number of components transfused.<sup>213</sup> That is a reasonable speculation. In addition, excess Scottish red cell production was 'exported' to England, reducing the proportion of components produced that were actually used in Scotland.

**3.204** Dr Soldan did not deal with these issues. It cannot be over-emphasised that it is accepted that Dr Soldan's work was a ground-breaking attempt to provide an estimate of the extent of the problem of post-transfusion HCV infection. The issues that may arise

<sup>210</sup> Soldan *et al*, 'The contribution of transfusion to HCV infection in England', *Epidemiology and Infection*, 2002; 129:587–591 [PEN.013.1580] at 1581–2 and 1583.

<sup>211</sup> *Ibid* [PEN.013.1580] at 1583

<sup>212</sup> It should be noted that although Dr Soldan and Professor Goldberg used an infectivity ratio of 0.066% they were derived quite differently. Professor Goldberg's value was the observed Scottish rate of 0.088% discounted by 25% for the proportion assumed to be non-infective.

<sup>213</sup> Dr Gillon's response to further questions on statistics [PEN.019.1311] at 1312

from her original work do not have to be resolved so far as they relate solely to England. That is not within the scope of the terms of reference of the Inquiry. Some, however, have an indirect bearing on the figures brought out for Scotland.

**3.205** Statistical modelling is a complex exercise and may be influenced by the interaction of other values. It has to be emphasised that while it is relatively easy to draw negative conclusions on the assumptions made, that does not assist in providing a reliable estimate. Simple arithmetical adjustment for a single altered factor in a statistical analysis would be unsatisfactory. One cannot substitute one value for any given factor for another and express a different conclusion arithmetically. For example, if Dr Soldan did use the component yield observed in England (1.6 units per donation) in her Scottish exercise, that would have been one-third higher than the Goldberg/Schnier figure. The effect is likely to have been large. Without knowing the sensitivity of the model to a variation of that kind, the consequence in terms of the final number could not be estimated broadly.

**3.206** Professor Goldberg considered that the extrapolation of the data from the observed path to the other components was a reasonable approach, though not the only approach. As already commented (paragraph 3.164), Dr Soldan's approach was not seriously disputed in the evidence before the Inquiry, and it is appropriate to take the results of her calculations into account.

#### The Department of Health estimate and Dr Soldan's estimate for Scotland

**3.207** While the methodology for the DoH estimate of the total number of TT HCV infections in the United Kingdom between 1970 and 1991 is not clearly expressed, it seems likely that it is an extrapolation of Dr Soldan's figure for England, to take account of the whole UK population. On that basis, as noted above at paragraph 3.170, it is possible to back-calculate the DoH estimate and to suggest that the estimate for Scotland would be about 9% of 28,043, ie 2524.

**3.208** This figure for Scotland is significantly different from the figure brought out in Dr Soldan's original Scottish exercise. Her value of 3498 related to components issued from 1 January 1980 to 31 August 1991; it was already higher than the number deduced from the UK values for a much longer period. In relation to England, the assumption of 10,000 additional infections for the previous decade amounted to 74% of the estimate for the later period. Since that involved application of the same general assumptions for both periods, one might expect an equivalent approach to estimating figures for Scotland to have produced an additional number of about 2600, making the Scottish number about 6100 for the whole period 1970–1991. Adopting a flat HCV donor prevalence rate of 0.09%, and applying his model, Professor Goldberg later calculated a median value of 6784 for this period. The difference between 6100 and 6784 is not material given the margins of error implicit in the exercise. On either approach, the total for England and Scotland would already exceed the DoH total for the United Kingdom, and leave no room for numbers of infections in Wales and Northern Ireland.

**3.209** It is not possible in the circumstances to accept Dr Soldan's estimate for Scotland as a sufficient and acceptable basis for discussing the numbers put at risk in Scotland. Dr Soldan was not available to assist the Inquiry by reassessing the position.<sup>214</sup> Her estimate remains one result of statistical modelling. Without detailed examination, it cannot be

<sup>214</sup> Letter from Health Protection Agency dated 25 June 2010 [MIS.001.0299]

dismissed. On the other hand, the DoH figure of about 2500 for Scotland, while not supported by detailed description of methodology, has the benefit of proportionality, and has at least superficial support from that fact.

### The Goldberg/Schnier model

**3.210** As already indicated, there were two critical assumptions in the Goldberg/Schnier model that required particular examination: the adoption of the rate of growth of HCV infection in injecting drug users as the rate of change of HCV prevalence both in the population as a whole and in the donor population, and the impact of the SNBTS blood donor exclusion policy in and after 1984.

**3.211** The sensitivity of the Goldberg/Schnier model to variations in the prevalence of HCV infection in the donor population was demonstrated by the re-run of the model excluding the assumption that HCV prevalence in the donor population was directly proportional to the estimated prevalence in the IDU population. Irrespective of the numbers brought out, the assumption was significant.

**3.212** It appears to the Inquiry that proportionality implied both that:

- There was a direct relationship between the pattern of HCV prevalence in the general population of Scotland and the growth in the numbers of injecting drug users.
- There was a direct relationship between the pattern of HCV prevalence in the general population and in the blood donor population over the relevant period.

**3.213** Overall, the evidence before the Inquiry showed that the growth in numbers of HCV-positive IDUs came to be the major factor to influence the prevalence of HCV infection in the Scottish population as a whole. The issue for the Inquiry was whether the data supported the assumption of direct proportionality of relationship between the IDU population and the general population of Scotland between 1970 and 1990 (assumption iv). That was explained:

The rationale of assuming proportionality is that it is estimated that 90% of HCV infected individuals in Scotland acquired Infection directly through injecting drug use and that an appreciable proportion of the remainder will have acquired infection indirectly as a consequence of injecting drug use (eg being born to an infected IDU or having unprotected sex with an infected IDU) (Hutchinson et al., 2006)<sup>215</sup>

**3.214** The paper by Hutchinson and others published in 2006<sup>216</sup> analysed information on diagnosed HCV infection at December 2004, (18,571 individuals less 11% who had died, 16,500 net), and estimated the likely pattern of infection in 33,500 antibody positive individuals who had not been diagnosed. Allowance was made for 25% natural clearance. In each case 88% of chronic HCV-infected people were estimated to be IDUs and 12% were non-IDU's; 26.6% of whom were blood/blood factor recipients.

<sup>215</sup> Schnier and Goldberg, *Estimation of the number of individuals infected and alive as a consequence of blood transfusion in Scotland 1970–1991*, 1 March 2012 [PEN.019.0899] at 0900

<sup>216</sup> Hutchinson et al, 'Hepatitis C Virus Infection in Scotland: Epidemiological Review and Public Health Challenges', *Scottish Medical Journal*, 51; 8:15: [LIT.001.3943]

**3.215** The 2006 paper carried forward by a year a 2005 study by Hutchinson, Roy and others<sup>217</sup> of information to December 2003 which had, in turn, drawn on material from a 2004 paper by Professor Goldberg's group at the Scottish Centre for Infection and Environmental Health (SCIEH).<sup>218</sup> The 2004 paper noted that at 31 December 2003 a total of 18,109 individuals were known to be HCV antibody positive. 61% of those were known to have injected drugs at some time. Those individuals represented 90.5% of the total for whom risk information was available (67% of the total of 18,109).

**3.216** The SCIEH paper contained a detailed analysis of data for each NHS Board, and for Scotland as a whole, aggregating data to 1995 and thereafter presenting data annually. For the period to 1995 'blood factor'<sup>219</sup> accounted for 269 reported cases of HCV antibody-positive individuals, and IDUs accounted for 1029, a ratio of just under 1:4. For 1995 the ratio was 29:648: 1:22. Over the remainder of the period reported the ratio of 'blood factor' antibody positive recipients to IDUs continued to fall.

**3.217** It would have been inappropriate to subject these papers to further, more detailed critical analysis. It did not appear that the additional time and expense involved in instructing further expert opinion was justified, since it was clear that a further or different set of assumptions would be unlikely to result in a definitive conclusion. It is not inappropriate to note that the data underpinning the opinions expressed have at no time been comprehensive. Perhaps more significantly in terms of long term trends, inferences have been drawn from reference periods including the highest growth in HCV positive IDUs when, by sheer force of numbers, they were clearly the dominant factor affecting HCV prevalence in the general population. As the SCIEH report notes, for blood factor concentrate recipients there were no new infections after the introduction of effective heat treatment of factor concentrates in the mid-1980s.<sup>220</sup> From 1991 screening for antibodies to HCV prevented new infections from transfusion generally. Mortality among transfusion recipients was at all times skewed by the significant proportion of NHS patients who died within a short time of the procedure that had required transfusion.

**3.218** The Inquiry cannot exclude the direct linear numerical relationship between the increase in HCV among IDUs and the increase in the donor population over the period 1970 to 1991. It seemed appropriate, however, to seek further explanation of its basis. In relation to the principal issue raised with him, Professor Goldberg explained:

You contest that the change in HCV prevalence among blood donors over the two decades in question would not have mirrored the change in the estimated number of prevalent infections among injecting drug users over this period. While we cannot prove this was indeed the case, our view is that injecting drug use has been the principal driver of HCV infection in Scotland, even going back to the 1960s. As we pointed out, it was not just the direct effect but

<sup>217</sup> Hutchinson *et al*, 'Modelling the current and future disease burden of hepatitis C among injection drug users in Scotland', *Hepatology*, 2005; 42:711 [LIT.001.4373]

<sup>218</sup> Codere *et al*, 'Surveillance of known hepatitis C antibody positive cases in Scotland: Results to 31 December 2003', *SCIEH Weekly Report* [LIT.001.4176] at 4177

<sup>219</sup> In these data 'blood factor' numbers appear to refer exclusively to those who acquired HCV infection through coagulation products: footnote at page 4177. Transfusion recipients were included in the 'other' or 'not known' categories. This classification continues in the HPS Weekly Report for 23 October 2013; Volume 47 No. 2013/43; ISSN 1753-4224 (Online): <http://www.documents.hps.scot.nhs.uk/ewr/pdf2013/1343.pdf>. Table 2. The 'Other' category includes needlestick, bite, blood spillage, and blood transfusion, among other means of transmission. By comparison, the data in the Hutchinson paper of 2006 encompasses all transfusion-transmitted infections.

<sup>220</sup> Codere *et al*, 'Surveillance of known hepatitis C antibody positive cases in Scotland: Results to 31 December 2003', *SCIEH Weekly Report* [LIT.001.4176] at 4177

also the indirect one. What we mean by this is that people who did not inject drugs but acquired their infection through, for example, tattooing, are likely to have become infected with a virus which was originally circulating among individuals who injected drugs ...<sup>221</sup>

It seems appropriate to be cautious about accepting total equivalence, as is implicit in the exercise.

**3.219** The next step seems superficially difficult, involving the assimilation of the prevalence of infection in the general population and in the blood donor population. It appears generally to have been accepted that there were always significant differences between the prevalence of HCV infection in the blood donor and general populations, and that these had become more pronounced since the early 1980s. The donor population has always been selected by age and general health factors and, at least in parts of Scotland, by questioning about injecting drug use and observation of signs of injecting. In Professor Goldberg's view, the prevalence of HCV in the general population may have influenced the prevalence in the donor population to a greater extent in the past than in more recent times.<sup>222</sup> In general, however, a policy of deferral on the basis of intravenous drug use, despite the limitations inherent in the practices of the SNBTS donor teams, must have had some impact on the risk of IDUs both being accepted as donors, and giving blood that entered the pool of blood available for clinical use.

**3.220** There were, and are, demographic distinctions between the general population and the blood donor population. It is not at all clear that the cohort of HCV antibody-positive individuals coming to the notice of doctors as being IDUs was ever a major component of the blood donor population (and it is to be borne in mind that between 80 and 90% of that population are return donors). Some return donors at 1991 will have begun donating decades earlier, in some cases before injecting became a major issue.

**3.221** Assumption (iii) in the Goldberg/Schnier model was:

Deferral policy, introduced by SNBTS in 1984, was assumed to have reduced the HCV prevalence in the donor population constantly by 66%. This assumption was based on limited local data and expert opinion.<sup>223</sup>

**3.222** The 'local data and expert opinion' referred to information and advice provided by Dr Gillon and Dr McClelland. The paper explained:

In 1984, SNBTS introduced a deferral policy to reduce the number of donors with a higher risk of having blood born (sic) virus infections; therefore the prevalence of HCV-positive donors in the donor population during 1984 to 1991 was lower than it would have been, if the deferral policy had not been in operation. It was assumed that the deferral policy reduced HCV-prevalence in the donor population by 66%.<sup>224</sup>

**3.223** The need for an adjustment to reflect the general point made is clear and is accepted: the deferral policy must have had some impact, whenever it was implemented.

<sup>221</sup> Letter from Professor Goldberg in response to further queries on statistics from Professor Oliver James [PEN.019.0922] at 0923

<sup>222</sup> Professor Goldberg – Day 6, pages 96–97

<sup>223</sup> Schnier and Goldberg, *Estimation of the number of individuals infected and alive as a consequence of blood transfusion in Scotland 1970–1991*, 1 March 2012 [PEN.019.0899] at 0900

<sup>224</sup> Ibid [PEN.019.0899] at 0902

The year 1984 was perhaps too early in the evolution of SNBTS management systems to find that there was a 'policy' introduced by SNBTS: the era of regional autonomy had not yet passed, and there were variations in the dates when practice changed across Scotland. Further, as already noted, the policy of Edinburgh and south east Scotland, which became the basis of the general model, still reflected an erroneous view of the duration of risk presented by a carrier of HCV RNA. The question was whether 66% was an acceptable estimate for the impact of the policy change from 1984 to 1991.

**3.224** The Goldberg/Schnier number of 6784 recipients of HCV-contaminated units, was based on a flat rate prevalence of 0.09%. Even at that level, the contaminated units remain a tiny percentage of the total number of units transfused, at 0.16%. The Goldberg/Schnier data showed that 4,344,795 units were transfused over the period 1970 to 1991. In terms of the numbers of donors presenting, the percentage is even lower. Over the beginning of the period when voluntary deferral was in practice, SNBTS data on donors and deferrals indicate the difficulty in drawing inferences. The pattern was as shown in Table 3.14.<sup>225</sup>

**Table 3.14: Donors and donors deferred 1981–82 to 1987–88**

**SNBTS**

	Total attendances		New donor attendances	
	Attended	% deferred	Attended	% deferred
1981–82	322,304	9.30	51,729	16.5
1982–83	328,086	9.10	50,241	14.5
1983–84	336,802	8.10	54,046	12.5
1984–85	338,278	9.00	50,004	9.5
1985–86	341,307	8.59	48,858	15.8
1986–87	340,890	8.78	48,350	13.5
1987–88	323,837	9.10	39,580	13.6

**3.225** In relation to total attendances, the fall in the number of donors influenced by a change in deferral policy is problematic. These were individuals whose blood had been accepted, perhaps often, in the past or who had been deferred temporarily and had returned. In 1984–85 approximately 30,500 return donors were deferred. These were, by definition, individuals who had not been deterred by the policy from attending to offer blood. None who attended and were deferred on grounds of evidence of intravenous drug use could be included with those persuaded by the leaflets and other material to self-defer. The number deterred by the policy and not attending at all must be speculative. There was a significant fall in new donors presenting at centres in 1985–86, and there was a relatively high incidence of deferrals in that cohort in that year alone compared to subsequent years. If it were possible to draw any inference from these data, it would be that the reducing numbers of new donors might have reflected the effectiveness of the policy more than would the numbers of return donors. The year on year cumulative

<sup>225</sup> The SNBTS data relate to years ended 31 March. However, applying the percentage deferral rates for total attendance, and averaging to accommodate the timing differences, the data reconcile reasonably closely with the Goldberg/Schnier data for observed donations.

reduction in new donors attending between 1983–84 and 1987–88 was 27%. The increase in deferrals in the new donor group after 1984–85 might suggest that other factors were affecting the situation.

**3.226** There is a danger in using the figures set out in Table 3.14 directly. The numbers of infected donors, returning and new, would be small relative to the totals in each group, and the relative percentage movements might have been affected by quite small changes in numbers. For the period September to December 1991, there were 33 infected donations from new donors. The number for 1992 was 55. They were, of necessity, included in the numbers who were not dissuaded from giving blood. One cannot tell what number would have attended to give blood but for the impact of the policy change, although it is not obvious that it would be large.

**3.227** Dr McClelland and Dr Gillon were asked to reconsider this area. From their responses, it appears that, with very limited relevant factual data, they attempted to make a conservative estimate.<sup>226</sup> Dr Gillon's explanation tends to underline the lack of numerical underpinning for the estimate:

We knew that the donor selection procedures introduced by November 1984, including as they did a signed declaration by each donor that he or she was not in the defined risk categories, led to the exclusion of a steady number of such donors throughout the period leading up to HCV screening in 1991. I received a written confidential report on every such donor, and therefore had first hand, if somewhat impressionistic knowledge of the apparent effectiveness of the procedures. In order to try to give this a numerical basis, we tried to extrapolate backwards as best we could from the reports on population prevalences published in the early 1990s and subsequently, in order to estimate what proportion of potentially infected donors we were managing to exclude ....

After commenting on HIV among intravenous drug users in Scotland, the discussion continued:

[W]e knew that the initial period of screening for HCV in 1991/2 produced a donor prevalence of 0.09%. Balogun et al (2002) estimated that the population prevalence in England and Wales peaked in 1986, at just over 1%. By 2005 the HPA (Hepatitis C in the UK. 2011 Report) estimated a prevalence in adults of 0.67%.

We interpreted these data as evidence that the entirety of donor selection policies and procedures, including publicity and donor education, reduced the risk of an infectious unit entering the blood supply by at least an order of magnitude ... We agreed in discussion that it would be appropriate to be very conservative in the final assumption, but we acknowledge that there are residual reservations about the assumptions on population prevalences. It was therefore correct to state that Assumption 3 derived in part from our expert professional opinions.

---

<sup>226</sup> Dr Gillon's response to further questions on statistics [PEN.019.1311] and Dr McClelland's response to further questions on statistics [PEN.019.1315]

**3.228** The Goldberg/Schnier report noted that 149 of 180,000 donors tested in the study period from September 1991 to February 1992 tested HCV antibody-positive. The adjusted value of 0.066% was the prevalence among those who presented at donor sessions, a cohort within the general population of potential donors but not co-extensive with that population. It was a difficult exercise to retrospectively apply that prevalence on the basis of limited data on the prevalence overall, whether in the IDU population or in the general population.

**3.229** Neither Dr Gillon nor Dr McClelland offered any computational support for the percentage applied in the Goldberg/Schnier exercise, nor any source data that were relevant to the estimate. It remains heavily dependent on limited data, their local knowledge and their professional judgement. Their local knowledge and their professional judgement are undoubtedly wide-ranging, and generally reliable, but cannot be assumed to be infallible.

**3.230** So far, this assumption has been discussed in terms of Scotland as a whole, as it was presented, and by reference to the time-frame selected. There are grounds for concern that detailed aspects of the assumption may not stand examination. The introduction of a deferral policy has to be set in context of other steps taken to reduce the risk of transmission of hepatitis, and the differing chronologies that emerged across Scotland. As discussed in Chapter 26, *Donor Selection – Higher Risk Donors*, collection of blood in penal institutions had been phased out by 1984. Edinburgh and South East Scotland BTS last collected blood from prisons in 1981; with the exception of Glasgow and south west Scotland, all other regions last collected in prisons in 1983; Glasgow and south west Scotland made their final (and much reduced) collection in 1984.<sup>227</sup> Though a small percentage of total collections while the practice of prison sessions continued, they carried a disproportionately high level of risk of transmission and, if the policy was valid, its implementation must have affected the prevalence of HCV infection in the donor population before the revised deferral policy came into effect.

**3.231** There were policy differences underlying the differing dates of phasing out of prison collections. There were similar policy differences relating to minimising the risk of transmission by donor selection and self-deferral. In Edinburgh and south east Scotland, Dr McClelland drafted a leaflet in 1983 promoting self-deferral.<sup>228</sup> It was tabled at a meeting of the SNBTS Coordinating Group on 24 May 1983.<sup>229</sup> At that meeting Dr Mitchell commented that he had introduced to the donor health questionnaire a question inviting those who were worried about AIDS to consult the doctor at the session. The Glasgow leaflet did not include a question on whether the donor had ever injected drugs, nor did a donor leaflet seemingly in use in England and Wales in 1983.<sup>230</sup> Dr Urbaniak, Director in the Aberdeen Centre, had decided after consideration not to do anything locally.<sup>231</sup> Dr McClelland's leaflet attracted adverse criticism from the Scottish Homosexual Rights Group.<sup>232</sup> Following constructive dialogue, a revised form of the leaflet was prepared. The

<sup>227</sup> Chapter 26, *Donor Selection – Higher Risk Donors*; paragraph 26.42, Table 26.6

<sup>228</sup> Chapter 28, *Donor Selection – AIDS*, paragraph 28.8

<sup>229</sup> *Ibid* paragraph 28.11

<sup>230</sup> The leaflet is [SGF.001.0397] and was enclosed with a letter dated 12 September 1983 by Dr Entwistle, Chairman of the Working Group on the Selection and Care of Donors, to Dr Brookes, Director of the Dundee and East BTS, who was the Scottish representative on the working party [SGF.001.0375]. Professor Leikola was examined on how donor sessions were conducted in Finland and did not think that the donor questionnaire in use in Finland in the late 1970s/early 1980s included a question on whether the donor had ever injected or used drugs. That changed in 1983 with the arrival of AIDS: Day 13, pages 20 and 73.

<sup>231</sup> Minutes of SNBTS co-ordinating group meeting on 24 May 1983 [SNB.003.7116] at 7120

<sup>232</sup> Chapter 28, *Donor Selection – AIDS*, paragraph 28.15



revised form was distributed on 15 June 1983.<sup>233</sup> The position in other regions remained as before. There was now a second significant, though relatively short-lived, difference in policy between Edinburgh and south east Scotland and the rest of the country that had the potential to affect the prevalence of infection in the donor population.

**3.232** A leaflet for UK-wide distribution was ready for use by 1 September 1983.<sup>234</sup> It seems likely that it was available in Glasgow and the west of Scotland thereafter.<sup>235</sup> However, the means of distribution and the terms of the leaflet continued to attract debate. The tortuous process of revision of the text, and of the steps to be taken for distribution, saw major developments in February, June, August and November of 1984.<sup>236</sup>

**3.233** On 9 February 1984 at a meeting on the infectious hazards of blood products at the National Institute for Biological Standards and Control (NIBSC), attended by Drs Cash and McClelland, it was reported that:

The policies adopted in Scotland to minimise the risk of transmission of infection were explained. The three main strategies were 1) avoidance of high risk communities (such as prisons, known homosexual areas, etc); 2) detection of clinical abnormalities by examination and careful questioning; 3) exclusion of the high risk donor, or his blood ....<sup>237</sup>

**3.234** Against this background the selection of a date, or period, when deferral policy had a significant impact on the risk of transmission of NANB hepatitis in Scotland is problematic, as is the rigour with which deferral may initially have been carried out. There was no uniformity of policy or practice between the two major transfusion regions. The cessation of prison donation sessions had already altered the distribution of risk by excluding one potentially major contributor to the total pattern of risk, but so recently that its impact on total risk cannot have been known.

**3.235** Dr Hay emphasised that it was difficult to know the extent to which donor self-exclusion reduced the number of donors presenting a risk of transmission of infection, because HIV testing began shortly after the self-exclusion programme started. He proceeded on the basis that HIV testing and donor self-exclusion taken together reduced the number of high-risk donors giving blood.<sup>238</sup> He reported:

It is difficult to quantify the effect of donor self-exclusion and HIV testing on the risk of non-A, non-B hepatitis because there were no reliable diagnostic criteria for non-A, non-B hepatitis in the early 1980s. The prevalence of chronic non-A, non-B hepatitis also varied geographically. The condition appears to have been commoner in the USA than in Northern Europe. Contemporary studies suggest that the prevalence of non-A, non-B hepatitis in Northern European blood donors was approximately 0.4–1.0% in the early 1980s. In contrast, Contreras reported a much lower rate of infectivity of 0.085% per donor unit amongst 387 UK patients transfused an average of 3 units of blood each in 1987 and tested using an hepatitis C antibody ELISA. This suggests an approximately tenfold reduction in the risk of post-transfusion hepatitis C, in

<sup>233</sup> Ibid paragraph 28.23

<sup>234</sup> Ibid paragraph 28.39

<sup>235</sup> Ibid paragraph 28.75

<sup>236</sup> Ibid paragraphs 28.52–28.57

<sup>237</sup> Draft minutes of meeting on the infectious hazards of blood products, 9 February 1984 [SNB.004.8628] at 8633 and 8634

<sup>238</sup> Dr Hay's report to the Inquiry on communication to patients about hepatitis 1974–1995 [PEN.018.1186] at 1191

the UK during the course of the 1980s, following the introduction of donor self-exclusion and HIV testing ...<sup>239</sup>

**3.236** He explained further in oral testimony. The risk groups for Hepatitis C and for HIV were similar and steps to exclude one virus would have an effect on attempts to exclude the other. While this would not make much difference to the risk from the concentrate derived from plasma in a large donor pool, the risk of transmission from single donor units such as cryoprecipitate or red cells was considerably reduced.<sup>240</sup>

**3.237** Other assumptions in the Goldberg/Schnier model included the yield of components per donation (1.25) which was a value provided by Dr Gillon and agreed by Dr McClelland.<sup>241</sup> The value was derived from data generated by the SNBTS look-back. SNBTS national statistics for the period 1981–82 to 1993–94 suggest that the yield of 1.25 was reasonably accurate. As calculated by the Inquiry, units placed at issue per donor,<sup>242</sup> including total cryoprecipitate, varied over the period but ranged between 1.18 and 1.31. The yield adopted was therefore an appropriate value for the purpose of estimating the number of recipients put at risk.

**3.238** Similarly, the assumption (number 6 in the Goldberg/Schnier list) that 56% of the donated blood was assumed to have been transfused,<sup>243</sup> with all units having the same probability of being transfused, appears to have been conservative when compared with SNBTS national statistics for the period 1981–82 to 1993–94. Dr Gillon re-examined this assumption at the request of the Inquiry and concluded that the Scottish percentage should be 66%.<sup>244</sup> That is still less than indicated by available SNBTS national statistics, but Dr Gillon's conclusion is accepted that the variation he found was not statistically significant, and it appears that little turns on this factor.

**3.239** Assumption 8 (a flat profile of the age distribution of recipients of blood transfusion justifying the application of up-to-date data over the whole period),<sup>245</sup> seems consistent with the assumption that the donor population, including IDUs, was homogeneous, but like that general assumption is questionable on the ground of lack of evidence. Return donors seem likely, as a matter of general impression, to have spanned a wider age range than new donors, including injecting drug users. The donor's age at first recruitment does not change, but increases so long as they returns to give blood. However, there are not enough hard data to enable comment on the extent of any differences.

**3.240** It is necessary to be cautious with even these assumptions. Dr Gillon observed that:

[T]he inherent unreliability of this set of assumptions, encapsulating as they do significant numbers of components which could not be traced, would make statistical calculations meaningless.<sup>246</sup>

<sup>239</sup> Ibid [PEN.018.1186] at 1192

<sup>240</sup> Dr Hay – Day 83, page 82

<sup>241</sup> Dr Gillon's response to further questions on statistics [PEN.019.1311] and Dr McClelland's response to further questions on statistics [PEN.019.1315]

<sup>242</sup> Units of blood available for transfusion

<sup>243</sup> Schnier and Goldberg, *Estimation of the number of individuals infected and alive as a consequence of blood transfusion in Scotland 1970–1991*, 1 March 2012 [PEN.019.0899] at 0901

<sup>244</sup> Dr Gillon's response to further questions on statistics [PEN.019.1311] at 1312

<sup>245</sup> Schnier and Goldberg, *Estimation of the number of individuals infected and alive as a consequence of blood transfusion in Scotland 1970–1991*, 1 March 2012 [PEN.019.0899] at 0901

<sup>246</sup> Dr Gillon's response to further questions on statistics [PEN.019.1311] at 1312

**3.241** It would be inappropriate to reject statistical exercises generally on that basis. On any view they make a valuable contribution to the overall picture and assist in arriving at an opinion. This observation underlines the need for caution. Having regard to the difficulties with the assumptions in all of the models discussed above, it would be inappropriate to accept the estimates made as conclusive of the extent of transmission of HCV by transfusion.

### General considerations

**3.242** On the evidence available, both expert approaches appear to have followed valid principles of statistical modelling, but each depended on the application of unverifiable and possibly erroneous assumptions, as they freely acknowledged. It is necessary to treat any estimates of prevalence with considerable caution. While it is inevitable that opinions reflecting calculation have to be expressed numerically, it is particularly necessary to avoid being misled by spurious mathematical precision.

**3.243** At the end of the day, all that can be done is to set out a range of estimates which vary depending on the different assumptions made. Professor Goldberg's calculation using a flat rate projection of 0.09% prevalence was worthwhile as indicating a possible maximum number of 6784. It demonstrated the response of his model to the revised assumption, but it was not an assumption for which he offered support. On that basis, the estimate produced by Professor Goldberg's statistical model is that a median number of 1533 patients in Scotland may have been infected with Hepatitis C as a result of blood transfusion between 1970 and the introduction of donor screening in September 1991. Dr Soldan's figure remains 3498 for the period 1980–91.

**3.244** Of the two approaches to the problem in Scotland, Professor Goldberg's approach has the advantage of using more relevant hard data, but remains heavily dependent on assumptions which cannot be objectively verified. Dr Soldan uses less local data, and again her assumptions cannot be verified objectively. Since Dr Soldan was not available as a witness, it was not possible to explore the qualifications expressed in her report.<sup>247</sup> The estimate of 2524 derived from the DoH report falls between the two. As already noted, the methodology adopted in arriving at the figures in the report is not disclosed.

**3.245** So far as Term of Reference 4 is concerned, it is clear (a) that recorded data cannot provide an accurate measurement of the extent of HCV infection in Scotland over the reference period, or of the risk of post-transfusion transmission; and (b) that such statistical models as have been developed to date remain, to a greater or lesser extent, of questionable validity as indicators of total exposure to risk and of transmission. The fundamental problem is that hard data are lacking and assumptions have to substitute for measurement over too wide a range of factors.

### Skipton and other data

**3.246** Professor Goldberg thought the Skipton data to be 'insufficiently robust'<sup>248</sup> and the Inquiry has identified one example in which it is unreliable. However, in the context of so much general uncertainty about other approaches, it has to be considered whether it is for present purposes of assistance in developing an estimate of numbers.

---

<sup>247</sup> Dr Soldan, *Estimated number of individuals infected by blood transfusion in Scotland* [SGH.005.7203]

<sup>248</sup> Letter from Professor Goldberg in response to further queries on statistics from Professor Oliver James [PEN.019.0922]

**3.247** Of the total number of stage 1 payments made by the fund (670) 10 were paid to the estates of people who had died before 2003. Six stage 2 payments were made to a further six estates.<sup>249</sup> Since the 670 included haemophilia patients co-infected with HIV, who had a relatively high mortality, it can reasonably be inferred that there were very few if any payments made to non-bleeding disorder beneficiaries who had died before 2003, and that the number is immaterial for estimating purposes. In any event, on this approach, to assume that all of the additional individuals are transfusion-associated cases is the more conservative approach. Since 2003, there have been deaths among those receiving stage 2 payments: of the 162 stage 2 payments, 37 were known to have died and there were up to 54 possible deaths among the total recipients, with 71 continuing to receive regular payments. The fate of the 54 is unknown, but Mr Fish (the administrator of the Skipton Fund) assumes that many will have died, on the basis that they have ceased to come forward to claim their regular payments. There are no survivorship data for those receiving stage 1 payments only.

**3.248** The number of post-transfusion HCV-infected individuals, estimated on the basis of Skipton data to 1 March 2012 at 439 (paragraph 3.142 above), must have included representatives of individuals who had died. Of the total qualifying recipients (670) at least 24 infected individuals had died. If all of those were assumed to be post-transfusion recipients (the most conservative assumption) there would have been 415 individuals in that group alive in 2012. This number can be contrasted with the finding in the 2011 Goldberg/Schnier model of an estimated median 222 HCV RNA-positive post-transfusion recipients (paragraph 3.192).

**3.249** The Scottish look-back found that 536 (60%) of the 880 recipients of infected components had died by 1995. Since a balance of recipients had not been identified, and Skipton's reference date of 2003 was later, by which time more patients would have died, it can conservatively be estimated from the Skipton non-haemophiliac recipient numbers and using similar mortality data, that a minimum of 1100 patients would have been infected. That is still considerably lower than the DoH figure and the statistically derived figures.

**3.250** The look-back exercise, as devised and implemented, was itself incapable of tracing more recipients than could be associated with the infected donations received after the introduction of screening. A more widely based approach is required to ascertain whether there was support for an estimate based on the DoH exercise.

### Look-back study in Denmark

**3.251** A Danish post-transfusion look-back exercise in 2009 by Just and others, traced the outcome for 960 patients (1018 less 58 untraced after 1996) who prior to 1991 had been exposed to donations from 150 HCV-positive donors.<sup>250</sup> By 1996, 730 had died. Of the 288 alive in 1996, 58 had to be excluded from the study because no personal identification had been supplied and they were untraced. Of the remaining 230, it was found that the pattern of infection was as set out in Table 3.15.

<sup>249</sup> Letter from Nick Fish, Scheme Administrator dated 1 March 2012 [PEN.019.0104]

<sup>250</sup> Just *et al*, 'Long-term follow-up among Danish transfusion recipients identified in the national hepatitis C lookback', *Transfusion*, 2012; 52:582–8 [PEN.018.0507]

**Table 3.15: Danish look-back data**

<b>HCV exposure in 230 Danish patients</b>			
Groups			
Infected individuals: <i>of whom:</i> Patients with cirrhosis Patients who had died	124	23	51
Uninfected individuals: <i>of whom:</i> Patients with cirrhosis Patients who had died	43	3	10
Unknown infection status: <i>of whom:</i> Patients with cirrhosis Patients who had died	63	3	46
Total	230	29	107

**3.252** The number of infected individuals alive in 2009 was 121 (two who left the country during follow-up were excluded) which represented 12.6% of the original cohort of 960 known to have been exposed to blood from HCV-positive donors prior to 1991.

**3.253** If that percentage were applied to the Skipton number of 439, it would indicate a starting cohort of 3484. However, the reference periods are not consistent. Skipton counted patients identified after 2003. Between 2003 and 2009 some of the Danish cohort would have died. There was an observed mortality rate of 4.91%. The deceased members of the cohort over the interval have to be added back to obtain a comparable number at the end of 2003. Assuming five years decrement at 4.91%, the comparable figure for Scotland is 2709, based on the 2003 Skipton numbers and the extrapolated Danish survival data.

**3.254** There are, as always, issues over the reliability of the approach. In relation to the haemophilia population, Danish experience of HTLV-III exposure was compared with experience in Glasgow in a study by Melbye, Froebel and others that is discussed in Chapter 10, *Knowledge of the Geographical Spread and Prevalence of HIV/AIDS 2*.<sup>251</sup> In that context, there was a clear distinction in therapy regimes that distinguished the two populations of Denmark and Glasgow. But no other distinctions were noted. Denmark had a well-developed health service and the Danish look-back, which took place at a time after the introduction of screening was very similar to the Scottish exercise. The most significant difference was that the Danish Health Information systems were apparently better organised than those in the UK. Comparison with Denmark provides a further figure, based on a comparable population, that may be used as a control: 2700 would be the number of persons assumed to have been infected in Scotland on this basis, and that is not dissimilar to the results of the DoH exercise (2524 individuals).

<sup>251</sup> See paragraphs 10.7–10.10. Melbye *et al*, 'HTLV-III seropositivity in European haemophiliacs exposed to Factor VIII concentrate imported from the USA', *The Lancet*, December 22–29 1984 [LIT.001.1702]

### *Conclusions on transfusion-transmitted HCV infection*

**3.255** None of the exercises described is capable of producing a firm and reliable estimate of the likely number of NHS patients, transfused in Scotland, who became chronically infected with HCV as a result of receiving infected blood or blood components.

**3.256** Excluding the extremes, a wide range of values remain as indications of the possible incidence of infection. Only a rough and speculative estimate is possible, and the balance suggests a number of around 2500. From Skipton Fund data, extrapolated to 2012, perhaps about 400 of these individuals remained alive in 2012, the last year for which an estimate can be made using available data. A further unknown number of still 'silently' infected individuals probably exists, 23 years after screening began. This number cannot be ascertained reliably. Any attempt to estimate it would be affected by the fundamental lack of hard data reflected in this chapter as a whole. It might be speculated that the number would not be large. But that would involve a dangerous step into unknown territory.

**3.257** Given that throughout most of the earlier years of the reference period it would not have been possible to have measured directly those contracting Hepatitis C from blood transfusion, it would never have been possible through contemporaneous records to arrive at a precise and final figure for those infected, and in particular for those infected and still alive. Estimates supported by statistical analysis would inevitably have been required. Now, even with the best support from expert epidemiologists, it is impossible to use the data available to provide a very satisfactory and reliable number.

**3.258** The work carried out by and for the Inquiry suggests that further epidemiological investigation would not produce a more reliable estimate. Nothing can be done now to improve the contemporaneous records, or to provide hard data indicating objectively the scale of the problem. The reporting system, such as it was, was never designed and operated so as to be likely to be effective, even if it was enforced when means of identifying infected individuals became available. If the Scottish Government is persuaded that, for health policy and strategy, or budgeting or other reasons, it is necessary to develop a more accurate figure, it may be that further research and further expert opinion might eventually converge. That cannot, however, be recommended by this Inquiry given the extensive investigations already carried out.

### *Hepatitis C as a cause of death among transfused patients*

**3.259** Dr Gillon gave evidence that of the 133 patients identified by the HCV look-back exercise who contracted Hepatitis C as a result of transfusion, 49 patients were known to be alive as at January 2011.<sup>252</sup> Information on the recorded causes of death was available for 53 out of the 54 patients known to have died.<sup>253</sup> Dr Gillon's interpretation of data was that Hepatitis C was the cause of death or had made a material contribution to the death of eight of the 53 patients for whom causes of death are known.<sup>254</sup>

**3.260** Professor Goldberg provided evidence that of the 304 individuals recorded by HPS as having contracted Hepatitis C as a result of blood transfusion, 85 individuals were known to be dead as at December 2009 and 219 individuals were not known to be dead

<sup>252</sup> Dr Gillon's statement on statistics relating to transfusion-transmitted HCV [PEN.001.0043] at 0047, question 4; Table 8 above

<sup>253</sup> Appendix 3 to Dr Gillon's statement on statistics relating to transfusion-transmitted HCV [PEN.019.1455]

<sup>254</sup> Dr Gillon's statement on statistics relating to transfusion-transmitted HCV, [PEN.001.0043] at 0047, question 5 and Day 6, pages 54–58

as at that date.<sup>255</sup> Of the 85 individuals known to have died, 18 had a primary liver-related cause of death recorded on their death certificate, 13 had a secondary liver-related cause of death recorded (including viral hepatitis, liver cancer, alcoholic and non-alcoholic liver disease) and 54 had other causes of death recorded.<sup>256</sup> Professor Goldberg was asked whether a death certificate was a reliable guide to whether an individual had died from Hepatitis C; he replied:

It's not a reliable guide and that's one of the reasons why we use the Hepatitis C diagnosis database in association with the death register, to identify individuals with Hepatitis C who have died, rather than going straight to the death certification register and just relying on the source of that information. It just is completely unreliable in that respect.<sup>257</sup>

**3.261** While the above figures are of some assistance, they require to be treated with caution given that they are based largely on the information contained in each deceased's death certificate which, in turn, depends on the thoroughness and accuracy of the investigation, recording and reporting of each death.

**3.262** The mortality figures spoken to in evidence, both for patients with post-transfusion Hepatitis C and for haemophiliac patients, correlate reasonably well with well-modelled studies from outwith the United Kingdom.<sup>258</sup>

### **Patients with bleeding disorders infected with HIV as a result of treatment with blood products**

**3.263.** The third group of patients to be considered is referred to in paragraph 3.2, item iii, and consists of patients with bleeding disorders, primarily haemophilia, who were exposed to infection with HIV through their treatment with blood products.

**3.264** The Preliminary Report set out the information available to the Inquiry prior to the oral hearings. As with other data, the information has been significantly corrected and updated at and after those hearings.

### ***Evidence of Dr Hay***

**3.265** When Dr Hay first gave oral evidence to the Inquiry on 18 March 2011, it was already understood that the data provided earlier were inaccurate. Dr Hay noted that in retrospect there were not many people thought to have been infected with HIV in 1980: the majority were infected from 1981 through to 1983. The details in the Preliminary Report referred to the date of reporting when a sample had tested positive, not to the date of infection.<sup>259</sup> As a result, the tabulated data were skewed to later dates than the dates of actual transmission, and gave an inaccurate impression of emerging risk.

<sup>255</sup> Professor Goldberg's statement on statistics relating to transfusion-transmitted HCV [PEN.013.0014], question 4; and Penrose HCV Transfusion Stats [PEN.013.0024]

<sup>256</sup> Professor Goldberg's statement on statistics relating to transfusion-transmitted HCV [PEN.013.0014] at 0015, question 5; and Penrose HCV Transfusion Stats [PEN.013.0024]

<sup>257</sup> Professor Goldberg – Day 6, page 113

<sup>258</sup> Seeff *et al*, 'Long-term mortality and morbidity of transfusion-associated non-A, non-B, and Type C hepatitis: a National Heart, Lung and Blood Institute collaborative study', *Hepatology*, 2001; 33:2 [LIT.001.3951]; Thein *et al*, 'Prognosis of Hepatitis C virus-infected Canadian post transfusion compensation claimant cohort', *Viral hepatitis*, 2009; 16:802–813 [LIT.001.4184]; Just *et al*, 'Long-term follow-up among Danish transfusion recipients identified in the national hepatitis C lookback', *Transfusion*, 2012; 52:582–8 [PEN.018.0507]

<sup>259</sup> Dr Hay – Day 8, page 37

**3.266** Further, at that stage Dr Hay's data did not necessarily reflect the numbers of patients who were infected with HIV in Scotland: they showed at best how many patients managed in Scotland were infected with the virus. In a number of cases so managed, HIV infection was first reported by a centre outside Scotland.<sup>260</sup> There were 1382 registered UK patients who were known at May 2010 to have been infected with HIV. Of those, 72 were registered at Scottish centres. Some of the patients registered at English centres had received treatment in Scotland and might have been infected there.<sup>261</sup> Where a patient was managed at more than one centre, identification of the centre at which he was infected was problematic and could involve duplication.<sup>262</sup> There was epidemiological evidence that heavy users of Factor VIII were more likely to contract HIV infection than those using smaller amounts, but that did not assist in determining total numbers likely to have been infected.<sup>263</sup>

**3.267** Before the oral hearings, UKHCDO data had been examined by the organisation and by the Scottish Directors in an attempt to determine how many of the HIV-infected patients registered as managed in Scotland may have been infected at Scottish centres. When Dr Hay first gave evidence, the attempt to reconcile the data from all sources had not been concluded. He thought that without going through each individual's records, it might be impossible to determine exactly where they were when they contracted HIV, and even if that were done, if there were no archived samples it might never be known for certain.<sup>264</sup> At this stage (in 2010) the Scottish Haemophilia Directors were working on UKHCDO data that had yet to be corrected. There was no satisfactory reconciliation.

**3.268** In an effort to resolve the uncertainties and discrepancies in these data, the UKHCDO, led by Dr Hay, and the Scottish Haemophilia Directors, notably Dr Tait (Glasgow) and Professor Ludlam (Edinburgh), conducted a series of data checking and data reconciliation exercises for HIV in parallel with those already described for HCV.

#### *Reconciliation of UKHCDO and Scottish data*

**3.269** It was necessary for there to be a review of all the data available to try to establish reliable numbers. The Directors of the Scottish Haemophilia centres and the UKHCDO examined the data recorded for each patient on the UKHCDO list, to try to determine whether the patient was likely to have become infected with HIV as a result of treatment in Scotland and, if so, at which Scottish centre.

**3.270** A number of issues arose in the comprehensive review that followed of all data available to Scottish Haemophilia centres. There remained the basic problem of double counting of patients. Each centre, operating in isolation, had returned data to the UKHCDO database at Oxford (the National Haemophilia Database) for each patient treated, whether or not the patient was otherwise registered at the centre. For example, a patient registered in Edinburgh who visited Inverness and there received necessary treatment, would be recorded as a separate patient receiving treatment in each centre.<sup>265</sup> For earlier periods, data were returned manually and later entered into the national computer system. It appeared that there had been some transcription errors and other misunderstandings.

---

<sup>260</sup> Ibid page 26

<sup>261</sup> UKHCDO data reproduced in the Preliminary Report at Appendix 1, introduction to Table 3 [PEN.013.1433] at 1458.

<sup>262</sup> Dr Hay – Day 8, page 27

<sup>263</sup> Ibid page 32

<sup>264</sup> Ibid page 26

<sup>265</sup> Professor Ludlam – Day 14, pages 12–13



The Scottish Haemophilia Directors each prepared a methodology to attempt resolution of the problems with the data.<sup>266</sup>

**3.271** The starting point was the tabulated patient-specific data provided by the UKHCDO relating to patients treated in Scotland who were known to have been HIV positive. The data included the dates of the last negative HIV and first positive HIV tests, and the products with which the patient had been treated year by year, including treatment outwith Scotland. In some cases a cause of death was recorded.

**3.272** The UKHCDO data were reviewed at each centre, and some patients were removed from the lists on the basis that they had been HIV positive when they first arrived at a Scottish centre.<sup>267</sup> Professor Ludlam described in some detail the procedure in Edinburgh and south east Scotland. In the Edinburgh Centre alone, identification of patients known to have been positive on first attendance at the centre, served to remove six patients from the original 29 reported by the UKHCDO. Discussions then took place to exclude duplication as between Scottish centres, and in the case of patients treated at more than one centre, to agree at which centre it was most likely that the patient contracted HIV. In cases where there was little or no information available as to the likely date of infection, a judgement required to be made as to the centre at which the patient was likely to have been infected. On review of local records it was found that UKHCDO data included all patients known to the individual centres. Local data were added where available.

**3.273** Professor Ludlam thought it unlikely that there were haemophilia patients in treatment with concentrates who were not registered at a centre. Patients who received treatment outwith a haemophilia centre for a bleeding problem were quickly referred to such a centre, following local laboratory tests.<sup>268</sup> There was a possibility that patients listed by the UKHCDO as English or Welsh patients might have been infected in Scotland if they had been treated in Scotland before moving to England or Wales in the early 1980s. But no such patient was known, and differences in treatment regimes would in any event make it difficult to form a view.<sup>269</sup>

**3.274** After undertaking that exercise the Scottish Haemophilia Directors gave the following evidence as to the number of haemophilia patients infected at their respective centres.

### Royal Infirmary of Edinburgh

**3.275** Professor Ludlam stated that 23 haemophilia patients were infected with HIV as a result of treatment at the Edinburgh centre.<sup>270</sup> All 23 patients had severe Haemophilia A.<sup>271</sup> Eighteen of the 23 patients had received treatment with material from a single batch of SNBTS product (PFC Factor VIII) during the relevant period, and comprised the 'Edinburgh Cohort'.<sup>272</sup> Five patients had received treatment with other SNBTS and commercial products.<sup>273</sup>

<sup>266</sup> For example, Professor Ludlam's statement on the methodology for collation of HIV patients in Edinburgh [PEN.012.0153]

<sup>267</sup> Professor Ludlam – Day 14, pages 34–35

<sup>268</sup> Ibid pages 13–14

<sup>269</sup> Ibid pages 14–15

<sup>270</sup> Professor Ludlam's statement on the methodology for collation of HIV patients in Edinburgh, dated 25 March 2011 [PEN.012.0153], at 0154. See also Dr Tait – Day 14, pages 68–69.

<sup>271</sup> Edinburgh spreadsheet [PEN.019.1461]

<sup>272</sup> Professor Ludlam, Day 14, pages 19–20. The 18 patients forming the Edinburgh Cohort are patients 1–4, 6–15, 17, 18, 20 and 23 on the Edinburgh spreadsheet [PEN.019.1461]. Patients 5, 16, 19, 21 and 22 do not form part of the Edinburgh Cohort.

<sup>273</sup> The commercial products used were all Factor VIII concentrates, namely Cutter 'Koate', Armour 'Factorate' and Immuno 'Kryobulin'.

**3.276** The adjusted list of patients thought to have been infected in Edinburgh was submitted to HPS for any additional information from their register of HIV-infected individuals, including information from death certificates.

**3.277** Routine blood samples from the 1970s were regularly stored by Edinburgh virologists as part of a study of Hepatitis B infection and its transmission in haemophilia.<sup>274</sup> It was therefore possible in many cases to decide retrospectively when the patient had seroconverted to HIV. It was this information that identified as new patients those who were already seropositive when they had arrived in Scotland. This procedure was adopted at all Scottish centres.

**3.278** It was originally thought that all members of the Edinburgh Cohort were infected between March and May 1984 after exposure to a single common batch of Scottish Factor VIII concentrate. Following phylogenetic analysis, there are now thought to have been at least two batches of contaminated Factor VIII responsible for infections in the group. It appears that two or three HIV-infected donors, who were not intravenous drug users or heterosexual males, contributed to the plasma pools.<sup>275</sup>

**3.279** One individual (E22 in the table below) is known to have been infected by Armour Factorate between 16 March and 1 December 1981 (the dates of the last sample testing negative and the first testing positive). One (E16) had samples that tested positive in 1983. One (E19) tested positive in November 1986, having tested negative in January 1985. Two (E17 and E20) were under 16 at the time of their first positive sample.<sup>276</sup> The overall picture is set out in Table 3.16.

---

<sup>274</sup> Professor Ludlam – Day 14, pages 17–18

<sup>275</sup> Holmes *et al*, 'The Molecular Epidemiology of Human Immunodeficiency Virus Type 1 in Edinburgh', *The Journal of Infectious Diseases*, 1995;171: 45–53 [PEN.012.1679]

<sup>276</sup> Professor Ludlam – Day 14, page 23

**Table 3.16: Royal Infirmary of Edinburgh HIV infections**

	Last negative	First positive	Treatment	Year assigned	Source
E1	16.08.1984	19.11.1984	PFC	1984	PFC
E2	05.04.1984	06.10.1984	PFC	1984	PFC
E3	13.09.1983	13.06.1984	PFC	1984	PFC
E4	13.09.1984	30.10.1984	PFC	1984	PFC
E5	21.06.1982	18.10.1984	PFC	1983–84	PFC
E6	26.10.1983	08.05.1984	PFC	1984	PFC
E7	18.01.1984	26.06.1984	PFC	1984	PFC
E8	29.05.1984	22.11.1984	PFC	1984	PFC
E9	16.04.1984	20.07.1984	PFC	1984	PFC
E10	27.03.1984	29.05.1984	PFC	1984	PFC
E11	02.03.1983	22.08.1984	PFC	1984	PFC
E12	01.02.1984	29.05.1984	PFC	1984	PFC
E13	09.04.1984	29.05.1984	PFC	1984	PFC
E14	26.06.1984	10.08.1984	PFC	1984	PFC
E15	14.12.1983	17.04.1984	PFC	1984	PFC
E16	05.08.1982	15.09.1983	PFC	1983	PFC
E17	29.03.1984	24.05.1984	PFC	1984	PFC
E18	28.11.1983	20.06.1984	PFC	1984	PFC
E19	01.01.1985	17.11.1986	PFC	1985	PFC
E20	17.04.1984	23.04.1984	Mixed	1984	PFC
E21	15.05.1984	11.10.1984	PFC	1984	PFC
E22	16.03.1981	01.12.1981	Mixed	1981	Armour
E23	06.08.1984	2.10.1984	PFC	1984	PFC

**3.280** Four of the 23 patients infected with HIV at the Edinburgh centre were still alive at the time of the oral hearings in 2011 and 19 had died. Of the 19 patients who had died, 14 had either died of HIV/AIDS or HIV/AIDS was a factor contributing to their death.<sup>277</sup> While that information was compiled by Professor Ludlam from information provided by HPS (based on the patient's death certificate) and the UKHCDO database, the latter contained 'very little information' as to the cause of death and more assistance was derived from the information in the death certificates.<sup>278</sup> Professor Ludlam explained that of the five patients whose deaths did not appear to have been caused or aggravated by HIV/AIDS, three deaths were due to a major catastrophic haemorrhage and that one patient clearly

<sup>277</sup> Professor Ludlam – Day 14, pages 22–23, 27–30 and 46–48. Professor Ludlam's statement on the methodology for collation of HIV patients in Edinburgh, dated 25 March 2011 [PEN.012.0153] at 0154

<sup>278</sup> Professor Ludlam – Day 14, pages 44–45

had a condition which was not related to HIV/AIDS at all.<sup>279</sup> Professor Ludlam had the benefit of having been the patients' treating clinician and was able to make an informed judgement on each patient's likely cause of death, rather than having to rely solely on the information recorded in each death certificate.<sup>280</sup>

### Glasgow Royal Infirmary

**3.281** Dr Campbell Tait, Director of the Haemophilia Centre at Glasgow Royal Infirmary (GRI), gave evidence about the results of the exercise in Glasgow.<sup>281</sup> In the final count, 12 patients contracted HIV infection while attending the GRI Haemophilia Centre.<sup>282</sup> Reconciled data are set out in Table 3.17.

**Table 3.17: Glasgow Royal Infirmary HIV infections**<sup>283</sup>

	Last negative	First positive	Treatment	Year assigned	Source
G1	01.01.1982	15.09.1986	Mixed	1982–1986	Imported/PFC
G2	Unknown	15.05.1984	Mixed	?–1984	PFC
G3	15.12.1984	15.11.1985	Mixed	1985	Imported
G4	15.05.1982	15.01.1984	Mixed	1982–1983	Imported/PFC
G5	15.07.1982	15.12.1983	Mixed	1982–1983	PFC
G6	15.05.1981	15.09.1982	Mixed	1981–1982	Imported/PFC
G7	Unknown	15.11.1982	PFC	?–1982	PFC
G8	01.01.1982	15.02.1984	Mixed	1982–1984	PFC
G9	15.10.1984	15.10.1985	Mixed	1984–1985	PFC
G10	Unknown	15.11.1985	DEFIX	?–1985	PFC
G11	15.10.1985	15.07.1986	DEFIX	1985–1986	PFC
G12	Unknown	15.04.1981	Mixed	?–1981	Imported/PFC

**3.282** Ten of the 12 patients had Haemophilia A (eight severe and two moderate), and two had Haemophilia B (patients G10 and G11). Most of the patients received both commercial products and SNBTS products and it is not always possible to be confident of a robust allocation of imported or PFC products as being the cause of HIV infection. The cause of infection in three cases (G3, G6 and G12) appears clearly to have been the use of imported Factor VIII. Three patients received only PFC Factor VIII between their last negative and first positive HIV test and it appears that these three patients were very probably infected by an SNBTS product.<sup>284</sup> Retrospective testing of stored data, where available, showed that of the 12 patients infected with HIV, one patient seroconverted in 1981–82, two in 1982–83, one between 1982 and 1984, one between 1982–1986, one in 1984–85, one in 1985–86, one during 1985 and, for four patients whose date of last

<sup>279</sup> Ibid pages 46–47

<sup>280</sup> Ibid pages 48–49

<sup>281</sup> Dr Tait – Day 14, page 58 onwards

<sup>282</sup> GRI spreadsheet [PEN.019.1456]

<sup>283</sup> Ibid [PEN.019.1456]

<sup>284</sup> GRI spreadsheet [PEN.019.1456] patients 5, 8 and 9. Dr Tait, Day 14, page 63. That was also the opinion of Dr Bruce Cuthbertson on behalf of the SNBTS: Response by Dr Cuthbertson dated 5 June 2011 [PEN.012.1633]. Dr Cuthbertson also considered it likely that patient 10 was infected with HIV from an SNBTS product.

negative HIV test is not known, the first HIV positive tests were, respectively, April 1981, November 1982, May 1984 and November 1985.<sup>285</sup> Ten of the 12 patients infected with HIV were dead by 2011, five from an HIV/AIDS-related cause, one possibly from an HIV/AIDS-related cause, two patients' cause of death appears to have been liver cirrhosis and one patient's death was probably the result of a haemorrhage.<sup>286</sup> Dr Tait's view on the cause of death was based solely on the death certificate codes provided by HPS for each patient.<sup>287</sup> Dr Tait started at the GRI in 1999 and, unlike Professor Ludlam in relation to the Edinburgh patients, had probably not met any of the patients who had died.

**3.283** It is highly likely that the trend of infection from the use of PFC Factor VIII in the GRI was similar to the trend in Edinburgh, namely that these infections were later in time than infections from commercial product. On the evidence available to the Inquiry, heat treatment of Factor VIII from December 1984 eliminated transmission of HIV by SNBTS factor concentrates processed after that date. The distribution of the infections over the period cannot be more precisely estimated.

### Royal Hospital for Sick Children, Yorkhill

**3.284** Dr Elizabeth Chalmers, Director of the Haemophilia Centre at the Royal Hospital for Sick Children (RHSC), Yorkhill, Glasgow, provided evidence that 21 children were infected with HIV as a result of their treatment at RHSC.<sup>288</sup> All 21 children had Haemophilia A (19 had severe haemophilia and two had moderate haemophilia). Imported Factor VIII concentrates were used extensively at the RHSC until 1982,<sup>289</sup> and infections have been identified at earlier periods than elsewhere.

**3.285** All 21 children received both SNBTS product (PFC Factor VIII and cryoprecipitate) and commercial product, in particular 'Factorate' produced by Armour. For 12 of the 21 children, the dates of the last negative and first positive HIV tests are known. Two of the 12 children seroconverted between January 1980 and January 1981, one child seroconverted in 1981, three children seroconverted in 1981–82, four children seroconverted in 1982–83, one child seroconverted between 1981–83 and one child seroconverted between 1982–84.<sup>290</sup> For nine of the 21 children, the date of the last negative test for HIV is not known. The date of the first sample from these nine children to test positive for HIV ranged from September 1982 to May 1985.

**3.286** It appears likely that about five of these 21 children were infected before the first cases of AIDS in haemophilia patients were described in the USA, and that up to 16 were infected before the first case of AIDS in a haemophilia patient was described in the UK.

**3.287** The 21 children were infected with HIV relatively early in the HIV crisis, probably as a result of the widespread use by the RHSC of the commercial product 'Factorate'. Eight of the 21 children infected with HIV have died. Of those eight, five deaths were due to HIV/AIDS, two deaths do not appear to have been due to HIV/AIDS and the cause of one death is unknown.

<sup>285</sup> GRI spreadsheet [PEN.019.1456]

<sup>286</sup> GRI Spreadsheet [PEN.019.1456] and Dr Tait – Day 14, pages 101–103

<sup>287</sup> Dr Tait – Day 14, page 101

<sup>288</sup> Dr Chalmers' statement on the methodology for collation of HIV patients in Glasgow (RHSC), dated 28 March 2011 [PEN.012.0155] and RHSC spreadsheet [PEN.019.1457]

<sup>289</sup> Chapter 21, *Haemophilia Therapy – Use of Blood Products*, paragraph 21.292, figure 9

<sup>290</sup> RHSC spreadsheet [PEN.019.1457]

**3.288** The full data available for Yorkhill is as set out in Table 3.18.

**Table 3.18: RHSC, Yorkhill HIV infections**

	Last negative sample	First positive	Treatment	Year assigned	Source
Y1	Unknown	05.04.1985	Mixed	?–1985	Imported/PFC
Y2	01.01.1980	01.01.1981	Mixed	1980	Imported
Y3	15.04.1981	15.05.1982	Armour	1981–1982	Imported
Y4	Unknown	15.02.1983	Mixed	1982–1983	Imported
Y5	15.06.1981	15.10.1981	Armour	1981	Imported
Y6	Unknown	15.12.1982	Armour	1981–1982	Imported
Y7	Unknown	15.05.1985	Mixed	?	Imported/PFC
Y8	Unknown	15.02.1983	Armour	?–1983	Imported
Y9	29.01.1982	10.03.1983	Mixed	1982–1983	Imported
Y10	Unknown	15.01.1985	Mixed	?–1984	Imported/PFC
Y11	01.01.1981	19.03.1982	Armour	1981–1982	Imported
Y12	Unknown	01.01.1985	Armour	?–1984	Imported
Y13	15.01.1980	01.01.1981	Armour	1980	Imported
Y14	Unknown	29.11.1982	Mixed	?–1982	Imported
Y15	21.05.1982	08.08.1984	PFC	1982–1984	PFC
Y16	08.04.1981	11.03.1983	Mixed	1981–1983	Imported/PFC
Y17	Unknown	01.09.1982	Armour	?–1982	Imported
Y18	24.02.1982	06.04.1983	Mixed	1982–1983	Imported/PFC
Y19	17.11.1982	06.04.1983	Mixed	1982–1983	Imported/PFC
Y20	15.05.1981	15.11.1982	Mixed	1981–1982	Imported
Y21	01.01.1982	01.01.1983	Mixed	1982	Imported

### Aberdeen Royal Infirmary, Foresterhill

**3.289** Dr Henry Watson, Director of the Aberdeen Haemophilia Centre, provided written evidence that three patients were considered to have acquired HIV as a result of treatment at Aberdeen on the basis that these patients had been treated only at the Aberdeen centre or had received minimal treatment elsewhere.<sup>291</sup> All three patients had Haemophilia A (two with severe haemophilia and one with moderate haemophilia).<sup>292</sup> One patient had been treated only with SNBTS product (PFC Factor VIII and cryoprecipitate) during the relevant period.<sup>293</sup> This patient's last negative test for HIV was 14 July 1983 and he first tested positive for HIV on 18 December 1984.<sup>294</sup> One patient received commercial product

<sup>291</sup> Dr Watson's statement on the methodology for provision of data on HIV infection from Aberdeen haemophilia centre, dated 28 March 2011 [PEN.012.0156]

<sup>292</sup> Aberdeen spreadsheet [PEN.019.1471]. The three patients who were infected with HIV at Aberdeen are patients 1, 2 and 3 on the spreadsheet. See the observations on the spreadsheet by Senior Counsel to the Inquiry, Day 14, pages 2–9.

<sup>293</sup> Aberdeen spreadsheet [PEN.019.1471], patient 3

<sup>294</sup> Report dated 6 April 2011 from Dr Cuthbertson to the Inquiry [PEN.012.1644]

in small amounts in 1978 and 1979 (Baxter 'Hemofil') but otherwise received treatment only with SNBTS product (PFC FVIII and cryoprecipitate).<sup>295</sup> This patient's last negative test for HIV is not known and the patient first tested positive for HIV in January 1985. One patient regularly received commercial product and from time to time received PFC product.<sup>296</sup> Again, this patient's last negative test for HIV is not known and the patient first tested positive for HIV on 1 January 1985. Two of these patients were known to have died. If these patients were infected by Scottish products (which was clearly the position in the first and third cases), all had PFC Factor VIII in 1983 and 1984. Patient A3 is likely to have been infected by the batch implicated in the infection of the Edinburgh Cohort.<sup>297</sup>

### Ninewells Hospital, Dundee

**3.290** Dr Ron Kerr, Director of the Dundee Haemophilia Centre, advised that no haemophilia patients were considered to have been infected with HIV as a result of treatment at Dundee.<sup>298</sup>

### Raigmore Hospital, Inverness

**3.291** Dr Christopher Lush, Director of the Inverness Haemophilia Centre, advised that no haemophilia patients were considered to have been infected with HIV as a result of treatment at Inverness.<sup>299</sup>

### *Results of Scottish Haemophilia Centre Directors' review of UKHCDO data*

**3.292** According to the Directors' evidence, the revised total number of haemophilia patients who contracted HIV while receiving treatment and care at Scottish centres was therefore 59.

**Table 3.19: Total HIV infections**

	Total	Dead	AIDS deaths*	Alive
Royal Infirmary of Edinburgh	23	19	14	4
Glasgow Royal Infirmary	12	10	6	2
Glasgow Yorkhill Hospital	21	8	5	13
Aberdeen Royal Infirmary	3	2	1	1
Total	59	39	26	20

\*This column lists deaths attributable or possibly attributable to AIDS

### *UKHCDO updated report*

**3.293** Following the oral hearings, the UKHCDO undertook further work on its data and provided an updated statistics report.<sup>300</sup> That report listed 73 patients with bleeding disorders first reported to the UKHCDO by Scottish haemophilia centres as testing positive for HIV.<sup>301</sup> The report noted:

<sup>295</sup> Aberdeen spreadsheet [PEN.019.1471], patient 1

<sup>296</sup> Aberdeen spreadsheet [PEN.019.1471], patient 2. This patient received PFC FVIII in 1977, 1978 and 1983 and received Baxter FEIBA between 1979–1983 and again in 1985 (the patient also received Speywood Porcine in 1983, which product is made from pig blood and is not capable of transmitting HIV).

<sup>297</sup> Dr Ludlam – Day 35, page 89; Dr Perry – Day 38, pages 41, 44 and 49 and Dr Cuthbertson – Day 46, page 86.

<sup>298</sup> Letter from Dr Kerr to Tracey Turnbull, dated 1 February 2010 [PEN.001.0234]

<sup>299</sup> Letter from Dr Lush to Tracey Turnbull, dated 31 January 2011 [PEN.001.0235]

<sup>300</sup> UKHCDO report *National Haemophilia Database: Bleeding disorder statistics for the Penrose Inquiry*, 2012 [PEN.019.0927]

<sup>301</sup> Ibid page 29 [PEN.019.0927] at 0961

Scotland accounts for about 10% of the UK haemophilia population but only about 5% of the patients with bleeding disorders infected with HIV. 1383 patients with bleeding disorders are known to have been infected with HIV in the UK and were reported to NHD, of whom 73 were first reported to NHD by Scottish Centres.

**3.294** Of the 73 patients who tested positive for HIV, 29 were reported from the Edinburgh centre, 24 from Glasgow Royal Infirmary, 11 from the RHSC, Glasgow, seven from Aberdeen, two from Inverness and none from Dundee.<sup>302</sup>

**3.295** The UKHCDO then analysed all of the data available on the National Haemophilia Database (NHD) to determine (a) which patients in the list of 73 were probably not infected in Scotland; and (b) which patients first reported to NHD by centres outwith Scotland were probably infected in Scotland. Five patients were probably infected outwith Scotland. The position of one additional patient was unclear: he was a severe Haemophilia B patient who had been treated extensively in Scotland and England in the nine months within which he seroconverted, with a variety of NHS and commercial products. Detailed analysis of the records of patients in the second group identified one patient who was probably infected in Scotland and two more who might have been infected either in Scotland or in England, where the data indicate treatment in both countries at critical periods but could not identify a single place where infection probably occurred.

**3.296** According to the UKHCDO, at that stage the range of patients probably infected in Scotland, taking account of the uncertain cases, was therefore 68–70.<sup>303</sup>

#### *HPS HIV Diagnosis Database*

**3.297** Professor Goldberg gave evidence that following the development of an HIV antibody test in 1985, HPS (then known as the Communicable Diseases (Scotland) Unit) established an HIV Diagnosis Database for Scotland.<sup>304</sup> The database holds data on all individuals diagnosed HIV antibody positive in Scotland and individuals previously diagnosed outside Scotland who came to reside in Scotland. Since 1989 a standardised National HIV Test Request Form has been used by laboratories; the form is made available to clinicians in clinical settings, allowing relevant information to be recorded by the clinician at the time of blood sampling.

**3.298** In a letter dated 23 March 2011 from HPS to the NHS Scotland Central Legal Office, it was stated that, 'As at 31 December 2010, HPS had recorded 46 deaths among 76 haemophiliac cases who are presumed to have been infected via the receipt of contaminated blood products in Scotland'.<sup>305</sup>

#### *Further investigation*

**3.299** Discrepancies in the numbers of patients considered likely to have become infected with HIV as a result of treatment in Scotland for blood coagulation disorders, prompted a request to Dr Hay and Professor Ludlam to explain the differences and, if possible, to reconcile the data. They carried out a further exercise and on 27 February 2013 produced a

<sup>302</sup> Ibid pages 34–35, table 3 [PEN.019.0927] at 0966 and 0967

<sup>303</sup> 73 less 5 clear and 1 possible cases plus 1 clear additional case = 68; 68 plus the two possible additional cases = 70.

<sup>304</sup> Professor Goldberg's statement on statistics relating to haemophilia patients infected with HCV, dated 1 February 2011 [PEN.001.0206] at 0210

<sup>305</sup> Letter from Glenn Codere, HPS, to Tracey Turnbull, CLO [PEN.012.0151]



short report that dealt comprehensively with the main questions posed.<sup>306</sup> Professor Lowe and Dr Tait (Glasgow) and Dr Watson (Aberdeen), along with staff of the UK National Haemophilia Database (NHD) were involved in the collaboration.

**3.300** Using patient data held locally, including details not recorded in the NHD, and the NHD data for treatments at centres other than those at which the patient was registered, enabled an accurate estimate to be made of the time each patient contracted HIV and the centre which administered the treatment responsible for the infection. In the course of the work of reviewing the records, a Scottish patient was identified who had not been registered or treated at any Scottish Haemophilia Centre but had probably been infected by treatment at a non-specialist Scottish Centre. It was concluded that this patient should be added to the Scottish Haemophilia Directors' previous total of 59, giving a new total of 60.

**3.301** All 59 members of the Scottish Haemophilia Directors' initial group were included in the NHD data. The total number derived from preliminary review of the NHD as probably or likely to have been infected in Scotland was 74, one more than published in the report of April 2012. On detailed analysis of the treatment records and HIV blood test results of the patients, it was found that three patients were probably infected in England. Ten patients who had arrived in Scotland from abroad, and were registered directly at Scottish Haemophilia Centres, were shown to have been HIV positive when they arrived. One further patient from abroad was found to be anti-HIV negative on arrival in Scotland, but HIV positive shortly thereafter. On review of his treatment records it was concluded that he had been infected before arrival, but was in the 'window period' following infection, before antibodies were detectable, 'incubating' the disease on arrival. That was thought to fit better with the known incubation period of HIV than the alternative, which would have required infection immediately on arrival in Scotland, and an unusually short incubation time.

**3.302** The result was that NHD data were fully reconciled with the SNBTS Haemophilia Directors' data. Sixty patients with bleeding disorders were infected with HIV in Scotland by treatment in Scotland.

**3.303** The results from the collaborative investigation carried out by the Scottish Haemophilia Directors and Dr Hay with the cooperation of the UKHCDO are accepted as accurate. Health Protection Scotland's data are an accurate reflection of the information collected. However, the patients notified to HPS were those with a positive HIV test who were classified on the request form submitted to the virology laboratory in Scotland as either having haemophilia or having been a recipient of a clotting factor concentrate. HPS does not have access to information about where patients were likely to have acquired HIV infection. As a result, some data are likely to relate to individuals infected outwith Scotland who subsequently were tested in Scotland. The need to adjust the UKHCDO data for this factor demonstrates that it may be sufficiently significant in itself to undermine the reliability of the HPS numbers for present purposes. Overall however, the investigations carried out by Dr Hay, Professor Ludlam and others have now been sufficiently specific and detailed to make the outcome preferable to inferences drawn from HPS data.

---

<sup>306</sup> Dr Hay and Professor Ludlam's joint response, dated February 2013 [PEN.019.1328]

**3.304** Not all deaths due to AIDS were registered as such, and reporting of the condition while patients were alive may also have been less than complete because of the stigma associated with HIV infection and the AIDS complex of diseases. The detailed work undertaken in the course of the collaborative exercise underlines the difficulty in arriving at any conclusive view on the actual prevalence of HIV infection, even in a closely monitored cohort such as haemophilia patients, given the lack of precise information on some individual patients' cases. Although the figure of 60 may not be absolutely accurate it is unlikely that more precise figures will ever be established than those available from the collaborative exercise.

#### ***Source of infection – SNBTS or commercial product***

**3.305** Dr Bruce Cuthbertson gave evidence that the SNBTS considered it likely that in total 25 patients were infected as a result of treatment with SNBTS products (comprising 19 patients in Edinburgh, four patients at Glasgow Royal Infirmary and two patients in Aberdeen).<sup>307</sup>

**3.306** While in many cases it is difficult to identify the particular product that infected a patient with HIV, it appears in general that commercial blood products carried a greater risk of transmission of HIV than products produced by the SNBTS from plasma from Scottish blood donors.

**3.307** Dr Cuthbertson said:

For those who were known to have received both SNBTS and commercial products, the assignment of probability [as to the source of infection] will partly be determined by date of first detection of antibody to HIV and the date of the last negative HIV test result. For those patients who received both products within a time period consistent with HIV infection, it is more likely that the source of infection was the commercial product. This supposition is based on SNBTS current understanding of the frequency of HIV transmission by commercial and NHS products at that time, and is further supported by the much lower HIV infection rate in Scotland when compared with those haemophilia populations which were treated exclusively with commercial FVIII of US manufacture .... This difference is found in many publications, including that from Moffat, Bloom and Mortimer, 1985 (*Lancet* 1, p935)<sup>308</sup> who found a significant difference ... between the infection rate in patients treated with US FVIII concentrate and those treated with UK concentrate. Similarly, Kroner et al, 1994 (*J. Acquired Immune Deficiency Syndromes*, 7:279–286) reported that more than 90% of moderate and severe haemophiliacs treated with American product seroconverted to HIV.<sup>309</sup>

**3.308** While it does appear that there is support for the assumption relied on in allocating contentious cases, it has to be observed that the Scottish product was infectious in some cases, and, as the UKHCDO April 2012 report shows, allocation can still be problematic. Dr Cuthbertson's evidence is accepted, but with a note of caution: so far as it is based on assumption it is not wholly based on hard data and cannot be accepted as absolutely accurate.

<sup>307</sup> Report dated 5 June 2011 from Dr Cuthbertson to the Inquiry [PEN.012.1633]

<sup>308</sup> Moffat et al, 'HTLV-III antibody status and immunological abnormalities in haemophilic patients', *The Lancet*, April 20, 1985 [PEN.016.0432]

<sup>309</sup> Report dated 5 June 2011 from Dr Cuthbertson to the Inquiry [PEN.012.1633]

**3.309** The updated UKHCDO statistics report notes that Scotland accounts for about 10% of the UK haemophilia population but only about 5% of patients with bleeding disorders in the UK infected with HIV.<sup>310</sup> In the updated report Dr Hay observed:

The relatively low proportion of Scottish patients infected with HIV reflects the fact that Scotland was more self-sufficient in blood and blood products from PFC than England during the period of risk. BPL fractionated most of England's requirement for factor IX but only approximately 40% of England's requirement for factor VIII. England was therefore far more dependent on imported factor VIII concentrates than Scotland. These imported products were largely manufactured from US-sourced plasma and plasma obtained from various other countries, including Africa. HIV spread earlier through the US and African donor population than the UK donor population and so patients using commercial products had a much higher risk of contracting HIV, especially early in the HIV epidemic in 1980, 1981 and 1982. Where English patients were maintained on a single brand of concentrate during the period of risk the risk of contracting HIV was much higher (approaching 100% in some centres) in those patients using US-sourced concentrates.<sup>311</sup>

**3.310** Newcastle and Liverpool were centres in that last category. Referring mainly to severely affected patients, Dr Hay explained:

In some centres, including the one that I worked in as a junior doctor, people were kept on one brand of concentrate as long as possible. It was felt that that might minimise their chance of contracting non-A non-B hepatitis. In fact, that proved to be completely false. It didn't really matter which concentrate they got from that perspective but it did provide us with evidence that those that just used English Factor VIII had approximately half the incidence of HIV observed in the group treated with commercial concentrates. I think that that was largely because HIV spread earlier into the US donor population than into the UK donor population. Of course, there may have been differences in the donor population between Scotland and England.<sup>312</sup>

**3.311** That there was a greater risk of HIV from commercial concentrates appears to be illustrated by the respective incidence of HIV infection in the Scottish centres.

**3.312** From the figures supplied by the Scottish Haemophilia Directors, all but two of the 59 patients with haemophilia identified by them as infected with HIV as a result of treatment at a Scottish centre, had Haemophilia A. Approximately five per cent of patients with Haemophilia A registered at GRI were infected with HIV as a result of their treatment at that centre (10/211).<sup>313</sup> Similarly, approximately 5% of patients with Haemophilia A registered at Aberdeen were infected with HIV as a result of their treatment at that centre (3/60). No haemophilia patients were considered to have been infected with HIV as a result of their treatment at the Dundee or Inverness centres.

<sup>310</sup> 1383 patients with bleeding disorders are known to have been infected with HIV in the UK, of whom 73 were first reported to the UKHCDO by Scottish centres: UKHCDO report *National Haemophilia Database: Bleeding disorder statistics for the Penrose Inquiry*, 2012, [PEN.019.0927] at 0961

<sup>311</sup> *Ibid* page 33 [PEN.019.0927] at 0965

<sup>312</sup> Dr Hay – Day 8, page 31

<sup>313</sup> The numbers of patients with each type of bleeding disorder registered at each Scottish haemophilia centre at five yearly intervals between 1970 and 2011 are provided in the UKHCDO updated report, April 2012, table 2. The registered patients at each Scottish centre in 1985 are shown at page 25 of the updated report.

In the early 1980s all of these centres used primarily SNBTS rather than commercial products.<sup>314</sup>

**3.313** The Edinburgh Centre used mainly SNBTS products in the early 1980s. While there was a greater incidence of HIV at the Edinburgh Centre compared with the other adult centres in Scotland (approximately 13% (23/172) of patients with Haemophilia A registered at Edinburgh in 1985 were infected with HIV as a result of their treatment at that centre) it appears, as discussed above, that 18 of the 23 patients infected at Edinburgh were infected by a small number of batches of SNBTS/PFC Factor VIII. Infection by these batches of concentrate made up about 38% of the total number of Scottish infections.

**3.314** In contrast, the greatest user of commercial concentrate in the Scottish centres in the early 1980s was RHSC Yorkhill, where almost 30% of the children with Haemophilia A registered at that centre in 1985 were infected with HIV (21/73).

**3.315** In conclusion, in Scotland, as was the case elsewhere, commercial concentrates produced by US companies appear to have carried the greatest risk of transmitting HIV.

#### *HIV – Secondary transmission*

**3.316** As noted in this Report at Chapter 8, *Knowledge of HIV/AIDS Now*, paragraph 8.24, secondary transmission of HIV is a real risk, whether from mother to baby or as a result of sexual contact, though reported numbers are small. Professor Ludlam advised that he was not aware of any partners of HIV positive haemophilia patients who became infected with HIV.<sup>315</sup> Dr Tait advised that to the recollection of staff in Edinburgh and Glasgow, no partners of haemophilia patients were HIV positive, albeit there were limited data in that regard.<sup>316</sup> Dr Henry Watson, at Aberdeen, stated that there were no accurate data relating to HIV infection in the partners of infected patients.<sup>317</sup> Beyond noting that some patients who contracted HIV as a result of infected blood or blood products may have inadvertently infected others, it is not possible for the Inquiry to make precise findings or estimates in that regard.

#### *HIV as cause of death*

**3.317** As noted at paragraph 3.302 above, 60 patients with bleeding disorders were infected with HIV in Scotland by treatment in Scotland. Examination of the histories of 59 of those patients, reported in Table 3.19 above, showed that 26 had died of AIDS-related causes. The remaining patient was also recorded as having died of AIDS.<sup>318</sup> Thus, of the 60 patients infected by treatment in Scotland, 27 died of AIDS-related causes.

**3.318** This figure does not represent the total number of deaths from AIDS-related causes among patients in Scotland with bleeding disorders. Figures from the UKHCDO of 48 deaths<sup>319</sup> and from HPS of 46 deaths<sup>320</sup> include cases where the patient's HIV infection was acquired from treatment outwith Scotland.

<sup>314</sup> UKHCDO report *National Haemophilia Database: Bleeding disorder statistics for the Penrose Inquiry*, 2012, pages 3–23, table 1 [PEN.019.0927] at 0935–0955.

<sup>315</sup> Professor Ludlam's statement on the methodology for collation of HIV patients in Edinburgh, dated 25 March 2011, [PEN.012.0153] and Day 14, page 16

<sup>316</sup> Dr Tait's statement on methodology for collation of HIV patients in Glasgow (GRI), dated 25 March 2011 [PEN.012.0152] at paragraph 5

<sup>317</sup> Dr Watson's statement on the methodology for provision of data on HIV infection from Aberdeen Haemophilia Centre, dated 28 March 2011 [PEN.012.0156]

<sup>318</sup> Dr Hay and Professor Ludlam's joint response, dated February 2013 [PEN.019.1328] at 1330

<sup>319</sup> UKHCDO report *National Haemophilia Database: Bleeding disorder statistics for the Penrose Inquiry*, 2012, page 54, table 9 [PEN.019.0927] at 0986

<sup>320</sup> Letter from Glenn Codere, HPS, to Tracey Turnbull, CLO [PEN.012.0151]

**3.319** The recent data provided by the UKHCDO do not include direct data on the patients registered with Scottish haemophilia centres who died of HIV. The data do, however, disclose that of 158 patients with Haemophilia A treated at Scottish Haemophilia Centres and who died between 1969 and 2011, 48 patients died of HIV (ie just over 30%).

**3.320** In addition, as noted at paragraph 3.298 above, HPS noted that, as at 31 December 2010, they had recorded 46 deaths among 76 people with haemophilia assumed to have been infected through blood products in Scotland.

**3.321** The pattern of deaths among HIV-infected patients shown in Table 3.19 above illustrates the relative mortality risks among patients who were young or old at the time of infection. Patients at RHSC, Glasgow have a significantly better survival record historically and, having survived into the era of effective treatment, a much better prognosis and life expectancy than patients who were older at the date of infection.

### **Patients infected with HIV as a result of blood transfusion**

**3.322** The fourth group of patients to be considered is referred to in paragraph 3.2, item iv, and consists of patients who were exposed to infection with HIV through transfusion with blood or blood components.

**3.323** An HIV look-back exercise started in 1985 as a UK-wide initiative of the Health Protection Agency.<sup>321</sup> The Blood Transfusion Services in England, Wales and Scotland agreed to participate when assured that the data would be sufficiently anonymised for no patient to be identified through it, and that the data would remain available to clinicians throughout the United Kingdom for research.<sup>322</sup>

**3.324** From the date of formal commencement of routine testing (15 October 1985) the look-back exercise traced the fate of all blood components from donations made during the preceding five years, by donors who were after that date found to be anti-HIV positive on returning to make a repeat donation. From a starting point of 39 anti-HIV positive donors with a history of previous donation, this process identified 10 anti-HIV positive patients in Scotland. In addition the SNBTS had information from the sporadic reports of clinicians, about patients with HIV infection where the sole risk factor was transfusion.

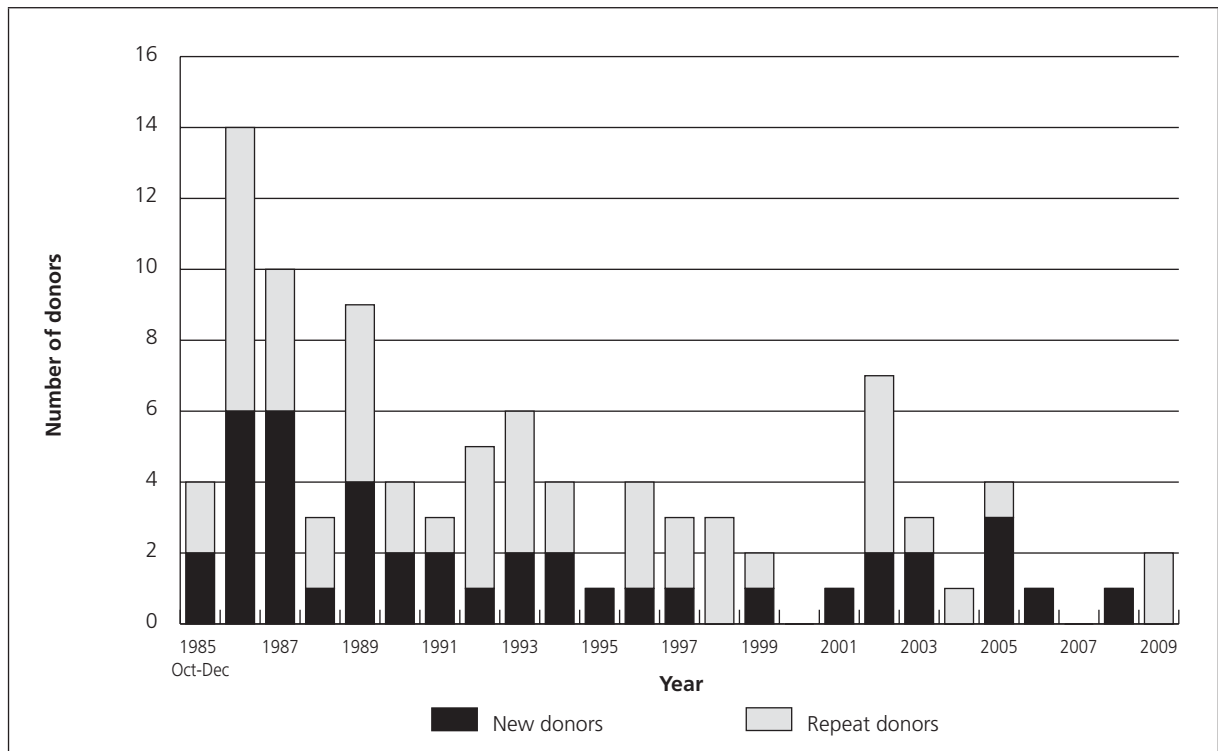
---

<sup>321</sup> Dr Gillon – Day 6, page 59

<sup>322</sup> Ibid page 71

**3.325** The data for infected donors in Scotland are shown in bar form in Figure 3.6.

**Figure 3.6: HIV-infected blood donations: Scotland**



**3.326** The 39 anti-HIV positive return donors represented the numbers presenting at donor sessions between October 1985 and the end of 1997. Fourteen return donors were found to be HIV-positive between 1998 and 2009. The look-back exercise targeted the period when the highest concentrations of infected return donors presented and were tested, but it was not comprehensive. Return donors who continued to appear and test positive after the reference period for the look-back study were not included. While the possibility of additional return donors since 2009 appears remote, the inclusion of any who did appear might have led to identification of additional patients who received infected components. It is not possible, however, to deduce from these data the numbers of possible return donations after 2009.

**3.327** A further difficulty that arose with the look-back exercise was that comprehensive archive samples were not available for the whole period of risk of transmission of HIV. Systematic storage of archive samples began in Edinburgh in mid-1984 and in Glasgow in 1986.<sup>323</sup> In the circumstances, reliable information on numbers of infected donations was available from about 1985.

**3.328** There was a supplementary source of data in returns from virology laboratories to HPS. As already noted at paragraph 3.297, in 1985 HPS (formerly SCIEH) put in place a reporting system throughout Scotland. The system used a single unified referral form for clinicians' use in requesting virology laboratories to carry out an HIV test. SCIEH automatically received a copy of the referral form for every test that proved positive. From that time, every transfusion patient testing positive for HIV at a Scottish virology laboratory was reported.<sup>324</sup> But the data were anonymised, limiting the scope for further

<sup>323</sup> Ibid page 60

<sup>324</sup> Ibid pages 9–10; Professor Goldberg – Day 6, page 147

investigation.<sup>325</sup> In 1985, the virus had only been present in the general population, and therefore by inference in the donor population, for about five years. When the test was introduced, the number of potentially dangerous previous donations from any individual donor was limited to that period.<sup>326</sup> So far as available, the data were reflected in the final figures presented by the SNBTS/HPS.

**3.329** As a result of concerns about the published information, all available data were reviewed for the Inquiry with a view to developing a more reliable picture of the information collected. The evidence was presented by Dr Gillon on behalf of the SNBTS and HPS. In total 18 patients are known to have contracted HIV infection as a result of blood transfusion in Scotland.<sup>327</sup> Ten of these patients were identified through the targeted look-back exercise by the SNBTS following the introduction of HIV screening in October 1985. Eight patients were reported by their clinicians, independently of the look-back exercise, as possible transfusion-transmitted infections. In four of these eight cases it was possible to identify an HIV positive blood donor as the likely source of infection. Of the remaining four, a circumstantial connection was established in three cases, but it was not possible to establish a date of transfusion. Each of the three patients had received more than one transfusion, transfusion had occurred before testing for HIV had begun, and there were no archived samples. But the patient had no other likely source of infection.<sup>328</sup> The remaining patient was reported to SCIEH by clinical staff at the Western Infirmary, Glasgow, but was not known to the SNBTS.<sup>329</sup>

**3.330** After further research, Dr Gillon provided a table showing information on probable dates of infection for all 18 patients.<sup>330</sup>

**3.331** In chronological order, the dates of transfusion of HIV-infected blood or blood components in these patients are shown in Table 3.20. These data represent the best information available to the SNBTS.

---

<sup>325</sup> Dr Gillon – Day 6, page 63

<sup>326</sup> *Ibid* page 18

<sup>327</sup> Dr Gillon's statement on statistics relating to transfusion-transmitted HIV, dated 31 January 2011 [PEN.001.0038] at 0038

<sup>328</sup> Dr Gillon – Day 6, pages 58–59 and Witness Statement [PEN.001.0038]

<sup>329</sup> Dr Gillon's statement on statistics relating to transfusion-transmitted HIV, dated 31 January 2011 [PEN.001.0038] and Day 6, Page 58

<sup>330</sup> *Ibid* [PEN.001.0038] at 0039 and 0042

**Table 3.20: Transfusion-transmitted HIV infection: dates of transfusion**

Patient	Date of transfusion	Annual total
1	13 August 1983	
7	31 December 1983	
2	1983 or 1984	1983:2/3
6	11 January 1984	
8	January 1984	
4	March 1984	
3	April 1984	
14	25 April 1984	
13	'early' 1984	
12	Before June 1984	
10	9 June 1984	
15	September 1984	
17	30 October 1984	
5	November 1984	
9	1984	1984:12/13
16	September 1985	1985:1
11	August 1986	
18	August 1986	1986:2

**3.332** For two patients, infective transfusion in August 1986, well after HIV screening of donors had been introduced, tends to confirm that the early anti-HIV tests were not 100% reliable in detecting infected donors.<sup>331</sup> In particular, as antibody tests, they could not detect infection during the window period following infection and before antibodies were produced.

**3.333** Eight patients were infected in Lothian, six in Greater Glasgow, three in Tayside and one in Lanarkshire health board areas. The distribution by Regional Transfusion Service was:

- Edinburgh and south east: eight
- Glasgow and west of Scotland: seven
- Dundee and Tayside: three.<sup>332</sup>

Neither of the other two regions, Highlands and Grampian, had any cases of transfusion-transmitted HIV/AIDS.<sup>333</sup>

<sup>331</sup> Ibid [PEN.001.0038] at 0042

<sup>332</sup> Ibid [PEN.001.0038]

<sup>333</sup> Dr Gillon – Day 6, page 65



**3.334** The most critical years for confirmed infection were 1983 and 1984, a factor that will become significant when the date of introduction of testing is considered. It will also be significant that the first nine months of 1985 saw one case only of transfusion-transmitted HIV infection.

**3.335** Fifteen of the 18 patients were known to have died as at 31 December 2010. The causes of death were not known, but Dr Gillon commented that, based on HPS data, many of these patients will have died of AIDS.<sup>334</sup>

**3.336** The figure of 18 patients known to have contracted HIV as a result of blood transfusion in Scotland is probably an underestimate. The actual incidence of HIV in Scottish donors between the assumed arrival of the HIV virus in the Scottish blood supply (around 1982) and the commencement of HIV screening of donors (October 1985) is not known. On general grounds, a significant (though not necessarily large) number of individuals infected with HIV by transfusion probably died of the underlying illness for which they were treated, or from other unrelated causes (such as the diseases associated with advancing age), before AIDS-related symptoms appeared. Similarly, an inherent problem of look-back is that some donors may have made HIV-infected donations before October 1985 but not presented to make further donations after the commencement of the exercise. The possible number of patients infected by such donors is likely to have been small, yet it remains unknown.

**3.337** On the other hand, it is unlikely that there were more than a very few post-transfusion AIDS or AIDS-related deaths which remained unidentified among those who survived the typical asymptomatic post infection period. AIDS and the AIDS-related complex present as very serious, usually fatal, illnesses once they develop, and it is highly likely that almost every Scottish AIDS case will have had a cause attributed to it: eight of the 18 known cases were reported by clinicians.

**3.338** The Preliminary Report included, at appendix 4, a table from the SCIEH (now HPS), showing the cumulative total, of AIDS cases as at 30 September 1999, AIDS deaths and HIV-infected persons registered or reported in Scotland. The table indicated that there were 33 recipients of blood or blood products recorded as being HIV positive, 18 male and 15 female. For the purposes of the table, 'blood product' does not appear to include blood products prescribed to haemophilia patients (e.g. clotting factor concentrate), as haemophilia patients are shown separately in the table. While not all of these 33 individuals necessarily received the infective blood transfusion in Scotland,<sup>335</sup> the record does perhaps suggest that the figure of 18 patients discussed above may be a little low, albeit the true figure will not be as high as 33. The HPS figure included patients who might have been infected outside Scotland.

**3.339** It is not possible to be more precise on the evidence available.

### Co-infection with HIV and Hepatitis C

**3.340** It is not known whether any of the 18 patients known to have been infected with HIV as a result of blood transfusion in Scotland were also infected with Hepatitis C.<sup>336</sup>

<sup>334</sup> Ibid page 66

<sup>335</sup> Note 1 to the table notes that, 'Some cases have arisen from transmission which occurred outwith the UK'.

<sup>336</sup> Dr Gillon – Day 6, pages 77–79

**3.341** It is likely, however, that all haemophilia patients who contracted HIV as a result of treatment with blood products made from large pools of plasma also contracted Hepatitis C. Dr Tait stated:

As we know, unfortunately some of the HIV patients would have died before Hepatitis C testing became available but I think it's a fairly reasonable assumption that virtually all HIV positive patients would also have been Hepatitis C positive.<sup>337</sup>

### Summary of conclusions

- Generally, contemporaneous records, whether of patients exposed to risk or of the incidence of infection, were either not maintained at all or were or have become over time, incomplete and unreliable.
- In the case of each of HIV/AIDS and HCV, there was a period when the agent of transmission was not identified, and no reliable diagnostic tests were available, and when effective recording of comprehensive data on the incidence of disease would therefore have been impossible.
- The Public Health (Infectious Diseases) (Scotland) Regulations 1975 did not achieve the reporting of viral hepatitis, pre-dated any requirement for the reporting of HIV and in any event were never enforced.
- Throughout the period when transmission of the index infections by blood, blood components and blood products exposed NHS patients to risk, there were no regulatory or other administrative systems capable of recording and monitoring the numbers of NHS patients in Scotland treated with blood and blood products, or the numbers exposed to risk of infection with the Hepatitis C virus and HIV, or the numbers contracting either or both such infections as a consequence of such treatment.
- The Blood Safety and Quality Regulations 2005 and the Public Health etc. (Scotland) Act 2008 have provided a statutory framework for improved reporting and recording of infection, and should be effective provided they are enforced and are supported by appropriate procedural rules.
- So far as patients with blood disorders are concerned, the National Haemophilia Database maintained by the UKHCDO and the records of individual haemophilia centres, as now adjusted, have provided the best evidence. However, due to anonymisation and reliance on voluntary compliance with requests for information and reporting, the records may not have yielded comprehensive information relating to infection and the consequences of infection for NHS patients.
- In the case of each of the index infections, the data extracted from records of known or recorded cases of transfusion-transmitted virus infection represent minimum numbers of patients who were infected. They probably do not reflect the actual number of patients who are likely to have contracted the disease in that way.
- So far as Term of Reference 4 is concerned, it is clear that recorded data cannot provide an accurate measurement of the extent of HCV or HIV infection in Scotland over the reference period, or of the risk of transmission of infection.

<sup>337</sup> Dr Tait – Day 14, page 132

- None of the statistical analyses carried out provided a single reliable source of information. A sensitivity analysis was not carried out to test the assumptions made in varying conditions. Such statistical models as have been developed to date remain of doubtful validity as indicators of total exposure to risk and of transmission. The fundamental problem is that hard data are lacking and assumptions have to substitute for measurement over too wide a range of factors.
- The work carried out by and for the Inquiry suggests that further epidemiological investigation would not produce a more reliable estimate, at least without disproportionate expense. Nothing can be done now to improve the contemporaneous records, or to provide hard data indicating objectively the scale of the problem. The reporting system, such as it was, was never designed and assembled so as to be likely to be effective even if enforced. If the Scottish Government is persuaded that, for health policy and strategy, or budgeting or other reasons, it is necessary to develop a more accurate figure, it may be that further research and further expert opinion might eventually converge. That cannot be recommended by this Inquiry.
- Excluding the extremes, a wide range of values remain as indications of the possible incidence of infection. Only a rough and speculative estimate is possible, as set out in Table 3.21.

**Table 3.21: Estimated numbers of NHS patients infected and outcomes**

Infection	Estimated number infected	Estimated number of deaths from liver-related causes (HCV infection) or AIDS (HIV infection)
Bleeding disorder HCV	478 <sup>338</sup>	Unknown overall: 21 to 30 deaths reported from various studies <sup>339</sup>
Transfusion-transmitted HCV	Around 2,500 <sup>340</sup>	Unknown overall: 8 of 133, per Dr Gillon; 31 of 304 per Professor Goldberg <sup>341</sup>
Bleeding disorder HIV	60 <sup>342</sup>	27 AIDS or AIDS-related deaths <sup>343</sup>
Transfusion-transmitted HIV/AIDS	18 minimum <sup>344</sup>	Up to 15 <sup>345</sup>

**3.342** Whatever the exact number of cases of transfusion-transmitted HCV might be, there are individuals currently infected with HCV as a result of blood transfusion who may not have been diagnosed. This topic is taken up in Chapter 35, *An Investigation into the Steps Taken to Identify the Individuals who were Infected (Look-back)*. The question of further investigations to identify these patients is discussed there. Any data recovered would incidentally have a bearing on the statistics. The primary focus should clearly be on identifying those who may benefit from treatment and who, despite previous attempts to identify them, remain unknown to the NHS.

<sup>338</sup> See paragraph 3.77

<sup>339</sup> See paragraphs 3.78 to 3.85

<sup>340</sup> See paragraph 3.256

<sup>341</sup> See paragraph 3.259 for Dr Gillon's evidence, paragraph 3.260 for Professor Goldberg's evidence.

<sup>342</sup> See paragraph 3.302

<sup>343</sup> See paragraph 3.317

<sup>344</sup> See paragraph 3.329

<sup>345</sup> See paragraph 3.335

## CHAPTER 4

### EXPERIENCES OF THE PATIENTS AND THEIR FAMILIES – WITNESS STATEMENTS

#### Introduction

#### 4.1 Term of Reference 10 requires the Inquiry:

To examine any particular adverse consequences for patients treated by the NHS in Scotland and their families of infection through blood and blood products with Hepatitis C and HIV, including the treatment offered.

This chapter and the following two chapters will explore the evidence available to the Inquiry from patients and their families about their experiences of the infections and of the impact of these on their lives.

**4.2** At the stage of preparation of the Preliminary Report, published in 2010, many patients who had acquired either or both HIV and Hepatitis C infection from blood or blood products, and their relatives, had provided written statements to the Inquiry. Details of how these witness statements were taken are narrated in paragraphs 4.18–4.23 of the Preliminary Report. Seventy-eight witness statements were finalised prior to the publication of the Preliminary Report and these witness statements alone provided the basis for Chapter 4. Since publication, further witness statements have been obtained by the Inquiry. In total the Inquiry has taken statements from 159 patients and relatives relevant to the reference period.<sup>1</sup>

**4.3** From these 159 patients and relatives, the Inquiry selected six witnesses to give oral evidence in respect of the effects of infection with HIV, including the effects of treatment, on patients and their families,<sup>2</sup> and seven witnesses to give oral evidence in respect of the effects of infection with Hepatitis C, including the effects of treatment, on patients and their families.<sup>3</sup> The evidence relating to these thirteen witnesses is dealt with in detail in the two chapters that follow this one. The approach used to select these witnesses is narrated in Appendix 1, *Inquiry Procedures*.

**4.4** What follows is a summary of the remaining witness statements (excluding the witness statements of the 13 witnesses who gave oral evidence and their 11 relatives) consisting of the witness statements of 90 patients and 45 relatives. Certain issues were raised by witnesses in the original 78 statements and referred to in Chapter 4 of the Preliminary Report, namely: the information given to patients (or their parents) about the risk of AIDS and about the risk of non-A, non-B Hepatitis, before their treatment with blood or blood products; the tracing and testing of patients who might have been exposed to the viruses through their treatment with blood or blood products; and the information given to patients who might have been infected, or who were found to be infected, and their families. During the oral hearings these issues were explored in evidence as part of the Topics B5 and C5 and the outcome of this is detailed in Chapters

<sup>1</sup> This figure excludes the witness statements taken from the relatives of those whose deaths were specifically referred to the Inquiry under Term of Reference 6. See Chapter 7, *An Investigation into the deaths of the Reverend David Black, Mrs Eileen O'Hara, Mr Alexander Black Laing, and Mr Victor Tamburrini*.

<sup>2</sup> See Chapter 5, *An Examination of the Effects of Infection with HIV on Patients and their Families, Including Treatment*.

<sup>3</sup> See Chapter 6, *An Examination of the Effects of Infection with Hepatitis C on the Patients and their Families, Including Treatment*.

33 and 34.<sup>4</sup> This summary of the witness statements does not rehearse these points but it focuses, in particular, on Term of Reference 10.

**4.5** It is not appropriate to weigh individual witnesses' evidence on too fine a scale. Inevitably, some specific accounts might fail to persuade one of the reliability of the evidence on particular points of detail. Taken as a whole, however, the cumulative impression from the evidence is that it has a high degree of coherence and consistency and provides great confidence in its overall reliability. It paints a distressing picture of seriously debilitating and sometimes fatal illness that makes its own impact without further comment in this Report.

**4.6** It should not be inferred, however, that every patient infected with either virus has experienced or will experience all of the consequences described. In some cases the diseases have been relatively benign and for some patients infection has been asymptomatic. Treatment is now available that can deal with many of the consequences described, though with side-effects that can themselves be distressing and difficult to manage on an individual basis. Inevitably those who have come forward are individuals with an account of the impact of infection that they wish to describe. Relatively few are motivated to come forward and explain that they have not been affected, or affected to any material extent, by infection. The evidence described is eloquent of what does happen, and what can happen. It does not provide a forecast of what will inevitably happen in every case.

## The witnesses

### 4.7 Table 4.1: Summary of the 90 patient witness statements

Means of infection	Witness infected with Hepatitis C	Witness infected with both HIV and Hepatitis C	Total number of witnesses
Treatment for Haemophilia A	19	2	21
Treatment for Haemophilia B	7		7
Treatment for other blood disorders, i.e. von Willebrand disease and Platelet Storage Pool Deficiency	6		6
Blood transfusion	50		50
Treatment with Immunoglobulin and Anti-Rh antibodies	2		2
Secondary infection	4		4
<b>Total</b>	<b>88</b>	<b>2</b>	<b>90</b>

**4.8** The Inquiry is aware that several patient witnesses who provided statements have since, sadly, died.

<sup>4</sup> Topic B5a) The information given to patients (or their parents) about the risk of AIDS before their treatment with blood or blood products; b) the tracing and testing of patients who might have been exposed to the virus through their treatment with blood or blood products; and c) the information given to patients who might have been infected, or who were found to be infected, and their families.

Topic C5a) The information given to patients (or their parents) about the risk of non A, non B Hepatitis before their treatment with blood or blood products; b) the tracing and testing of patients who might have been exposed to the virus through their treatment with blood or blood products; and c) the information given to patients who might have been infected, or who were found to be infected, and their families.

### *Summary of the witness statements of the relatives*

- Twenty-nine witnesses were relatives of patients who had also provided the Inquiry with a witness statement. Of those witnesses, 13 relatives made statements about six patients between them, and the remaining relatives gave a statement about 16 individual patients;
- Seven witnesses were relatives of eight patients (one witness was related to two patients) who acquired HIV and/or Hepatitis C from their treatment for haemophilia. Of these eight patients, three were co-infected with HIV and Hepatitis C from their treatment; one patient had acquired HIV and his relative suspected that he had also acquired Hepatitis C; one patient had acquired HIV and his relative was unaware if he had been tested for Hepatitis C; and two patients had acquired Hepatitis C only. Four of the eight patients had died.
- Nine witnesses were relatives of eight patients (two of the relatives were related to the same patient) who had acquired HIV and/or Hepatitis C from blood transfusions. One patient had acquired both HIV and Hepatitis C from a blood transfusion, and the remaining seven patients had acquired Hepatitis C from a transfusion. Seven out of the eight patients had died.

### **The reaction of patients and relatives to diagnosis with HIV and/or Hepatitis C**

#### *Diagnosis with HIV*

**4.9** Invariably the patients who were diagnosed with HIV and their relatives felt fear, and some of them also felt anger. In the mid-1980s the publicity surrounding HIV was horrific and the prognosis for someone diagnosed with HIV was very poor.<sup>5</sup>

**4.10** One witness was told, within six months of her haemophiliac brother dying of AIDS contracted from infected blood products, that her seven-year-old son had acquired HIV from his haemophilia treatment. This witness' son subsequently died in 1994, aged 16, of AIDS.

**4.11** A mother of a 14-year-old boy described hearing the news that her son had been infected with HIV as being 'like a sledgehammer to the face'. Her son stated that, initially, when he was told his diagnosis, he did not take in the enormity of it. When he did understand his diagnosis he changed from doing fairly well at school to dropping out of school at the age of 16 with no qualifications. He started drinking alcohol and he stated that he was probably an alcoholic by the time he was 18 years old.

**4.12** Another patient described the time he was diagnosed with HIV as being 'an extremely stressful time' for both him and his wife due to the poor information available about the virus, and their concern for the future.

#### *Diagnosis with Hepatitis C*

**4.13** Most of the patients who were diagnosed with Hepatitis C, and their relatives, had not previously heard of the virus. They did not know the implications of it and, in the early years of the emergence of the virus, doctors were unable to provide them with much information about it.<sup>6</sup>

---

<sup>5</sup> See Chapter 5, *An Examination of the Effects of Infection with HIV on Patients and their Families, Including Treatment*, paragraph 5.17.

<sup>6</sup> See Chapter 34, *An Investigation into the Systems in Place for Informing the Patients About the Risks – Hepatitis C*, paragraphs 34.7–34.8.

**4.14** The patients and their relatives were shocked and upset when the patients were diagnosed with Hepatitis C. They described feelings of disbelief, uncertainty and fear. The lack of certainty about what the diagnosis might mean for the patients in terms of symptoms and prognosis exacerbated witnesses' fears. Many patients believed that diagnosis with the virus meant that they had a shortened life expectancy. When patients and their relatives discovered that the patient had been infected with the virus for a number of years, many believed that this meant that the patient's life expectancy was even shorter. At the same time, for many patients, their diagnosis with Hepatitis C provided them with an explanation for how they had been feeling, some for a long period of time.

**4.15** Some patients described experiencing feelings of shame and of feeling 'dirty' as a result of their diagnosis with Hepatitis C. The questions, which many patients were asked by medical professionals at the time they were diagnosed with the virus, may have contributed to such feelings. Many patients were asked if they had abused intravenous drugs, abused alcohol, been promiscuous or had tattoos. One patient, who suffered from obsessive compulsive disorder at the time of her diagnosis with Hepatitis C, stated that after her diagnosis she scrubbed herself until she bled.

**4.16** For those patients with haemophilia, who had already endured the outbreak of HIV, being diagnosed with Hepatitis C was a new blow. As one patient stated 'I was flabbergasted. I thought I was going to die. I asked myself when my bad news was ever going to end. We had just come through the highly publicised AIDS scare'.

**4.17** A patient described her shock when she was diagnosed with Hepatitis C after previously being diagnosed with HIV, both acquired from a blood transfusion. She stated that it was 'quite a lot to take in'. She felt shocked, hurt and angry. She became hysterical.

**4.18** Some patients were very worried that, having been unaware that they had Hepatitis C, they might have infected others, in particular their close relatives. One said:

Discovering I was Hepatitis C positive was a nightmare, a total nightmare. I was devastated at the thought of having potentially infected my wife and children. I was extremely relieved that my wife is negative for Hepatitis C.

**4.19** Two patients had given birth to children after acquiring the virus, but before their diagnosis with it. They were both extremely worried that they had passed the virus to their children. The children, who were subsequently tested for the virus, were found to be negative. Another mother worried that she had passed the virus to her daughter when her daughter had attended to a cut on her mother's foot. They both endured an anxious wait for the daughter's Hepatitis C test results, which were negative. A few patients had donated blood while they were unaware that they had Hepatitis C.

**4.20** In addition to the worry about having infected family members and others, many patients were concerned about the impact their diagnosis with Hepatitis C would have on their family. They were concerned that their symptoms would mean that they would be unable to care for their family or that they would die leaving their family members to cope without them.

**4.21** Some witnesses tried to ignore the diagnosis and others tried to find out more information about the virus themselves. This was difficult for those who were diagnosed with the virus, and for their families, before the advent of the internet. Even after the

availability of the internet, not all homes had access to it. Some of the information witnesses found frightened them. A patient who was infected with Hepatitis C stated that she was horrified by information she discovered on a website which told her how to arrange her own funeral and how her body would be treated after her death. She stated that this information 'profoundly affected her'.

### **Symptoms of HIV**

**4.22** The natural history of HIV and AIDS, including the signs and symptoms of infection, as now understood, is discussed in Chapter 8, *Knowledge of HIV/AIDS Now*. This provides a general background to the witnesses' evidence.

**4.23** One witness stated that when her son developed AIDS, 'everything focussed on getting [her son] to eat'. Her son did not eat enough and he suffered great weight loss. He developed eye disease and then tunnel vision. This witness stated, 'The worst thing about the whole business was that [my son] gradually went blind. None of the other kids [who attended the same Haemophilia Unit and had AIDS] had this and it made him depressed and vulnerable'. Her son subsequently died of AIDS aged 16.

**4.24** Another witness described the decline of his wife before she died from AIDS, aged 51 years. She became weaker over the years and suffered significant weight loss. 'Even the smell of food made her sick' and latterly she was tube fed. She weighed less than six stone when she died.

**4.25** A patient who was diagnosed with HIV as a teenager stated that he developed a bad chest infection when he was in his 20s. This required treatment in hospital. When he was in his late 20s he was diagnosed with non-Hodgkin's lymphoma, an AIDS-related cancer. He stated that he now has HIV-related mental health symptoms including dementia and post-traumatic stress disorder. He suffers from violent and aggressive thoughts, poor memory and cognitive processes, flashbacks and sleep disturbance.

**4.26** One patient, who was diagnosed with HIV when he was 30 years old and then later with Hepatitis C, has developed type 1 diabetes. He is now insulin dependent. He has been admitted to hospital with diverticulitis (a digestive condition affecting the large intestine), pneumonia and pleurisy. He now has cirrhosis. He has suffered from fluid retention, 'yellow tinges' in his eyes, varices, spider naevi (red veins resembling the shape of a spider beneath the surface of the skin) and encephalopathy (damage to the brain characterised by confusion, cognitive impairment and lethargy). These latter symptoms are attributable to Hepatitis C.

**4.27** A witness whose two sons acquired both HIV and Hepatitis C from their haemophilia treatment stated that they had both developed AIDS. One son developed sores on his back, bleeds in his stomach, liver and kidney problems, loss of weight and general weakness to the extent that he could barely walk. His other son also lost a lot of weight and developed arthritis, the latter perhaps due to the Hepatitis C virus (HCV) as opposed to HIV. Both sons suffer from severe depression.

**4.28** The wife of a man with both HIV and Hepatitis C stated that her husband's health has deteriorated 'dramatically' over the past 14 years to the extent that he now requires 24-hour care. He has little energy, tires easily and sleeps a lot of the time.



## Symptoms of Hepatitis C

**4.29** The symptoms of Hepatitis C described by the patients and relatives ranged from no symptoms at all to a number of severe symptoms. Most of the patients reported a gradual onset of symptoms and often, initially, patients thought the symptoms were caused by something else, for example having a young family or working hard. A number of patients stated that they 'did not feel right', highlighting the unspecific nature of the symptoms of Hepatitis C.

**4.30** Specific physical symptoms reported by patients and attributed by them to their infection with HCV were:

- Lethargy, tiredness, exhaustion, reduced physical ability, heart palpitations after physical activity.
- Night sweats, insomnia, erratic sleep – one witness stated that he would never wake up feeling as if he had experienced a good night's sleep.
- Little or no appetite, indigestion, nausea, vomiting, weight loss.
- Anaemia.
- Jaundice.
- Discomfort and/or pain in the abdominal area.
- Irritated and/or itchy skin, skin discolouration, red hands, rosacea, boils, spots, bruising easily.
- Muscle pain, joint pain, stiffness, cramp, rheumatoid arthritis.
- Neuralgia and neuropathy (damage to the nerves and nervous system).
- Headaches.
- Having a compromised immune system and being prone to infection.
- Hot flushes, feeling the cold, uncontrollable shaking.
- Low mood and mood swings, depression, poor concentration, poor memory, poor motivation, irritability, confusion, anxiety and panic attacks, suicidal thoughts, incidents of self-harm.

**4.31** The more serious symptoms described by a smaller number of patients and attributable to severe liver disease were ascites (accumulation of fluid in the abdomen), varices (varicose veins), inflammation of the liver and of the spleen, hepatocellular carcinoma and encephalopathy (damage to the brain characterised by confusion, cognitive impairment and lethargy).

## Treatment for HIV

**4.32** The treatment for HIV, including the development of it over the years, is described in Chapter 9, *Knowledge of HIV/AIDS Now*.

**4.33** The first treatment which doctors prescribed for HIV was Zidovudine (also known as AZT). A witness, whose son was treated with Zidovudine in the mid-1980s when he was eight years old, believes that the start of her son's treatment with Zidovudine coincided with the start of his declining health. She now wonders if he was prescribed too large a

dose of the drug. Her son was also treated for eye disease with an intravenous drug which took two hours to administer. He was prescribed antiemetic medication to control nausea. Her son subsequently died. Another witness described how her husband was wary of Zidovudine, having seen a number of his friends and relatives take it and subsequently die. Her husband refused treatment with Zidovudine.<sup>7</sup> He later suffered a psychotic reaction to his treatment with Efavirenz.<sup>8</sup>

**4.34** One patient described having to take his antiretroviral medication every four hours. He used to have to wake himself up at four o'clock every morning to take the dose due then. He found this treatment disruptive and upsetting. The same patient stated that there were a lot of 'harsh' side-effects from antiretroviral medication and that this was especially true of the first-generation products. He said, 'I knew I had to take them if I was to live'. The side-effects from which he suffered as a result of his treatment for HIV over the years have included a burning feeling in his stomach, nausea, vomiting, malaise, generally feeling unwell, anxiety, depression, insomnia, peripheral neuropathy (damage to the nerves and nervous system), joint and muscle pain, sexual dysfunction, diarrhoea, flatulence, headaches, depression, anxiety, loss of concentration, poor sleeping and difficulties eating. This same patient was also treated with chemotherapy and radiotherapy for his AIDS-related non-Hodgkin's lymphoma.

**4.35** Another patient stated that his treatment with antiretroviral medication has caused a thinning of his bones. As a result of this he sustained a spiral fracture of his femur after falling down stairs. Whilst being treated for this in hospital he acquired an infection with E-coli.

**4.36** Another witness' wife was treated with Zidovudine, Didanosine and Immunoglobulin before she died of AIDS. This witness stated that he had 'every praise' for the staff who treated his wife and the care which she received.

### **Treatment for Hepatitis C**

**4.37** Further detail about treatment for Hepatitis C is narrated in Chapter 13, *Knowledge of Viral Hepatitis Now*. In summary, it may include monitoring of a patient's condition by examination, blood tests, ultrasound, CT scan, MRI scan, Fibroscan and liver biopsy and treatment with medication and, if necessary, a liver transplant. The medication to treat Hepatitis C was initially Interferon, then Interferon and Ribavirin and is now Pegylated Interferon with Ribavirin.

**4.38** One aspect of treatment for Hepatitis C, which a number of patients commented upon, was the fact that they had to attend the infectious diseases unit of the hospital for their treatment at the same time as those who had become infected as a result of drug misuse. 'Most people attending the clinic had a drug problem. All conversations in the waiting area were about getting access to drugs. This was a complete culture shock to me.'

**4.39** Two patients described attending clinic appointments at the same time as heavily guarded and handcuffed prisoners. One patient stated that if the prisoners 'kicked off' they would be seen before her. She found the experience 'uncomfortable'. The other patient found it upsetting attending her appointment at the same time as prisoners. She

---

<sup>7</sup> See Chapter 8, *Knowledge of HIV/AIDS Now*, paragraph 8.36.

<sup>8</sup> Efavirenz is a non-nucleoside reverse transcriptase inhibitor used to treat HIV since about 1998.

was also very concerned that someone she knew would see her attending the infectious diseases unit. In fact, one of her work colleagues saw her there and asked her about her illness. She stated that rumours about her then circulated at work.

**4.40** A patient who was diagnosed with Hepatitis C in 2009 has described his treatment as chaotic. When his wife phoned the hospital, in 2010, for test results she was told by the doctor's secretary that she had to understand that 'hepatitis was a chaotic illness which meant that it was a chaotic clinic for people with chaotic lifestyles'. The patient's wife said, 'I appreciate it is a chaotic clinic for people with chaotic lifestyles but we are not like that'. A number of patients spoke about their clinic appointments being cancelled.

### ***Medication for Hepatitis C***

**4.41** It was apparent from the witness statements that a number of factors affected a patient's decision to start treatment with medication for Hepatitis C, and often made the decision about whether and when to start treatment difficult. These factors included the uncertainty about the best time to undergo treatment, the potentially severe side-effects which the medication can cause and the poor prospects of success of the treatment. It was particularly difficult for patients who had no symptoms of the virus, to embark on a course of treatment which might cause them very significant side-effects and which might fail.

**4.42** A number of patients chose not to undergo treatment with medication for Hepatitis C. Their reasons for this decision included: believing that the treatment would not help them and might, in fact, make their condition worse; being too scared to start the course of treatment; and a concern that the medication would worsen a witness's pre-existing mental health or physical symptoms. Some patients were required to undergo a psychiatric assessment before being allowed to start treatment.

**4.43** Other patients chose to delay their treatment mainly for family reasons, for example having young children or wishing to start a family. Some of these patients then faced a delay when they decided they were ready to start the treatment. This was a difficult period for them and caused them anxiety.

**4.44** For some patients starting treatment for Hepatitis C brought home their diagnosis with the virus. One patient stated:

The worst thing about starting the Interferon was it forced me to acknowledge that I had this life threatening virus in my blood. At that point my future was impossible to contemplate and I found myself thinking what music I would like at my funeral. That's how it made me feel. I always felt I was a strong individual and that I could handle anything von Willebrand's disorder threw at me. This was something else, far beyond my control and it loomed over me blocking out the light.

### ***Side-effects of Interferon and Interferon combined with Ribavirin***

**4.45** Most patients were warned about the side-effects they might experience from their treatment with Interferon and Interferon and Ribavirin but many stated that the treatment was much worse than they had expected. While a few patients experienced some or no side-effects, the majority experienced a number of different side-effects. The impact of these ranged from having little effect on a patient's life to rendering a patient bed-bound and incapable of taking part in work, family or home life. These impacts are described in more detail in paragraphs 4.47–4.49 below.

**4.46** Treatment with Interferon was administered by way of injection usually given three times a week. In more recent years, treatment with Pegylated Interferon may be injected weekly. Patients were taught to inject themselves. Some had difficulty with this and either their family members helped them, or they attended their GP's surgery and the treatment was administered there. Some patients took their weekly treatment on a Friday evening in the hope that they would recover from the worst effects of it over the weekend, and be fit for work on the following Monday. Many patients were advised to take paracetamol at the same time as their dose of Interferon and some patients found that this helped the side-effects.

**4.47** Side-effects reported by witnesses and attributed by them to treatment with Interferon were:

- Flu-like symptoms – raised temperature, headaches, sweating, feeling hot and cold, tiredness, lack of energy, loss of appetite, weight loss.
- Insomnia, disturbed sleep and exhaustion.
- Nausea, vomiting, stomach cramps, diarrhoea, dehydration (requiring in-patient treatment).
- Insatiable thirst, change in sense of taste.
- Depression (requiring treatment with antidepressants), irritability and anger, mood swings, anxiety attacks, confusion, cognitive impairment.
- Worsening of joint pain.
- Vertigo.
- Developing an underactive thyroid (which requires permanent thyroid replacement treatment).
- Loss of hair.
- Itchy skin, hardening of the skin and a smell coming through the skin.
- Uncontrollable shaking.
- Seizures.

**4.48** Additional side-effects reported by witnesses and attributed by them to treatment with Interferon or Pegylated Interferon together with Ribavirin were:

- Dry skin.
- Dry mouth.
- Straightening of the hair.
- Anaemia.
- Hypertension.
- Dizziness and light headedness.
- 'Riba-rage',<sup>9</sup> panic attacks, disorientation.
- Constipation.
- Peripheral neuropathy.

---

<sup>9</sup> 'Riba-rage' is a term used for the intense depression and irritability that some patients taking treatment for Hepatitis C have experienced.

- Neutropenia (an abnormally low level of neutrophils, a type of white blood cell).
- Infections, for example dental abscesses.
- Mouth ulcers, thrush.
- Vivid nightmares.
- Palpitations and shortness of breath.<sup>10</sup>

**4.49** Examples of other, less common, side-effects experienced by patients were:

- One patient suffered blood loss during treatment with Interferon and Ribavirin and required a transfusion.
- Another patient developed septicaemia while being treated with Interferon and Ribavirin. He then developed swelling of his prostate gland which he was told was caused by the septicaemia. His treatment with Interferon and Ribavirin was stopped immediately.
- Another patient stated that his ALT level increased to four times the level it was prior to treatment.

**4.50** Some patients worried about the impact their treatment would have on pre-existing medical conditions. One patient stated that he was unable to take anti-inflammatory medication for arthritis during his treatment as he was unable to eat. Women taking the treatment were strongly advised not to become pregnant during the course of the treatment due to the risk of it causing birth defects or the death of the unborn baby. For the wife of one patient, this meant that there is now a greater age gap between her children than she would have liked.

**4.51** The treatment caused a wide range of mental health symptoms for a number of patients and often these were severe. Some patients were prescribed anti-depressant medication during their treatment for Hepatitis C. One patient became severely depressed and started taking an overdose of paracetamol before he was interrupted by a telephone call from his mother. He stated, 'That time felt like a dark hole with no way out'. Another patient described waking up one morning during his treatment and not knowing who he or his wife was. One patient was not allowed to be left alone with her young nephew in case she 'flipped'. Another patient stated:

As well as not feeling well, I felt at risk of blowing up with anger and frustration at small provocation. I tried to avoid getting into any such situation as far as I could. For example, at that time two of our children were at university and the two teenagers were at home, and I avoided anything which might lead to a dispute because I did not trust myself to be reasonable. My wife had to deal with things like that as well as with me.

**4.52** Some patients suffered a loss of confidence as a result of the treatment:

I was rarely able to go out. I had to pick my moments to go into shops. Sometimes I drove to the shops but had no confidence to get out of the car and so I just drove home again. A few times I drove when I really was not capable of driving safely as I had tunnel vision and could not see the road properly.

---

<sup>10</sup> See Chapter 13, *Knowledge of Viral Hepatitis Now*, paragraphs 13.106 and 13.107 for side-effects of these treatments, including the list set out in the SIGN guidelines of the side-effects of Pegylated Interferon and Ribavirin.

**4.53** For many patients their treatment with Interferon or Interferon and Ribavirin was the worst aspect of their infection with Hepatitis C. A number of patients and relatives described the treatment as horrendous:

The side effects of the treatment were horrific. It was the worst treatment I have had in my life and I would never do it again. It was like having the worst flu you can imagine. My immune system became so low I was totally open to infection. I got lots of infections. If I cut myself it took a long time for cuts to heal. I lost the sensation in my feet. My hair fell out, I lost a lot of weight and I looked like a corpse. I regularly collapsed into long stupors of sleep. On a few occasions when my husband came home and found me like this he thought that I had died. I suffered from spinal pain and from pain at the injection site. In the end I chose to stop the treatment due to the side effects.

I took the [Interferon and Ribavirin] treatment for 48 weeks. It was horrific and never again. I have had chemotherapy, a mastoid operation and deaths in the family and other personal stuff but I have never, ever experienced anything like the Interferon and Ribavirin treatment.

After approximately six weeks I began to notice changes in my sleeping and eating habits. I can sleep very easily now when I go to bed at 9.30pm – 10pm, whereas before I was a bit of a night owl, staying up until the early hours watching television, reading etc. Several days a week I feel tired, lethargic, listless, nauseous, uninterested and have no attention span in what is happening around me. Conversations, television and reading all leave me thinking afterwards, 'What actually happened there'. For a short-time I actually felt like hell. I was constantly nauseous, tired, 'wabbit', had indigestion, heartburn and I just lay in my bed suffering and feeling sorry for myself with absolutely no appetite.

**4.54** Some patients thought that they or their relatives were going to die during the treatment. One witness stated:

The treatment [Interferon and Ribavirin] my brother had was horrendous .... I do not know how he survived it. I think he should have been hospitalised but he was determined not to go in to hospital. He was very weak and suffered a lot of pain. He was unable to sleep and suffered from "shocks". He lost a lot of weight and was unable to eat. My brother always had someone in the house when he was having a bath as he was so weak. My son, my other brother or another member of the family was always there in case anything happened. I worried throughout the treatment that he was not going to survive it. I have seen my father and a friend die of cancer but watching my brother undergo this treatment for a year was worse than that. It was the worst thing I have ever seen. Unless you see someone go through this treatment you cannot understand how horrendous it is.

**4.55** The severity of the side-effects which some patients experienced, and which their relatives observed, caused some to have their dosage of the treatment reduced and others to have the treatment stopped altogether. This caused great disappointment to the patients being treated and their families as the patients faced an uncertain future. Many patients showed great strength and fortitude in managing to continue with their treatment despite experiencing severe side-effects. It was apparent that the hope of ridding themselves of the virus gave patients the motivation and determination to do this.

**4.56** For a number of patients and their relatives the treatment was successful. For the patients, this made what they had suffered by way of side-effects worth it. However, as well as their feelings of joy and relief, some patients described feelings of uncertainty and doubt as to whether they had cleared the virus for good or whether it might return. The uncertainty of doctors about this, particularly in the earlier years, is likely to have contributed to these feelings.

**4.57** The treatment of a similar number of patients was unsuccessful, in some cases after three or four different courses of treatment. Witnesses expressed their devastation and disappointment about this. The feelings of many patients were exacerbated by the severity of the side-effects they had endured. One mother described her shock at her son's second treatment failing as she 'felt sure there was no way a second treatment would fail. My son suffered two massive blows to his life and future health'. A number of patients stated that they would refuse to take the treatment again due to its side-effects.

**4.58** For some witnesses the disappointment of the treatment failing was compounded by the 'false hope' given by blood tests at the end of treatment indicating that a patient had cleared the virus, only for the blood test six months later to show that the virus had returned. One witness described how she felt after her husband's blood tests looked promising:

For the first time ever, I allowed myself to think about life without Hepatitis C and realised all the ways in which it overshadowed our lives like a persistent cloud; uncertainty, anger, long term financial implications, having to decide about and attempt future treatment; what that meant for job prospects and financial security; the ongoing risk of cross infection; the worry of my husband's health declining and what that would mean for my health, my children, my work, our income, our quality of life. When the virus reappeared in his blood soon after the treatment ended I found this extremely hard to cope with because having seen how improved our life would be if we were free of the virus, these hopes were then dashed.

**4.59** Some patients described the side-effects of the treatment persisting for some months, even years, after the treatment ended.

I have never recovered from the Interferon treatment. Physically, I looked as though I had aged ten years. My hair turned from black to grey. My back and posture became stooped. My sons thought I looked old. My sister-in-law was flabbergasted when she saw me. She barely recognised me. I never looked nor felt like a young man again. After the treatment ended I never bounced back. I still have to take antidepressants. My depression is not as severe but I still need to take the medication. My wife and I have no sexual relations. For two years this has been getting worse. In my opinion this loss of libido is directly linked to the side effects of Interferon treatment. I try to get out of the house to meet my male friends who all thought I was going to die during the treatment. They are also of the opinion that I aged tremendously after this treatment.

**4.60** One patient who suffered from side-effects of Interferon but whose treatment ultimately was successful, described the effect of the treatment as follows:

Luckily by December 1999 I knew that the treatment was working. I suddenly felt better and between December 1999 and July 2000 I started putting on weight and feeling better in myself. I had more energy, my colour improved

and I felt excellent. It was as though I had been blind and had just put my first glasses on. I soon realised how long I had been ill for. As I have already said I had got used to feeling ill and had forgotten what being healthy was all about.

### ***Other treatment***

**4.61** A few patients have undergone banding of oesophageal varices (varicose veins on the oesophagus). One patient stated that a varix burst as he underwent the procedure and he lost four pints of blood.

**4.62** One patient who received a liver transplant described how he felt afterwards:

Despite all the adversity I now feel like a 20 year old. I have never felt so well in my whole life. I am building up my fitness. I want to do so many things with my life which were previously denied to me due to illness. Hepatitis C ended my working career and career opportunities. With Haemophilia I always managed to work albeit with occasional absences. Hepatitis C caused my irreparable liver disease and I nearly died due to this. My end stage liver disease made me housebound and highly dependent on others to survive. I had no quality of life for years. Hepatitis C caused a sharp decline in my health from 1997 to 2009. I am keen to rebuild my life by going to night school. I am keen to learn how to play a musical instrument. I want to travel. I got my driving licence back in ... 2009. I now drive to my own appointments at the [hospital]. I have freedom to do these things because I am cured from Hepatitis C induced liver disease. I have energy again. I feel optimistic.

### ***Alternative therapies***

**4.63** Some patients have tried alternative therapies to alleviate their symptoms of Hepatitis C and believe that these have caused some improvement of their condition. Such therapies include milk thistle, meditation, aromatherapy, vitamin supplements, omega 3 supplements, herbs, acupuncture, tai chi, receiving treatment from a chiropractor, crystals and a healthy diet.

## **Other impacts of infection with HIV and/or Hepatitis C on patients and their relatives**

### ***Personality and lifestyle***

**4.64** A number of patients described their diagnosis with HIV and/or Hepatitis C and their fear for the future as weighing on their minds. One patient described his diagnosis with Hepatitis C as 'a weight around my neck. It's always there'. Patients have coped with this in different ways but it is apparent that the feelings they have experienced have been exacerbated by the stigma and isolation surrounding both viruses.<sup>11</sup>

**4.65** The following are excerpts from a number of the witness statements describing how infection with HIV and/or Hepatitis C had affected patients:

I don't have a life anymore. I exist. The Hepatitis C virus has taken everything. I don't know who [the witness's name] is anymore. I used to be so outgoing. I travelled a lot and was very sporty. I used to enjoy rock climbing, swimming and gardening. I rode a motorbike. I enjoyed socialising. Now I have just one

---

<sup>11</sup> These are discussed in more detail in paragraphs 4.95–4.113 below.



friend. The Hepatitis C virus has 100 per cent changed me. I feel a drain on everyone as I rely on everyone so much. I very rarely leave the house, only really to go to hospital appointments and this has been the case for about the last 10 years.

The impact of my infection with Hepatitis C has been huge. I suppose after all I have been through growing up with haemophilia it was the straw which broke the camel's back.

This diagnosis has changed me completely. I used to be a happy-go-lucky type of person. Now I stay at home and keep myself to myself. I go out once a week on a Wednesday when I go to the bank and pay bills. I keep thinking I am going to die. I cannot get it out of my head. It feels like a life sentence.

**4.66** A father stated that one of his sons 'went wild' when he was diagnosed with HIV as a teenager. His son thought that he was dying anyway and so what did his behaviour matter? His other son was also diagnosed with HIV. The family was devastated. Subsequently his sons watched a number of their friends, who attended the same haemophilia clinic as them, die of AIDS. Both his sons suffer from depression and he has had a nervous breakdown.

**4.67** The mother of a boy who died from AIDS when he was a teenager stated that her son withdrew from his friends as he became more ill as he thought that 'he was not much company'. She stated that, having been brought up with a brother with haemophilia and then subsequently having a son with haemophilia, she feels as if she has had 'a roller coaster life. I have lived with haemophilia all my life and you always put the sick person first'.

**4.68** A mother stated that her son had lost all his confidence since finding out he was infected with Hepatitis C and he did not have a good self-image. Another witness who was diagnosed with Hepatitis C when he was a teenager stated that, had he not been diagnosed with the virus, he would have gone out drinking and socialising more. He stated that his lifestyle would have been different. He was 'very careful' as a single man and did not have any short-term relationships.

**4.69** One patient described the change in his lifestyle as a result of his symptoms of Hepatitis C. Before his diagnosis with Hepatitis C he had a wife, a successful career, a house and a boat. Since suffering symptoms of Hepatitis C and the side-effects of treatment he has lost all of these. He is now separated from his wife, homeless and living on benefits. His sister stated that it was embarrassing for him to meet up with his old friends as people remembered him as 'so very generous'. Now he can no longer afford to be generous. She stated that her brother is lonely with no one to share his life with.

**4.70** Many witnesses spoke about themselves or their family members being unable to go on holiday or to take part in hobbies or activities which they previously enjoyed, due to being unwell as a result of the symptoms of the virus or their treatment for it. Others spoke of withdrawing from activities due to the fear of infecting others with the virus. A couple of patients with Hepatitis C spoke to feeling left out and conspicuous as a result of being unable to drink alcohol socially.

**4.71** Relatives spoke about their worry and concern for their family members who were infected and their fear for the future. The wife of a man diagnosed with HIV stated:

The consequences of what happened to us after [my husband] was told of his HIV positive status are vast and a lot of it is too difficult to tell in this statement. Before being told that [my husband] was infected we were a happy family with everything to look forward to. Life changed to fear, uncertainty, worry and most of all secrecy.

**4.72** Relatives also spoke to the changes in patients following their diagnosis with the virus:

It feels like our whole life has been turned upside down. It has left me married to a stranger. The happy-go-lucky person I married is no longer here. Our family life is a lot different now. If we went somewhere and were doing something, my husband used to be loud and lively. Now he can't be bothered. He used to see his brother every Friday night, now he can't be bothered. Even going grocery shopping is an escapade, half way round the shop he feels tired. He is now a crabbit, old besom. Some days he feels very depressed and some days he is too tired to do anything. He sometimes needs help out of the bath and to get downstairs. He is sometimes scared to be alone and wants company, then he doesn't like when he has company. My husband is not interested in anything. His whole life now revolves around sleep and being exhausted. He's like a stranger to folk now.

### ***Relationships and family life***

**4.73** Many patients described the strain which their own or their relative's infection with Hepatitis C and/or HIV placed on their marriage or relationship. A number of witnesses attributed the breakdown of their marriage or relationships to their own or their spouse's/partner's infection with HIV and/or Hepatitis C. Some patients thought that the implications of their own infection had been too much for their partner to cope with.

**4.74** One woman stated that, during their son's illness with AIDS, 'Needless to say our marriage was not important. Both of us focused on trying to keep [our son] alive'. Following the death of their son, she and her husband underwent some courses of IVF and worked at their marriage. Despite having 'a few good years' they are now in the process of divorcing.

**4.75** Another witness stated that her husband suddenly started to wash his own crockery and cutlery. He used the same two cups and would not let anyone else use them. He started to wash his own underwear. Then he told his wife to leave and she did so. They separated at that time. Later she discovered (after finding correspondence from the Skipton Fund) that her husband had acquired Hepatitis C. Her husband has since died.

**4.76** At the time one patient was diagnosed with Hepatitis C his partner was pregnant. Their baby was born with a cyst on the brain and subsequently died. His relationship with his partner broke up soon after as they were both devastated at the loss of their child and his partner believed, at that time, that the baby's health condition was 'in some way' caused by his Hepatitis C.

**4.77** Many witnesses stated that the nature of their relationship with their spouse or partner changed as their spouse or partner became his or her carer or they cared for their relative. Some carers found themselves torn between looking after their spouse or partner on the one hand and the rest of the family on the other. One woman described the impact of her husband's treatment for Hepatitis C:

The treatment and its side-effects have had an impact upon my role as mother and wife. I tried very hard to ensure that my husband's needs and daughters' needs are met. The children sometimes got the brunt of my husband's irritability and mood swings. I had to keep reassuring them and explaining that it was down to the medication. It is most unlike my husband because he is usually such a placid character. It is a fine balance and has been a difficult time. I wanted to keep everything as normal as possible. It was very challenging as I also continued to work full time and was actually awarded with a certificate for 100% attendance for the year. I don't know how I did it. I never said to anyone about the situation. I really struggled to keep upbeat. I confided in my GP about the pressure at home.

**4.78** One patient and her relatives described how her treatment for Hepatitis C affected her relationship with her husband in the last few months of his life. Her husband was undergoing chemotherapy treatment while she underwent treatment with Interferon. The side-effects of the Interferon treatment caused her to be short tempered with her husband. She became critical of him and spoke to him with venom. Her son stated that this was not natural and his mother had not spoken to his father like that during 40 years of marriage.

**4.79** A patient, who subsequently died after he and his wife had given their statements, described Hepatitis C as having 'destroyed' his relationship with his wife and their sex life. This patient's wife stated:

We don't go out and are unable to make plans. Our relationship has suffered severely. I feel I have gone from being his wife and friend to being his carer. We no longer have a sexual relationship or do anything together as a couple. I find he has become dependent on me for a lot of things, his concentration is not so good and he has lost some of his confidence. I also find it very hard to talk to him and to get him to talk to me. We are like brother and sister instead of husband and wife and I do not see this improving. I feel sad that this has happened through something which was not the fault of [her husband].

**4.80** A number of individuals spoke about the impact of HIV and Hepatitis C on their sexual relations. Some stopped having sexual relations with their spouses or partners after their diagnosis with HIV and/or Hepatitis C, for fear of infecting them. One stated that, other than when she and her husband conceived their children, they have had to use barrier methods of contraception at all times as opposed to other methods, like a vasectomy, which are open to their contemporaries. She said, 'We never expect to be free of the fear of transmission'. One patient, having read that the virus could be transmitted sexually, contacted all his previous girlfriends and explained the risks to them.

**4.81** One patient stated that he was in denial after being diagnosed with HIV, and he continued to have unprotected sex with his wife. She became pregnant and was advised that the baby could have HIV and would not have a good chance of survival. She underwent

a termination of the pregnancy. During this procedure his wife was treated as infectious and kept in a side room in the hospital. This experience was 'devastating' for his wife.

**4.82** A number of patients who are not in a relationship spoke of the difficulty in forming relationships when infected with Hepatitis C and/or HIV. A number posed the question, 'How do you tell someone (with whom you would like a relationship) that you are infected with Hepatitis C or HIV?'

**4.83** A husband who acquired Hepatitis C from his wife stated that his marriage came under 'an immense strain' when his wife was advised that they had different sub-types of the virus. They had been together since they were young and he felt that she would be wondering where he had got the virus from if he had not acquired it from her. His wife was later informed that she had two sub-types of the virus and that she had only infected him with one.

**4.84** Family members have described watching their relatives suffer from the symptoms of both viruses and from the side-effects of treatment. Some have watched their relatives die, which understandably has had a profound and lasting effect on them.

**4.85** Some witnesses spoke of their relative turning to alcohol as a way of dealing with the illness and its impacts. One witness stated that his father's death from Hepatitis C had 'a massive impact' on the whole family. The witness stated that he is now a binge drinker and, since his father's death, he has 'come off the rails' a few times.

**4.86** Another witness described the effect on him of his father's illness with HIV and subsequent death. He was eight years old when his father died. He remembered that his father was unable to do much actively with him although he used to take him fishing and told him a story every night. He remembers his father being in hospital most of the last year of his life and visiting him there. He remembers the night his mother told him that his father was dying. He stated 'It was devastating. I didn't see my father again'. His father's death completely changed his relationship with his paternal grandfather who unfortunately became very depressed and died a few years later. His maternal grandfather helped his mother raise him. After his father's death he felt that he was missing out not having a father to put him to bed or to tell him a story. He believes that his mother was looked down on by some people because she was a single parent. He stated that his father was a gifted musician but he never had the chance to learn from him. He would have loved his own children to have known their grandfather.

**4.87** Many patients expressed their concern, distress and fears about the effect that their illness has had and may have on their family in the future. Their fears include being unable to look after their family, needing to be looked after by them or dying and leaving the other members of their family to cope. Likewise, the relatives expressed their worries about their family members who are infected with HIV and/or Hepatitis C becoming ill or dying. One mother stated:

I used to worry that my son would not meet anyone to share his life with due to his Hepatitis C. I am so overjoyed that his new wife has accepted him and loves him as he is. They met at University and were close friends first. She is perfect for him. However despite my happiness I cannot stop being worried about the future. I worry about the risk of sexual transmission, the problems they may encounter should they decide to start a family and the worst case scenario of his new wife bringing up a family on her own should he predecease her due

to Hepatitis C. They do not have any children and I know that this is probably yet another huge blow to both of them whilst they weigh the risks up, given the risk of sexual transmission of the Hepatitis C virus. This is not something he talks about with his mother, but no doubt he has worried about this also. There remains a lot of uncertainty about his future prognosis.

**4.88** Witnesses described the strain on family relationships caused by their own or their relative's illness as a result of HIV and/or Hepatitis C.

When our children were very young they suffered by being separated from me on the numerous occasions I was in hospital. While young they were unaware of the serious health problems I was dealing with, but in their teenage years their lives were shaped by the anxiety of seeing their mother in extreme pain and suffering and they had to endure the worry of test results and hospital admissions. In their final years at school they both experienced emergency ambulances coming to the house on a number of occasions. They cared for me in every way they could but my husband and I did not want them to witness any more of the daily suffering I had to endure or feel responsible for my care .... Today when they visit, they voice their concerns about the large amount of medication I take each day and worry that I may die soon.

**4.89** Witnesses described seeing other family members, sometimes their parents, upset as they tried to cope with the full effects of the illness. They also spoke of the patient being unable to contribute to or to take part in family life as she or he did before:

I have seen my Dad's health deteriorate over the years and he has become increasingly dependent on the family to help him do everyday things and assist him attending appointments and GP surgeries. He cannot participate in a lot of family functions and activities and has been unable to go on holiday for a number of years. These are the things I miss most – being a family and being able to do things as a family. He is not the same person now and I am sure this affects him in many ways. I think it affects relationships and he is concerned about the future, both his and the family.... I know that my Dad becomes frustrated that he cannot do more with [her disabled brother] due to his condition and help my Mum .... I feel that this condition has seriously and adversely affected my life and that of my family. I do not feel that I had a normal childhood due to this....

**4.90** One relative described seeing his father lose all confidence in himself during and after his treatment with Interferon. His father suffered depression as a result of this treatment. While this relative was a student, he used to go to work meetings on his father's behalf while his father sat in the car outside. Eventually he stopped going to university for a while as he was so worried about his father. He stated that, at times, he had to be with his father as he was worried he would take his own life. There were periods when his relationship with his father was difficult and now he believes that this was probably due to his father's symptoms of the virus. He stated:

I do not feel good about this now .... It has been totally distressing for me to see Dad like this. I feel so helpless and I find it stressful. I worry about him. It is very difficult to see someone, who you have looked up to and seen as a good role model, go through what he has been through and understand why this has happened.

**4.91** A difficult matter for a number of patients was telling their children about their infection. Patients described their children reacting in a range of different ways on being told this – being supportive of the other parent; being scared; worrying in particular that their parent was going to die; becoming very emotional and developing mental illness such as depression and anorexia nervosa. One parent described one of her daughters changing from being an outgoing, successful athlete to becoming a recluse after being told of her mother's infection with Hepatitis C. She also developed myalgic encephalomyelitis (chronic fatigue syndrome, also known as ME) and depression. This parent stated, 'I should be able to look after her but cannot [due to her own symptoms of Hepatitis C]. We have to help one another to get through the day'.

**4.92** A number of patients with Hepatitis C are concerned about their ability to have a family, with some believing that this is an option denied to them as a result of their infection. One witness described her and her husband's inability to have children as one of the most distressing impacts of his diagnosis with Hepatitis C. She and her husband both have fertility problems. Her husband has another medical condition. Having unsuccessfully tried fertility treatment they decided to explore the possibility of adoption. Two independent adoption agencies turned them down on the basis that her husband's medical condition together with his infection with Hepatitis C, meant that adoption would not be in the best interests of the child. She found this very hard to take and became very depressed.

**4.93** A number of patients infected with HIV and/or Hepatitis C feared that they might pass the virus on to relatives or other persons.

On a day-to-day basis I have to be really careful with my two young sons regarding my toothbrush. When I'm doing anything in the house where I could cut myself I always wear gloves and take extra precautions. Any time I do injure myself I find it very difficult not to panic when my children are in the vicinity. I am very paranoid about passing this disorder on to my children. It is clear to me that there will be many limits to the activities that I can pursue with my children, for example, I have already avoided all contact sports due to the risk of passing on the virus. Many of the feelings I had when I first learned I had Hepatitis C resurface and this can be upsetting.

**4.94** One patient stated that she is terrified to give her grandchildren a hug or a kiss in case they catch the Hepatitis C virus from her. Others described keeping their home very clean, using their own glasses and crockery and being very careful around their relatives.

#### *Stigma, secrecy and isolation*

**4.95** Many witnesses described having to deal with the stigma associated with the viruses as being the worst aspect of the infection. A large number of patients have not told their family members (including close family), friends and colleagues about their infection. The result of this has been that they live their lives with secrecy, sometimes with lies and they have become isolated from family and friends.

#### **HIV**

**4.96** Due to the adverse publicity about HIV in the 1980s patients and their families were encouraged by medical professionals to keep their diagnosis with HIV a secret.

**4.97** A mother (whose brother also had HIV) described how she and her husband were 'obsessed' with keeping their son's diagnosis with HIV a secret. One newspaper published

an article about HIV with the headline 'Killer Blood' which referred to her brother. This witness and her husband were concerned that their son would be excluded from school if the school became aware that he had HIV, and they did not want the press to start investigating their son. After their son's death, they told people that he had died of leukaemia.

**4.98** Another witness whose wife died of AIDS stated that, at her funeral, her coffin was covered with a tarpaulin and the flowers were put on the floor. Following her death his sons changed their names so that their children would not be bullied because of the stigma associated with HIV and Hepatitis C. At the time of his wife's death, he worked part-time as a mechanic. After her death he was told not to return to work because his wife had died of AIDS. He felt that neighbours were talking about him after her death. In her diary this witness's wife wrote about her inability to put her diagnosis with HIV out of her mind due to the constant publicity about it. She stated that the news stories about HIV and 'the way they jumped out of newspapers' did not let patients like her forget that they had the virus.

**4.99** One witness stated that, as a result of their secrecy after her husband's diagnosis with HIV, the closeness they previously had with their families has now gone and 'is something that can never be fixed'. She stated that they could not face her family 'because of all the lies' as they had not told anyone about her husband's diagnosis with HIV. They still keep away from their families.

### Hepatitis C

**4.100** Even today there is ignorance and lack of understanding about the Hepatitis C virus. Some people associate it exclusively with the misuse of intravenous drugs, abuse of alcohol, tattoos and even promiscuity. As a result of the stigma associated with it, a number of patients described feeling ashamed, embarrassed, self-conscious, contaminated and stigmatised by their diagnosis with the virus.

**4.101** Many worried how their family, friends and work colleagues would react to their diagnosis and chose not to tell them. This secrecy put a great strain on witnesses and their relatives who knew of their diagnosis.

**4.102** A patient who was diagnosed with Hepatitis C when he was 15 years old stated:

My parents worried about the potential prejudice I may suffer from others and so we decided together to only inform the immediate family about Hepatitis C. We did not tell friends and the teachers at school. The pressure upon us to keep the diagnosis secret was, and is still, immense. It is very hard to withhold information about yourself which is so personally consuming. The pressure to conceal this diagnosis continues to be a source of pressure to this day for me, my wife and my family. Some of my closest friends know about my haemophilia but I have never discussed Hepatitis C at any time. A constant source of worry for me is if my employers should find out or have to be informed. Will they understand what Hepatitis C and Haemophilia are? Will they be prejudiced against me? Will they consider it is some way deceitful of me that I have never told them despite no compulsory medical disclosures ever having been required?

**4.103** Some witnesses have experienced adverse reactions of family and friends to their diagnosis with Hepatitis C. One witness stated that her husband, who died as a result of his infection with Hepatitis C, was embarrassed by his diagnosis with the virus and did not wish anyone to know about it. His children found out about it when he started treatment with Interferon. One of his children stopped bringing his own children to their house and would not allow the witness to hold her grandchildren even although she did not have Hepatitis C. She stated that she should have had a close and meaningful relationship with her family but she has now lost contact with them as a result of her husband's infection with Hepatitis C.

**4.104** A patient, who lived in a small village, told a friend of hers that she had Hepatitis C. Their children were friendly but suddenly her friend stopped inviting her children to play and there was talk of her children having a virus. This patient and her family moved to a different village for a fresh start.

**4.105** Another patient stated that a relative of his told someone in their local pub that he had Hepatitis C. Rumours then spread that he had HIV. One patient stated:

I want to get people to wake up to the fact that stigma causes more damage than the disease. The stigma attached to the Hepatitis C virus is insidious. I have been most affected by that. Once, due to my condition, I was asked not to make sandwiches for a children's party but to bring crisps instead.

**4.106** Some relatives expressed sadness that the patient had found it difficult to tell them about their infection and so had, initially, dealt with their diagnosis alone and without their support.

**4.107** A number of patients spoke of being treated differently by healthcare workers due to being infected with HIV and/or Hepatitis C.

**4.108** The husband of one patient, who had died, stated that, in the 1980s, 'HIV' was written in large letters on the front of her medical records. Also around the time when she was admitted to hospital, after the nurse found out that she was HIV-positive, her bed and her locker were moved into a side room. Other patients spoke of their Hepatitis C positive diagnosis being recorded in an obvious manner on their medical notes or on blood samples.

**4.109** A witness, whose son was diagnosed with HIV in the mid-1980s, stated that after this diagnosis her son's treatment in hospital was different. Her son was always kept in isolation. All those treating him wore gowns and gloves. When her son underwent any medical procedures the doctors wore face masks. Patients with haemophilia and HIV were given bright blue, thick bags to return their treatment refuse to the hospital. She stated that, gradually, those families who used these blue bags started to share their experiences with each other. Very quickly these precautions were applied to all haemophilia patients, irrespective of whether they had HIV or not.

**4.110** A patient who is HIV-positive stated that he has been made to feel unclean when he has been in hospital. One doctor would not touch him. In 2010 his GP said to him, 'No one told me you are HIV positive and I have been touching you without gloves on'.



**4.111** A number of patients spoke about healthcare professionals making assumptions about their symptoms being due to alcohol or drug abuse:

When I had to deal with nurses and doctors there was a complete lack of sensitivity to how I had contracted Hepatitis C through a blood transfusion. It was always assumed I had a history of drug taking. I eventually broke down one day and said 'I'm being labelled as a drug user'. The doctors and nurses admitted that this was true and it was a very stressful environment for me to attend but there was no support for a patient like me.

**4.112** Another patient stated that when he attends hospital and undergoes blood tests for other medical conditions, he always tells the staff that he has Hepatitis C. He stated that some of the staff give him 'dirty looks as if I was a needle-sharing junkie or similar' but that their attitude changes significantly when he tells them that he was infected by a blood transfusion.

**4.113** A number of patients stated that when they had undergone medical procedures they were put to the end of the operation list. A patient who underwent a surgical procedure in 2008 stated:

When I was in the ward waiting to go to theatre I reminded the admissions doctor that I had Hepatitis C. Prior to going to theatre I mentioned to a second doctor that I had Hepatitis C. I eventually got to theatre at 4.30pm when someone in the theatre said to me 'You've put the cat amongst the pigeons'. Apparently they had to empty the theatre of all unnecessary equipment and any equipment that couldn't be removed had to be covered in clingfilm because I had Hepatitis C. I eventually got the procedure.

### *Education and work*

**4.114** A few patients or their relatives stated that their education at school, college or university had been detrimentally affected as a result of the viruses. This was mainly due to absence as a result of suffering from the symptoms of the viruses or the side-effects of treatment, caring for a relative or worrying about a relative. As a result some patients were unable to complete the course they had started or did not obtain the qualifications they had hoped to gain. This affected their job prospects and career choice. Some relatives of patients provided statements to the same effect.

**4.115** Some patients stated that their choice of work, including whether they worked full-time or part-time, were employed or self-employed, the type of work they did and where they worked, was affected by their diagnosis with HIV and/or Hepatitis C.

**4.116** A few patients spoke of the difficulty they had obtaining work. One stated that, on numerous occasions, he had attended job interviews at which the prospective employers wished to discuss his medical history. He stated that as soon as he mentioned Hepatitis C these employers believed that he had been injecting illegal drugs. Others were too scared to try to obtain work or a promotion at work as they believed that, in order to do so, they would have to disclose their medical history.

**4.117** A number of patients showed great determination in persisting at work even when they were quite unwell. Notwithstanding this a large number of patients and their relatives had to reduce their working hours, change their role at work (often with a drop in salary),

stop working or sell their successful businesses as a result of the symptoms of the viruses or the side-effects of treatment.

**4.118** This has had numerous consequences for patients and their relatives. The financial impacts are described in paragraphs 4.126–4.139. Many witnesses have suffered stress and worry with regard to their own and their family's finances. Partners and spouses of those unable to work have felt additional responsibility and pressure as the only breadwinner in the family. One witness stated that this weight of responsibility caused her to become anxious about her own health in case she became unable to work. She also felt constantly insecure about the future.

**4.119** A number of patients described how devastated they felt at the loss of a job they had loved or relished. One patient described how he had recently been promoted at work to be a skipper. Due to his symptoms of Hepatitis C and the side-effects of the medication taken to treat it, he had had to stop work and was now unfit for this role. He stated:

This has been totally devastating for me. Your whole life you aspire to be something and then you get there and they take it away from you so easily, you are so easily replaced. My Dad would have been so proud of me being a skipper. I have spent down time crying about this. Also I have never been off work this length of time and it is killing me. I have worked since I left school and have never been idle. I don't do sitting about. It is very hard to fill the day although I like reading.

**4.120** Another patient who has haemophilia and Hepatitis C stated that, when he was young, his GP told his mother that it was unlikely he would ever work due to his haemophilia. This patient was determined to work and, at the age of 17, he found an apprenticeship in an ironmonger's shop. He stated:

It was not the safest working environment but I was so happy and excited to be able to work. I managed fine. Sometimes I worked all day with my knee swelling up due to a bleed and then I would go, by bus, to [...] Hospital in the evening for treatment.

**4.121** He managed to keep working until he was nearly 40 years old when he had to stop due to his symptoms of Hepatitis C.

**4.122** Many patients were reluctant for their employers to find out that they were infected with HIV and/or Hepatitis C for fear of jeopardising their employment or their future career prospects. A patient with HIV and Hepatitis C was asked to provide his employers with a copy of his medical records and to attend an assessment by a doctor after his health took a turn for the worse. He did not wish his employers to know that he was infected with these viruses and so he gave up work. Around this time, he was told by the consultant treating his HIV that he might only have a few more years to live so he should enjoy them. He stated that this was a very stressful time as he and his wife were unsure how they would manage financially.

**4.123** Another patient stated that she was very keen to work and had greater earning potential than her husband. Due to her symptoms of Hepatitis C, she was unfit for work for a period of six months. Before her return to work she was sent for a medical examination by her employers. She stated that there was no confidentiality and she was ostracised once her employers knew that she had Hepatitis C. She was made redundant and her role

was filled by someone from a different office. She found this whole experience 'extremely upsetting'. Another patient stated that she lost her job as a cleaner at a school as she was considered a health and safety risk due to her infection with Hepatitis C. She stated, 'I loved my job and really miss it'.

**4.124** A patient, whose employers are unaware that he has Haemophilia and Hepatitis C, stated that this is 'a huge worry for him'. He is concerned he may become unwell at work and his employers will not know what his underlying conditions are.

**4.125** On the other hand, a number of patients spoke of having confided in colleagues or managers at work about their condition and having been helped by them, for example, by being given less strenuous roles at work.

### *Financial*

**4.126** It is apparent from the witness statements that the financial impact of patients' infections with HIV and/or Hepatitis C has been significant both for the patients and their families.

### **Loss of earnings, pension and savings**

**4.127** A number of patients stated that they had lost substantial earnings as a result of having had to reduce their working hours or stop working altogether due to their symptoms or to the side-effects of treatment. Some had moved to a less well paid role in order to be able to continue working and others had stopped working overtime. A number of patients stated that they had not tried to gain promotion or to obtain a new, better paid job because of their condition and so they were deprived of the opportunity of increasing their earnings.

**4.128** Families of patients who died as a consequence of their infection with one or both of the viruses have been deprived of their relative's financial support. Relatives of those infected also reported having lost earnings as a result of caring for those suffering from the symptoms of the viruses or the side-effects of the treatment, accompanying their family members to hospital appointments or visiting them while they were in-patients in hospital and grieving for their deceased family members after their death.

**4.129** Many patients spoke of having been unable to afford to contribute to a pension or to save. Some had made fewer or lower contributions to their pensions than they had planned due to reduced or no earnings. Many witnesses were understandably anxious about how they would manage financially in the future.

### **Insurance**

**4.130** A number of patients highlighted the difficulties they had faced obtaining life assurance, travel insurance, critical illness cover and private health insurance as a result of their infection with HIV and/or Hepatitis C. A large number of patients were unable to obtain any of these, some having applied to a number of different insurers. Some patients had not tried to obtain any of these policies as they thought that they would be unsuccessful due to their infections with HIV and/or Hepatitis C. Other patients were too embarrassed to apply for such cover. One patient stated that he was worried that a refusal of his application for life insurance would go on 'record against [him] somewhere' or that the refusal would filter back to his mortgage lender.

**4.131** Some patients spoke of having been able to obtain life assurance and travel insurance but at the cost of increased premiums. A number of patients who were over 50 years of age had obtained life assurance cover which did not require medical information.

**4.132** The inability of patients to obtain or increase their life assurance has had a number of consequences for them. A number of patients have been unable to obtain a mortgage or to increase their mortgages. This has resulted in patients renting accommodation instead of buying their own property, remaining in their present home instead of moving to a larger or a more expensive home or obtaining a mortgage without life assurance to cover it. A number of patients stated that their mortgage was in their spouse's or partner's name alone.

**4.133** One patient with HIV and Hepatitis C stated that the only way he was able to obtain a mortgage was with the MacFarlane Trust acting as guarantor.

**4.134** With regard to travel insurance, a number of patients did not disclose their HIV or Hepatitis C diagnosis to insurers when they obtained their cover. Others obtained travel insurance which excluded cover in respect of their HIV and/or Hepatitis C.

**4.135** One patient helped her son buy a car. She applied for insurance to cover the bank loan but was refused this due to having Hepatitis C.

#### **The MacFarlane Trust, the Eileen Trust, the Skipton Fund and the Caxton Foundation**

**4.136** Most of the witnesses had received payments from the MacFarlane Trust, the Eileen Trust or the Skipton Fund.<sup>12</sup> The MacFarlane Trust has made lump sum payments from the late 1980s to those infected and annual discretionary payments thereafter. The payments made by the MacFarlane Trust to an infected individual and dependents, up to about 2011, ranged between £43,500 (where death occurred before or upon establishment of the scheme) to £150,000–£180,000 for those still living. The Eileen Trust, from 20 May 2009, made flat-rate recurrent annual payment of £12,800, with continuing scope for discretionary payments. The range of payment received by patients and dependents from the Eileen Trust, up to about 2011, ranged from £43,500 (where death occurred before or upon establishment of the scheme) to £80,000–£150,000 to those still living.<sup>13</sup> There are three payments currently available from the Skipton Fund. The first-stage payment is £20,000 for those patients who were infected with Hepatitis C through treatment with NHS blood or blood products prior to September 1991, or have acquired it from someone else who received such treatment. The second-stage payment is £50,000 for those who have received the first stage payment and whose Hepatitis C has advanced to the extent that the patient has undergone or is on the waiting list for a liver transplant or the patient has been diagnosed with primary liver cancer or the patient has been assessed as having cirrhosis or the patient has been diagnosed with B-cell non-Hodgkin's lymphoma. The third payment is for those who meet the criteria for the second-stage payment. It is a payment of £14,574 per year. Many patients and their relatives are of the view that the

---

<sup>12</sup> The MacFarlane Trust provides assistance to patients with haemophilia infected with HIV as a result of their treatment with blood products and their families in the United Kingdom ([www.macfarlane.org.uk](http://www.macfarlane.org.uk)). The Eileen Trust was set up to provide financial assistance to those infected with HIV through a blood transfusion or tissue transfer in the form of small regular payments or one off payments to affected persons. The Skipton Fund ([www.skiptonfund.org](http://www.skiptonfund.org)) is a UK-wide ex gratia payment scheme which makes payments to those infected with Hepatitis C through treatment with NHS blood or blood products prior to September 1991 – see paragraph 3.129 of Statistics chapter.

<sup>13</sup> Review of Support available to Individuals infected with Hepatitis C and/or HIV by NHS-supplied blood transfusions or blood products and their dependents as a result of Written Ministerial Statement, Department of Health 'Support for those affected by contaminated blood', Thursday 14 October 2010.

payments they receive from the Skipton Fund are insufficient. A new charity, The Caxton Foundation, also provides financial assistance by way of grants to individuals who have been infected with the Hepatitis C virus as a consequence of receiving NHS treatment using contaminated blood, blood products or tissues or to their relatives.<sup>14</sup>

### **State Benefits**

**4.137** There have been a number of changes to the UK's benefits system during the period of the Inquiry's Terms of Reference and since the witness statements were taken. Infection with HIV and/or Hepatitis C did and does not automatically give rise to an entitlement to state benefits. However, the effects of either virus, whether it be the symptoms, the consequences of these or the consequences of treatment, may result in a person meeting the eligibility criteria for certain benefits. Benefits claimed by patients who gave witness statements to the Inquiry included Income Support, Disability Living Allowance, Incapacity Benefit, Housing Benefit, Council Tax Benefit, Statutory Sick Pay and Pension Credit.

**4.138** A number of patients had to claim benefits as a result of their infection with Hepatitis C and/or HIV. This was difficult for many patients who had taken pride in their work and in being self-sufficient. Many patients described having to claim benefits as degrading and humiliating. A few patients described difficulties in the process of applying for benefits and in obtaining the benefits to which they were entitled. Delays in obtaining benefits caused further financial pressure for some patients.

### **Debt**

**4.139** A number of patients had accrued debt as a result of their infection with HIV and/or Hepatitis C, mainly due to their inability to work. The uncertainty about the future also caused patients and their families to accrue debt: a couple, both diagnosed with Hepatitis C in the early 1990s (the husband was infected with Hepatitis C by his wife) thought that they were going to die. So they gave up work, went on holiday and accrued 'a lot of debt'. Being in debt caused the patients and their respective family great distress and anxiety, particularly as those who were unfit for work had no means to repay their debt. A number of patients were declared bankrupt. Others had their homes and other possessions repossessed. Some patients received financial help from family members in the form of loans or gifts. Many patients were embarrassed by their financial situation.

### ***Additional expenses***

**4.140** Witnesses spoke to having incurred the following additional expenses as a result of their infection with HIV and/or Hepatitis C:

- Travel costs and car parking charges incurred attending hospital appointments or visiting a patient in hospital.
- Prescription charges, the cost of vitamin and mineral supplements and homeopathic remedies.
- Extra heating and fuel costs (many patients described feeling the cold more than they did before), the cost of extra washing and increased bathing.
- Employing a gardener, painter/decorator or person to help with DIY, as they were now unfit to do such chores themselves.
- Increased spending as a symptom of depression.

---

<sup>14</sup> See paragraph 3.129 of Statistics chapter; [www.caxtonfoundation.org.uk](http://www.caxtonfoundation.org.uk)

## CHAPTER 5

### AN EXAMINATION OF THE EFFECTS OF INFECTION WITH HIV ON PATIENTS AND THEIR FAMILIES, INCLUDING TREATMENT

#### Introduction

**5.1** This chapter deals specifically with the evidence given by six witnesses at the Oral Hearings on their own or their relative's infection with HIV.

**5.2** The hearings of evidence on this topic took place on 7, 8, 9, 10, 14, 15, 16 and 24 June 2011. The following patients or relative witnesses<sup>1</sup> gave evidence to the Inquiry in respect of this topic:

1. Christine
2. Amy
3. Frances
4. David
5. Elaine
6. Mark

**5.3** In addition, Professor Clifford Leen, a Consultant Physician at the Regional Infectious Diseases Unit at the Western General Hospital, Edinburgh and Honorary Professor in the Department of Medicine at the University of Edinburgh provided a written report to the Inquiry and gave evidence on this topic.<sup>2</sup> He provided a clinical view on the effects of infection with HIV on patients and their families and gave evidence on treatment for HIV.

#### Christine

**5.4** Christine was 55 years old when she gave evidence to the Inquiry. She is married. At times she was assisted in the evidence she gave by her husband. Christine wished her occupation to remain confidential.<sup>3</sup> Christine's evidence was twofold: firstly in relation to their elder son's infection with HIV and Hepatitis C, and secondly in relation to her own infection with Hepatitis C, both as a result of blood products.<sup>4</sup> For the purposes of this chapter Christine's elder son will be referred to as 'John'. John died aged 20 in the mid-1990s as a result of his infections.

#### *John's diagnosis with Haemophilia A and his treatment*

**5.5** Christine has a family history of haemophilia and as she stated, 'I have lived with it all my life'.<sup>5</sup> Two of her brothers were diagnosed with severe Haemophilia A and she also has a cousin and an uncle with haemophilia.<sup>6</sup> John was born in the mid-1970s. He was born from the breech position and was bruised from the neck down. Despite Christine disclosing her family history to the doctors, John was not diagnosed with haemophilia at that time. When he was about four months old, John developed spontaneous bruising of his right cheek. Christine informed her General Practitioner (GP) about this bruising

---

<sup>1</sup> As detailed in Appendix 1, in order to preserve the witnesses' anonymity, each witness was given a pseudonym.

<sup>2</sup> Professor Leen's report [PEN.012.1044]

<sup>3</sup> Day 28, page 3

<sup>4</sup> Her evidence in relation to the latter is narrated in Chapter 6, *An Examination of the Effects of Infection with Hepatitis C on the Patients and their Families, including Treatment*, paragraphs 6.361–6.371

<sup>5</sup> Day 28, page 15

<sup>6</sup> Ibid, pages 6 and 9

and she believes that the GP thought that they had abused him. He referred John to the Royal Hospital for Sick Children in Glasgow (also known as Yorkhill Hospital) where he was found to have severe Haemophilia A. At the same time Christine was found to be a carrier of Haemophilia A.<sup>7</sup>

**5.6** As a child, John was treated for his haemophilia at Yorkhill Hospital under the care of Dr Anna Pettigrew, a clinical assistant, and as an adult at the Glasgow Royal Infirmary (GRI) under the care of Professor Gordon Lowe. In 1980 the family moved to England for a few months, but returned to Scotland as they considered that the haemophilia care was better at Yorkhill Hospital than the hospital John had attended in England.<sup>8</sup> Initially, and until about 1980, John was treated with cryoprecipitate. Christine and her husband treated their elder son as 'a normal child' and 'we never mollycoddled him'.<sup>9</sup> As a toddler he had more frequent bleeds and so he needed more treatment during this part of his life. Each treatment involved John and one of his parents attending the hospital, being admitted (sometimes after a lengthy wait at the Accident and Emergency Department) and then receiving an infusion of cryoprecipitate, which took up to an hour.<sup>10</sup>

**5.7** In 1980, when John was five years old, he received his first treatment with Factor VIII concentrate. Christine stated 'we thought it was wonderful stuff' as it could be mixed so quickly and injected there and then.<sup>11</sup> John was treated with both Scottish National Blood Transfusion Service (SNBTS) products and American Factor VIII. It was explained to Christine and her husband that the American Factor VIII was much better because, when being made up, it dissolved more easily and it seemed to act more effectively in preventing the bleed from getting any worse.<sup>12</sup> In July 1981 Christine, alongside other parents, was taught to administer Factor VIII to John so that she could give him prophylactic treatment twice a week. This helped reduce the number of bleeds that he had. If he had a breakthrough bleed, Christine gave him further injections of Factor VIII and it was only if he had a particularly bad bleed that he needed to go to the hospital.<sup>13</sup> When he was 14 years old, John learned to give himself Factor VIII and from then on he injected himself.<sup>14</sup> Both Christine and John kept a detailed record of each treatment he had, including the batch number of the Factor VIII used, and the reason for each treatment. Once completed, these records were returned to the hospital.<sup>15</sup>

**5.8** When asked if they were warned of any risks associated with Factor VIII treatment Christine replied:

My husband did ask about risks and they said that, you know, there were risks with everything that was taken. It was just kind of brushed under the carpet when he asked about it.<sup>16</sup>

Christine said in her statement that they were not warned about the risk of infection with HIV or with Hepatitis C.<sup>17</sup> She stated:

---

<sup>7</sup> Ibid, page 5–7

<sup>8</sup> Ibid, pages 9–11

<sup>9</sup> Ibid, page 12

<sup>10</sup> Ibid, pages 11–14

<sup>11</sup> Ibid, page 16

<sup>12</sup> Ibid, page 20

<sup>13</sup> Ibid, pages 21–23; Christine's Witness Statement; a 'breakthrough bleed' happens when bleeding occurs despite prophylaxis treatment.

<sup>14</sup> Day 28, page 24

<sup>15</sup> Ibid, Page 23

<sup>16</sup> Ibid, page 17

<sup>17</sup> Christine's Witness Statement

The doctors were perceived by us to be gods. We trusted them and didn't question the treatment they were giving John. We accepted that they were giving him the best treatment available because that was what they told us.<sup>18</sup>

**5.9** Christine said that she was never warned that there was an increased risk from prophylactic treatment (as opposed to providing treatment in response to actual bleeds). She said that had she been warned of this risk she would never have given her son prophylactic treatment.<sup>19</sup>

**5.10** As Christine stated, what makes 'the whole tragedy' even harder to accept is that mothers and fathers may have given their own children Factor VIII infected with HIV.<sup>20</sup> She stated:

We thought we were doing the best thing for our children by giving them something that allowed them to live a more normal life. All the children in the training group from Yorkhill used the same batch of Factor VIII ... I think that all of the children have now died.<sup>21</sup>

**5.11** Christina Leitch, who worked as a senior social worker at Yorkhill Hospital during the mid-1980s, spoke of the guilt some parents experienced about giving their own children treatment with infected blood products. She also described the guilt some mothers, who were carriers of haemophilia, felt at having passed haemophilia to their children. She stated:

But for many of the parents that was greatly exacerbated by the fact that they were treating their children at home, and although they had not chosen the treatment, had ... no real responsibility for what that treatment had done, I think for many of them it was an incredibly painful thing to look back and consider that, whilst they had been giving their children treatment and believing that that was for the best, in reality that's what had made them ill and which might ultimately cost them their lives. And I think that that was a terrible burden for people to have to live with.<sup>22</sup>

**5.12** Having discovered that she was a carrier of haemophilia, Christine and her husband decided not to have any more children. They adopted a younger boy.<sup>23</sup>

### *John's diagnosis with HIV*

**5.13** In about 1984 or 1985, when John was about nine or ten years old, he and Christine attended one of his regular clinic appointments at Yorkhill Hospital. While they were waiting, Dr Pettigrew came and spoke to them. She apologised for the delay in them being seen by a doctor and explained that there were a lot of children there with HIV and that John was one of those children. Although John gave regular blood samples at his clinic appointments, Christine and her husband were unaware that he had been tested for HIV. Christine cannot remember who she saw after speaking to Dr Pettigrew. She remembers that she was told that the doctors did not know what effect the HIV would have, but that they would closely monitor him. She does not remember being told anything else about the virus or how John had acquired it.<sup>24</sup>

---

<sup>18</sup> Day 28, page 18

<sup>19</sup> Ibid, page 22

<sup>20</sup> Christine's Witness Statement

<sup>21</sup> Ibid

<sup>22</sup> Day 38, pages 135–136

<sup>23</sup> Ibid, pages 38–39

<sup>24</sup> Ibid, pages 39–43



**5.14** Christine returned home in shock and told her husband the news. As she stated, 'our world crashed down around us'.<sup>25</sup> They had heard that HIV was affecting people in Africa and in the gay community but that was all they knew.<sup>26</sup> John's diagnosis was 'devastating to the family'.<sup>27</sup> Christine and her husband had planned to adopt the sibling of their adopted son but as a result of John's diagnosis with HIV, they abandoned this plan. They were worried that John would feel 'pushed out' if they adopted two natural brothers.<sup>28</sup> They also considered that it was unfair to bring another baby into the house, not knowing what the effects of their elder son's diagnosis were likely to be. She said, 'We had to try and stabilise what we had and not add any more factors into it'.<sup>29</sup>

**5.15** Christine and her husband were not offered any counselling or support at the time of John's diagnosis with HIV. They were encouraged by both their GP and the staff at the hospital to keep his diagnosis with HIV a secret. At the time, Christine and her husband were running their own business and they lived in a small community. Their GP was concerned that they might be ostracised. He advised them that he had sealed John's case notes so that only senior partners in the medical practice could see them. The hospital staff seemed not to know much about HIV, and seemed keen to avoid any panic and to prevent anyone being shunned. The only person Christine and her husband told was one of Christine's brothers as he too was diagnosed with HIV at about the same time as John's diagnosis with it.<sup>30</sup> Christine understands why the doctors thought it was right to keep John's diagnosis a secret but, as she stated:

[The secrecy] was the worst part of our lives. We always had to put on a happy front to the general public. If we could change anything we would not have had the secrecy. Why should we have stigma? We didn't do anything wrong. Other people did something wrong. But they encouraged us to keep quiet about it. The secrecy was like a powder keg.<sup>31</sup>

**5.16** After John's diagnosis with HIV, Christine and her husband felt very isolated. They withdrew into their own family unit. They rarely went out and as a result they lost a lot of friends. When they did go out with friends, they found themselves becoming morose. She stated: 'The only person I could speak to about [John's] HIV was my husband and vice versa. The stress of only being able to speak to each other built up inside us and we took it out on each other'.<sup>32</sup> This caused Christine and her husband to argue with each other. Christine's husband tried to drown out the bad news by drinking too much alcohol. The stigma surrounding HIV was the most difficult aspect for them. Christine stated that they asked themselves constantly why they and John should be stigmatised when they had done nothing wrong.<sup>33</sup> Within a few months of John's diagnosis, Christine and her husband began to realise how serious HIV was from what they read in the newspapers and saw on the television. HIV was known then as the 'gay plague' and it was also linked to drug users in America.<sup>34</sup>

---

<sup>25</sup> Christine's Witness Statement; Day 28, pages 44–45

<sup>26</sup> Ibid, page 44

<sup>27</sup> Christine's Witness Statement

<sup>28</sup> Day 28, page 45

<sup>29</sup> Ibid, pages 45–46

<sup>30</sup> Ibid, pages 46–48

<sup>31</sup> Christine's Witness Statement

<sup>32</sup> Day 28, page 50; Christine's Witness Statement

<sup>33</sup> Day 28, pages 49–50

<sup>34</sup> Ibid, pages 51–52

**5.17** The Inquiry recovered some newspaper articles from around this time and examples of some of these are:

- Two newspaper articles in February 1985 reported that both fire brigade and ambulance unions had advised their members to avoid direct mouth-to-mouth resuscitation for fear of catching AIDS.<sup>35</sup>
- An article in *The Sun*, dated 19 February 1985, entitled 'Gays put Mrs Mopps in panic on AIDS' reported that cleaners at a theatre where gay actors were performing feared that sweeping up after a show would put them at risk of catching AIDS. The article reported that the cleaners were issued with rubber gloves and bottles of disinfectant.<sup>36</sup>
- In July 1985, the *Birmingham Post* published an article entitled 'Killer AIDS virus has hit 10,000 in Britain'.<sup>37</sup>
- On 3 September 1985 *The Standard* reported that the recording of a television interview with 'two AIDS victims went ahead today using volunteers after some Yorkshire TV staff refused to work in the same studio'.<sup>38</sup>
- In October 1985 a letter was printed in *The Sun* from 'Name and address supplied'. It was headed 'So cruel' and stated 'Your report (*The Sun*, September 23) gives the impression haemophiliacs are spreading AIDS. This is wrong and also cruel because these people suffer enough already. People are born with haemophilia. Their blood doesn't clot and they have injections to keep them alive. Now they are taking a gamble with their lives every time they have an injection. Haemophiliacs have enough to worry about without people spreading these malicious accusations'.<sup>39</sup>
- In July 1986 *The Sun* printed an article entitled 'Swimmers in danger from AIDS'. It reported that an expert, Professor Zuckerman, had warned that people with cuts and bruises could catch AIDS if they go swimming in badly cleaned pools.<sup>40</sup>

**5.18** The above articles are only a very small sample of the large number of reports about HIV which appeared in the press in the mid-1980s. As Dr Patricia Wilkie stated, in the mid-1980s, 'There was never a day when the press didn't have something. And it wasn't just the tabloids, it was also the broadsheets'.<sup>41</sup> Christina Leitch said, 'Some of the adverts on television would have struck fear into most people's hearts. It was a time where there was almost ... hysteria'.<sup>42</sup>

**5.19** About six months after John's diagnosis with HIV in 1984 or 1985, Christina Leitch set up a parents' support group. In her evidence she explained why she did so:

People were terrified that anyone would find out the child had HIV because of the impact that would have on the child and themselves.

So we are talking about parents who are living with an incredibly painful situation as parents and as families, but were also having to deal with this incredible fear

---

<sup>35</sup> [DHF.001.9322]

<sup>36</sup> [DHF.001.9316]

<sup>37</sup> [DHF.001.7443]

<sup>38</sup> [DHF.001.7790]

<sup>39</sup> [DHF.001.8015]

<sup>40</sup> [DHF.002.4628]

<sup>41</sup> Day 32, pages 27–28

<sup>42</sup> Day 38, page 131

of other people finding out, worried sick about how their children and they would be treated if they did. There were some schools that were anxious about having children with haemophilia and looking for reassurance around those things. It seemed to me that those parents were in an exceptionally difficult situation and unable to talk to anyone very much about it.

There was also a tension that had built up between the families and the hospital. Parents spoke about feeling angry. Sometimes that could be openly expressed and sometimes not, but expressed in different ways. There was a tension at times between the families and the hospital, and I think that was natural and understandable when parents felt that the hospital, the NHS, that was there to treat and care for their children had let them down, was how it was perceived.<sup>43</sup>

**5.20** Ms Leitch stated that, as well as allowing parents to talk to other parents, the support group also allowed couples to talk to one another. She stated:

[P]arents couldn't talk about something like [HIV] when they had children about the house. There was that awful fear that they couldn't even have a conversation within their own homes at the time. So I think the importance of giving them a safe place to talk was quite important and I think the need for that gradually came to an end.<sup>44</sup>

**5.21** Initially, Christine found the parents' group helpful, but there were only a few parents in the group and, once their children started to die, the group quickly broke up.<sup>45</sup>

**5.22** For a few years John remained unaware that he was HIV-positive. He carried on life 'as an active boy who had haemophilia'.<sup>46</sup> He enjoyed sports, particularly playing football and riding his bicycle and he was a member of the Scouts. He later went on to become the youngest Scout leader in Scotland.<sup>47</sup> He was a sociable boy who enjoyed spending time with his friends.

**5.23** Christine and her husband decided not to tell John's teachers about his diagnosis with HIV as they were worried that he would be ostracised, and might have to go to another school. Their worries were based on the difficulties Christine and her husband had, before John started school, persuading the staff that they could admit a boy with severe haemophilia. Prior to John's attendance there, his school had no experience of haemophilia and so Dr Pettigrew and one of the nurses attended to provide staff with information and reassurance about haemophilia. Christine and her husband also promised the school that, if anything happened to John, they would respond immediately. In addition, Christine usually had to accompany John on school trips. After his diagnosis with HIV, Christine was aware that the school had 'blood kits' which contained everything needed to deal with blood spills without the risk of contamination. John had also been taught from a very early age to try to keep his bleeds to himself. In 1987 there was concern about John experiencing a number of nose bleeds at school, and he was referred to a Consultant Ear Nose and Throat (ENT) Surgeon about this.<sup>48</sup>

---

<sup>43</sup> Ibid, pages 131–132

<sup>44</sup> Ibid, page 134

<sup>45</sup> Day 28, pages 67–68

<sup>46</sup> Ibid, page 52

<sup>47</sup> Ibid, page 115

<sup>48</sup> Ibid, pages 53–56; Excerpts from medical records recovered in respect of John

*John's symptoms of HIV*

**5.24** Until late 1985, John appears to have had no symptoms which could be ascribed to HIV. He attended the hospital regularly for monitoring of his condition. This monitoring included blood tests. In December 1985 it was noted that John had been well, apart from 'recent respiratory tract infections' and poor hearing.<sup>49</sup> The poor hearing was subsequently found to be caused by 'glue ear' and, in 1990, he had grommets inserted to rectify this. In 1986, John had a persistent cough from about October until December.<sup>50</sup> These symptoms may have been attributable to John's infection with HIV or they may have been childhood illnesses which are fairly common in children under 10 years of age. In June 1987 he was referred to a dermatologist due to a large, unsightly wart on his left middle finger which was causing him some discomfort. The dermatologist was advised that John was a 'high risk patient' and from this he surmised that John was HIV-positive.<sup>51</sup> The dermatologist thought that the wart was best left alone. In November 1987 John experienced recurrent tonsillitis, recurrent staphylococcal infections in his ear-lobe and dull hearing in his left ear.<sup>52</sup> Blood tests taken at this time showed that he had a 'healthy' T4/T8 ratio.<sup>53</sup> John was still experiencing recurrent tonsillitis in March 1988. At that time he also had an upper respiratory tract infection. He also continued to experience 'very troublesome' hand warts which were treated with liquid nitrogen. It was known that HIV-infected persons might be more susceptible to hand warts.<sup>54</sup>

**5.25** In April 1989, when John was 14 years old, he was admitted to Yorkhill Hospital with a four-day history of a sore throat, facial pain with facial swelling and purulent (containing pus) nasal discharge. On admission he was found to have a high temperature. Examination and x-rays revealed that he had acute maxillary sinusitis. He was treated for this with antibiotics. Christine stated that the first time John was admitted to Yorkhill Hospital after his diagnosis with HIV he was put into a side room on his own.<sup>55</sup>

He was not allowed to leave the room. Everything in the room was covered in polythene so that he couldn't infect anything. The television and video and all the medical equipment were covered in polythene. The staff would come into the room wearing masks and gowns when they gave him food. They used to put his food into a disposable container before they gave it to him so that it could be thrown away when he had finished eating. One day the home tutor (hospital teacher) dropped a pencil and she refused to pick it up and a member of staff had to go and put gloves on before they picked it up. My son had to grow up like this. He was treated by the NHS as though he was a leper.<sup>56</sup>

**5.26** Christina Leitch described a very similar episode. She stated that she was asked to visit a boy with HIV who had been admitted to hospital the night before. The patient was in a room on his own. She was told that she was expected to wear a disposable gown when she went into his room. Ms Leitch thought this unnecessary and so she refused to wear a gown. When she went into the room, the boys' parents were there. They too had

<sup>49</sup> Day 28, page 57; Excerpts from medical records recovered in respect of John

<sup>50</sup> Day 28, page 58; Excerpts from medical records recovered in respect of John

<sup>51</sup> Day 28, page 59; Excerpts from medical records recovered in respect of John

<sup>52</sup> Day 28, pages 60–61; Excerpts from medical records recovered in respect of John

<sup>53</sup> Day 28, page 61; Excerpts from medical records recovered in respect of John; The ratio of T4 cells ('helper' cells also known as CD4 cells) to T8 cells ('suppressor' cells also known as CD8 cells) provided a measure of the effectiveness of the immune system.

<sup>54</sup> Day 28, pages 61–62; Excerpts from medical records recovered in respect of John

<sup>55</sup> Day 28, page 63

<sup>56</sup> Christine's Witness Statement; Day 28, pages 63–64

been told to wear gowns. She said that the parents were very upset that their son had been admitted to hospital. She stated:

And they felt that their son was being treated as though he was the carrier of the plague. And he was sitting in bed and a nurse came in completely gowned and she had his lunch on a plate, one of the normal hospital plates, but with a paper plate on top of it, and she told him to hold out his hands and she slid the paper plate onto his hands. And I looked at the paper plate and there were – it was baked beans and mince and mashed potatoes. And I remember looking and thinking “How do you eat that from a paper plate?” And he looked and sort of laughed and said, “This is what it’s been like.” And while he was laughing, it was so obvious that he was deeply hurt by it. It was absolutely horrible and that incident has – it has remained very clearly in my mind for a very long time.<sup>57</sup>

**5.27** Christine used to take meals into the hospital for John so that ‘he could have his meal as a normal person rather than eating it out of this disposable dish’.<sup>58</sup> Christine saw other children with haemophilia being treated in the same way. Unsurprisingly, the parents complained about the way their children were being treated. The staff said that they were trying to be safe. At this time John was still unaware that he was HIV-positive. Christine does not know how he felt about this treatment, stating that John ‘was a boy that just took everything in his stride’.<sup>59</sup>

### *John is told of his diagnosis*

**5.28** In 1989, when John was 14 years old, Christine and her husband made the important decision to tell him about his HIV status. By this time they had known that John was infected with HIV for about four or five years. During this period they had been told by someone at the hospital that John had been infected by Factor VIII. Christine cannot remember when they were told this.<sup>60</sup> The reason Christine and her husband decided to tell their elder son that he was HIV-positive was that they were concerned that he might become sexually active. Christine’s husband discussed it with the doctors at one of John’s clinic appointments and they agreed that he was at an age where, possibly, he should be told. The doctors offered to tell John but Christine’s husband decided that they would tell him, as a family, at home. They were not given any advice by the hospital about how to tell him. Christine and her husband did not know any more about the virus than what they had read or seen on the television. They did not know what the long-term prognosis was for John. Christine’s husband explained to John that he had contracted HIV from infected Factor VIII. John burst into tears and asked when he was going to die.<sup>61</sup> John had heard about HIV by this time but all he knew about it was that it was ‘a gay plague’.<sup>62</sup> After being told his diagnosis, John was very quiet and withdrawn for a while. Christine and her husband tried to encourage him, as much as they could, to carry on as normal.<sup>63</sup> Christine stated that John then ‘pulled himself together and did cope, and just got on with his life for a long time, which was hard for a vulnerable 14-year old’.<sup>64</sup> As far as Christine

---

<sup>57</sup> Day 38, pages 142–143

<sup>58</sup> Day 28, page 64

<sup>59</sup> *Ibid*, page 65

<sup>60</sup> *Ibid*, page 112

<sup>61</sup> *Ibid*, page 65

<sup>62</sup> *Ibid*, page 66

<sup>63</sup> *Ibid*, page 70

<sup>64</sup> *Ibid*, page 65

is aware, John never told anyone that he was HIV-positive.<sup>65</sup> There was no support group for the children. Christine stated that if the HIV-positive children discussed their diagnosis with each other, they kept it to themselves and never told their parents that they did so.<sup>66</sup>

**5.29** Christine recalled that, in 1989, John took part in a clinical trial with a drug intended to fight infections of the lung. This is likely to have been a trial of Co-trimoxazole to prevent pneumocystis carinii pneumonia (PCP).<sup>67</sup> Christine does not know if John received the placebo or the drug during this trial.<sup>68</sup> In about 1990 joint clinics were started at Yorkhill Hospital which were attended by a doctor from Ruchill Hospital as well as a doctor from Yorkhill Hospital. At that time, Ruchill Hospital treated adults and children with HIV and AIDS. At a joint clinic in April 1990, John was noted to be in excellent health and asymptomatic in respect of his HIV infection. His CD4 cells remained at 'an acceptable level of 580 cells/mm<sup>3</sup>' with a CD8 count of 807 cells/mm<sup>3</sup>.<sup>69</sup>

**5.30** The CD4 cell count test became available in the mid-1980s. This was one of the earliest tests available to assess the status of the virus. In the early days of treatment it was one of a number of factors considered by clinicians when deciding when to treat a patient. The other factors were the toxicity of the early drugs to treat HIV, resistance to the treatment, and treatment fatigue versus the benefit of treatment over a long period of time. Clinicians' knowledge and understanding of the significance of a CD4 cell count was not as good in the mid-1980s as it is now. It evolved over the years and the CD4 cell count became one of the best measures of assessing the progression of the infection.<sup>70</sup> Now, the *British HIV Association guidelines for the treatment of HIV-1-infected adults with antiretroviral therapy 2008* recommend that treatment should be started in all patients with a CD4 count of fewer than 350 cells/uL (or cells/mm<sup>3</sup>) and in those patients with certain clinical symptoms.<sup>71</sup>

**5.31** John's doctors considered that there was no indication for antiretroviral therapy but stated that they would continue to monitor him closely. In October 1990, John experienced an episode of discharge from his left ear. At this time, Christine told the doctors that she was concerned that John was experiencing night sweats. Although he was telling her he was not having such episodes, he was putting his sheets out very regularly for washing. John was very private about such matters and Christine did not like to press him about this.<sup>72</sup> She stated:

It was a difficult balance. We had a relationship that if anything really worried him, we knew he would come and talk to us but we never pushed him on it. We asked him; if he denied it that was fine, even though we had other ideas on it.<sup>73</sup>

<sup>65</sup> Ibid, page 67

<sup>66</sup> Ibid, page 69

<sup>67</sup> Co-trimoxazole was used by clinicians to treat patients with PCP before HIV was identified, Professor Leen – Day 33, page 38. After PCP was diagnosed in the first patients with AIDS in the early 1980s, Co-trimoxazole was prescribed for patients with HIV as a prophylactic treatment, Professor Leen – Day 33, page 34

<sup>68</sup> Day 28, pages 70–71

<sup>69</sup> Ibid, page 73; Excerpts from medical records recovered in respect of John

<sup>70</sup> Professor Leen – Day 33, pages 35–36

<sup>71</sup> Symptoms included Kaposi's sarcoma, HCV-related comorbidity, Hepatitis B and Hepatitis C: British HIV Association guidelines for the treatment of HIV-1-infected adults with antiretroviral therapy 2008 [PEN.012.1130] at 1136

<sup>72</sup> Day 28, pages 74–75

<sup>73</sup> Ibid, page 75

**5.32** When checked in September 1990 John's CD4 cell count was 380 cells/mm<sup>3</sup>. The issue of whether to start treatment with Zidovudine (also known as AZT) was discussed with Christine and John, and it was decided at that time not to commence this treatment. At the time it was difficult to know when to start therapy as there was a body of opinion that Zidovudine therapy should be started when the CD4 cell count fell below 500 cells/mm<sup>3</sup>. However, that was not the policy of Ruchill Hospital. Although staff at the hospital started therapy with Zidovudine earlier than they had done before, they were concerned about the resistant strains of the virus.<sup>74</sup> Christine stated that they were told that if John started Zidovudine treatment, he would have to continue with it. If he subsequently stopped the treatment the virus would become resistant to the drugs and he would be unable to use that treatment again. Christine stated that it was John's decision when to start treatment and she and her husband supported his decision. On hearing that it was not 'absolutely imperative' that he start treatment, John decided not to at that time.<sup>75</sup>

**5.33** The development of antiretroviral therapy for HIV is discussed in Chapter 8, *Knowledge of HIV/AIDS Now*, paragraphs 8.35–8.40. In 1986 and 1987 there was uncertainty about the effectiveness of Zidovudine as a treatment for HIV. It caused a number of side-effects and it required to be taken every four hours. It was difficult for clinicians, like those treating John, to decide when to treat a patient who was still asymptomatic or very mildly symptomatic. Patients who were treated in the 1980s and early 1990s received very little support in adhering to their medication. Understandably, there was, and there continues to be, difficulty persuading children and teenagers, in particular, to take such medication.<sup>76</sup>

**5.34** In the early days of treatment with Zidovudine, there was bad publicity surrounding it. A television programme showed people that it was a toxic medication and reported that clinicians were being rushed into prescribing it. As Zidovudine was not particularly effective, patients sometimes saw their friends taking it and dying and so they associated the cause of the death with the drug. This caused patients to resist being prescribed Zidovudine.<sup>77</sup>

### *John's treatment with Zidovudine*

**5.35** In early 1991, when John was 15 years old, he started treatment with Zidovudine. It was noted that he remained 'in general good health' but that his CD4 count had fallen to 200–300 cells/mm<sup>3</sup> on the last two occasions it had been measured.<sup>78</sup> He was also prescribed nebulised Pentamidine as prophylactic treatment against PCP. The Zidovudine treatment consisted of tablets which John had to take five times a day. He had to take one of the tablets at school, but managed this without any problem. Christine and her husband encouraged John to keep taking the medication and, on the odd occasion, he needed reminding to do so.<sup>79</sup>

**5.36** In September 1991 John was noted to be very well apart from a recent upper respiratory tract infection. He had a number of lesions and red patches on the roof of his mouth which were thought to be viral in nature. His CD4 cell count remained stable, being 217 cells/mm<sup>3</sup>.<sup>80</sup> Between September and December 1991, John had a sore throat.

<sup>74</sup> Ibid, page 75; Excerpts from medical records recovered in respect of John; Chapter 8, *Knowledge of HIV/AIDS Now*, para 8.37

<sup>75</sup> Day 28, pages 76–77

<sup>76</sup> Professor Leen – Day 33, pages 62–63

<sup>77</sup> Ibid, pages 23–24

<sup>78</sup> Day 28, page 77; Excerpts from medical records recovered in respect of John

<sup>79</sup> Day 28, pages 78–79

<sup>80</sup> Ibid, pages 79–80

His appetite reduced and he lost about two and a half kilograms in weight. His recent CD4 count was 127 cells/mm<sup>3</sup> and Dr Gibson, consultant haematologist, was of the view that this, together with John's weight loss, was 'a rather concerning feature'.<sup>81</sup> Dr Gibson was concerned that if John's HIV disease was progressing it might produce more marrow toxicity related to his Zidovudine treatment and so she reduced his dose of Dapsone<sup>82</sup> (which John was by this time being prescribed to prevent PCP) to minimise the combined marrow suppressive effect of these drugs.

### *John's treatment at the Glasgow Royal Infirmary*

**5.37** In December 1991, as John was almost 17 years old, he was referred to adult services and to Professor Lowe, a consultant physician, Haemophilia and Thrombosis Unit at the GRI. In her referral letter Dr Gibson noted that John was positive for the antibody to Hepatitis C.<sup>83</sup> Christine stated that she did not know until after John died that he had Hepatitis C. She does not think that John knew either as she is sure he would have told them if he had known. After John died, Christine asked a nurse if John had contracted Hepatitis C. The nurse replied in 'a matter of fact, off the cuff' remark, 'Oh yes, all of our boys have got it'.<sup>84</sup> In her referral letter Dr Gibson stated that John was 'a delightful young man' and that she would be anxious to hear how he progressed.<sup>85</sup>

**5.38** John attended his first appointment at the GRI with his mother on 22 January 1992. There they met Professor Lowe and a doctor from the Infectious Disease Department at Ruchill Hospital. They also met the unit staff including nursing staff, physiotherapy staff and the medical social worker. John was noted to have a small boil on his right chin from shaving, wax in his ears, bilateral increase in tonsils and a few patches of redness on his palate. It was planned that he would continue to attend for monthly review.<sup>86</sup> In June 1992 he was noted to be experiencing sensitivity to light affecting his right eye. He was referred to an ophthalmology doctor who specialised in ocular disease in immune-compromised patients.<sup>87</sup> The doctor concluded that there was no evidence of ocular disease and he considered John's symptoms might be stress related.<sup>88</sup> Christine thought that John's eye problems were due to spending too long in front of a computer.<sup>89</sup>

**5.39** That summer John went on holiday with his family to Spain. During this holiday he was bothered with a cough which produced green spit for about two weeks. He also suffered from diarrhoea and developed a nose bleed which caused him to cough up some blood. When he attended his clinic appointment on 21 July 1992 he was noted to have some seborrhoeic dermatitis (an inflammatory skin condition) on his face.<sup>90</sup> Christine took John to a Chinese Herbal doctor who concluded that his dermatitis was caused by a reaction to the ingredients of food from a burger chain which John was eating regularly at that time. The dermatitis cleared up when he stopped eating this food. With regard to his chest symptoms, John underwent a chest x-ray and tests revealed that there was a heavy growth of haemophilus influenzae (a bacterium associated with acute and chronic respiratory infections). He was prescribed antibiotics for this. In August

<sup>81</sup> Ibid, page 80; Excerpts from medical records recovered in respect of John

<sup>82</sup> Dapsone was a second-line treatment for PCP

<sup>83</sup> A blood test dated 15 June 1990 confirmed that John was positive for the antibody to the Hepatitis C virus

<sup>84</sup> Day 28, page 18

<sup>85</sup> Ibid, page 81; Excerpts from medical records recovered in respect of John

<sup>86</sup> Day 28, pages 82–83; Excerpts from medical records recovered in respect of John

<sup>87</sup> Day 28, page 84; Excerpts from medical records recovered in respect of John

<sup>88</sup> Ibid

<sup>89</sup> Day 28, page 85

<sup>90</sup> Ibid, page 85; Excerpts from medical records recovered in respect of John



1992 John experienced a recurrence of sinusitis.<sup>91</sup> There was some improvement in his condition but he continued to be troubled by a cough. On one occasion his cough was blood-stained. On 11 September 1992 John was admitted to the GRI with lower left lobe pneumonia. He gave a history of an increasingly severe cough productive of green sputum, breathlessness principally on exertion, lethargy, malaise and occasional vomiting after paroxysms of coughing. It was thought that his infection was bacterial. He was prescribed antibiotics and was discharged from hospital when his condition improved.<sup>92</sup> In October 1992, John was admitted to hospital briefly and was prescribed further antibiotics as a sample once again showed haemophilus influenzae, and also candida albicans (a fungus which causes yeast infection). At this time, John also had facial folliculitis (inflammation of hair follicles causing rash, itch and pimples) and fungal infections of his thumbnails.<sup>93</sup> Christine described John's nails as looking as if they were rotting. John was referred to a dermatologist, who noted that, in addition to the fungal infections of his nails, John had developed a rash on both his scrotum and face. He was prescribed Terbinafine (an antifungal treatment). It was recommended that John undergo regular liver function tests while being on this medication.<sup>94</sup> On 12 November John was admitted to hospital with a haemophilus influenzae chest infection. Once again he was treated with antibiotics and was discharged home five days later.<sup>95</sup> Around this time, he underwent hyperbaric oxygen treatment which caused a great improvement in his chest symptoms.<sup>96</sup>

**5.40** John continued to suffer from a cough and chest symptoms. He also suffered from a right middle-ear infection. In March 1993 he was prescribed Zalcitabine in addition to Zidovudine.<sup>97</sup> According to a letter from a consultant physician at Ruchill Hospital to Professor Lowe, Zalcitabine was 'released on a compassionate basis' for John.<sup>98</sup>

**5.41** John was admitted to hospital on two separate occasions towards the end of March 1993. Both times he was admitted due to coughing up blood following bouts of coughing. During the first admission he was treated with high dose Factor VIII 12-hourly and, after his condition stabilised, he was discharged home the next day. The second time he was admitted to hospital, he had a high temperature. He underwent a bronchoscopy which revealed bronchiectasis (damage to the lung tissue leading to a build-up of mucus, which in turn makes the airways more prone to infection). John was prescribed intravenous antibiotics, and when his condition improved, after about four days, he was discharged home. During this admission, it became apparent that he had not been taking his anti-viral medication regularly. Prior to his discharge Christine spoke with Professor Lowe. He stressed to Christine how important it was that John keep taking his medication although he appreciated that, as he was an adult, it was harder for them to enforce this.<sup>99</sup>

**5.42** Christine and her husband had been unaware that John had stopped taking his medication. It had been emphasised to him that he needed to take his medication regularly, and that once he had started taking it he would need to keep taking it, otherwise the HIV

<sup>91</sup> Excerpts from medical records recovered in respect of John

<sup>92</sup> Day 28, pages 87–88; Excerpts from medical records recovered in respect of John

<sup>93</sup> Day 28, pages 86–87; Excerpts from medical records recovered in respect of John

<sup>94</sup> Day 28, page 87; Excerpts from medical records recovered in respect of John

<sup>95</sup> Day 28, pages 88–89; Excerpts from medical records recovered in respect of John

<sup>96</sup> Day 28, page 73

<sup>97</sup> See Chapter 8, *Knowledge of HIV/AIDS Now*, para 8.41 for information about Zalcitabine and other drugs used to treat HIV

<sup>98</sup> Day 28, page 89; Excerpts from medical records recovered in respect of John; the use of drugs being released on a compassionate basis may also be referred to as 'on a named patient basis'. 'Named patient basis' meant that, if a clinician considered that a patient would benefit from a medication prior to it being licensed, the clinician could request access to the medication for this patient from the manufacturers.

<sup>99</sup> Day 28, pages 92–93; Excerpts from medical records recovered in respect of John

symptoms would return with 'a vengeance'.<sup>100</sup> Despite this advice, John stopped taking the antiviral medication. The medication made him feel tired and sick. Christine and her husband often asked John if he had taken his medication and he told them that he had, when they now know he had not. She believes that John did not tell them he had stopped his medication as he could see how much stress they were under and did not wish to bother them.<sup>101</sup>

**5.43** In April 1993, John was suffering from nausea. Professor Lowe reduced his dose of Zidovudine and prescribed him Maxolon (an antiemetic medication) for this. In addition to these medications, he continued to be prescribed Zalcitabine and Co-trimoxazole. John continued to suffer from a regular cough, a rash on the right hand side of his face and neck and a fungal infection of his thumbnails.<sup>102</sup>

**5.44** In June 1993, John left school aged 18 years. Despite all his absences from school due to hospital admissions and appointments, he successfully obtained the exam results he needed to go to college to study an HNC in computing as he had hoped to do.<sup>103</sup> Christine stated that at school John was 'quite switched on' and, with the help of a friend who brought work home for him, he always made the effort to catch up on schoolwork that he had missed.<sup>104</sup> One summer, John went to a summer camp in the USA with other boys with haemophilia from Yorkhill Hospital. They were accompanied by staff from the hospital. The trip was partly funded by the Round Table, a local charity in Glasgow, and by the MacFarlane Trust.<sup>105</sup>

**5.45** In the summer of 1993 John went on holiday for a week to Europe with the Scouting group. He was unwell while he was there. When he attended a clinic appointment that August, he had marked facial dermatitis on the right side, looked tired and pale and had lost about 14lbs in weight. He continued to have chest problems, with a productive cough and purulent sputum. He was noted to have crepitus (crackling) and rhonchi (a coarse rattling sound) in his left lung. He had a lesion on his tongue. Dr Kennedy, the Consultant who saw John at this appointment, wrote to John's GP: 'I did not like the look of [John] today.' Dr Kennedy prescribed him a course of Erythromycin (an antibiotic used to treat bacterial infections).<sup>106</sup>

**5.46** In about August 1993 John started the computing course at college. His health stabilised for a while and he gained some weight. He also obtained part-time work delivering meals for a restaurant three or four nights a week. He thoroughly enjoyed this work, but he found it tiring and it took its toll on him.<sup>107</sup> In December 1993 John went with the family on holiday to Spain. This was the last family holiday they had together. John had a cough, diarrhoea and a nose bleed while they were away but Christine stated that, despite this, he had a good time.<sup>108</sup> On his return he was prescribed a course of antibiotics for chest symptoms and mouth ulcers. The treatment improved both.<sup>109</sup>

---

<sup>100</sup> Day 28, page 91

<sup>101</sup> Ibid, page 91

<sup>102</sup> Ibid, pages 94–95; Excerpts from medical records recovered in respect of John

<sup>103</sup> Day 28, page 82

<sup>104</sup> Ibid, page 62

<sup>105</sup> Ibid, pages 95–96

<sup>106</sup> Ibid, page 97; Excerpts from medical records recovered in respect of John

<sup>107</sup> Day 28, page 98; Excerpts from medical records recovered in respect of John

<sup>108</sup> Day 28, pages 98–99

<sup>109</sup> Ibid, page 99; Excerpts from medical records recovered in respect of John

**5.47** On 24 May 1994, John was admitted to the GRI as a result of gastrointestinal haemorrhage. On admission he had a two-day history of vomiting 'coffee ground fluid' (indicative of digested blood in the stomach) associated with general weakness, lack of energy, fever and an intermittent cough. His haemoglobin was found to be low, and he was transfused with three units of packed cells and Factor VIII. He was given a course of Magnapen (a penicillin-type antibiotic used to treat bacterial infections) and oral iron. He underwent an isotope red blood cell scan which showed bleeding in the ascending colon. He also underwent a colonoscopy. He was discharged on 22 June. At discharge, his haemoglobin had increased. He suffered a cough for three days with greenish spit, and was prescribed a further course of Amoxicillin.<sup>110</sup>

**5.48** After completing his computer course, John went to work full-time for a family-run catering business in their office. He went to work no matter how ill he felt.<sup>111</sup> He was keen to obtain a second job working part-time with a retail company. Christine and her husband were concerned about how tired John became working in the one job. They sat down with him and discussed the pros and cons of a second job, particularly with regard to his tiredness. John then agreed not to pursue the second job. It was apparent from Christine's evidence that she and her husband took great care to allow their elder son to lead as full and as independent a life as he wished which, in the circumstances, must have been difficult. She stated:

[W]e had to let him live his life. We didn't know how long it was going to last. We knew it would eventually – we weren't sure, we didn't know, so he had to make his own decisions. And he did appreciate our comments, when we felt we had to intervene, that we weren't nagging, that it was just constructive.<sup>112</sup>

**5.49** John managed to work at the catering business for three months. The owners of the business knew that he had haemophilia, but did not know that he had HIV. They were very supportive of him. There were times when they telephoned Christine's husband and asked him to come to collect John as he was so unwell. At times, Christine's husband had to collect him from work and take him straight to the hospital. John's employers were very upset when they had to let him go due to his ill-health.<sup>113</sup> One can only imagine how disappointed John must have felt.

**5.50** In the summer of 1994 John stopped taking his antiretroviral medication again, and his prophylactic Co-trimoxazole. Christine stated that, once again, he became 'fed up with having to take tablets all the time and how ill they were making him feel'<sup>114</sup> and 'the side effects were quite straining on him'.<sup>115</sup> He was trying to work, trying to just be normal and he felt the side-effects were just bringing him down. She stated:

He was fed up. I do not think that he thought it through properly when he came off the medication. We could not keep track because when he became an adult patient we lost control of managing his care. The hospital would not tell us anything. We could not search his room and count the tablets. He had made up his mind. He was very fit and went to the gym. Maybe he thought he would survive without medication. Perhaps he thought he was indestructible.<sup>116</sup>

---

<sup>110</sup> Day 28, page 99; Excerpts from medical records recovered in respect of John

<sup>111</sup> Day 28, page 100

<sup>112</sup> Ibid, page 101

<sup>113</sup> Ibid, pages 101–102

<sup>114</sup> Ibid, page 102

<sup>115</sup> Ibid, page 91

<sup>116</sup> Ibid, page 92

**5.51** John's condition continued to deteriorate. He suffered from repeated chest infections.<sup>117</sup> In about October or November 1994 he was admitted to Ruchill Hospital with PCP. This was successfully treated. In November John was still slightly wheezy, had a rash on his back, oral candidiasis (thrush) and a fungal skin eruption over his shoulder.

**5.52** In January 1995 John was admitted to Ruchill Hospital due to vomiting and a joint bleed. He underwent a gastroscopy and was found to have developed two ulcers.<sup>118</sup> His lungs were badly damaged. John was told that the ulcers could be treated. A few hours after the gastroscopy, he became paralysed and he could only move his head. The doctors did not know what had caused this. By this time he had lost a lot of weight and was unable to do anything for himself. He felt degraded. The doctors told Christine and her husband that John did not have long to live and so, on 13 February, they took him home.<sup>119</sup>

**5.53** At home, Christine and her husband made up a bedroom for John downstairs. Initially they tried to care for him themselves, but it became impossible for them to do so. He needed assistance with everything. Ruchill Hospital organised nurses to care for John overnight so that Christine and her husband were able to sleep. The only thing John asked them to do was to take him to the toilet during the night. He used a commode, and it took two people to lift him onto it so as not to hurt him.<sup>120</sup>

**5.54** John started having nose bleeds. Christine telephoned the GRI for help, and three days later someone came to the house to see him. This person cauterised the bleed, but by this stage John had blood in his lungs. He developed a further lung infection. He needed oxygen, and this was provided for him at their home. On 7 March 1995 John died while holding his parents' hands. Before dying he said, 'Dad, just leave me, I'm ok' and he told his parents that he loved them.<sup>121</sup>

**5.55** About two days after John's death, the possibility of a post mortem being carried out was raised with Christine and her husband. Initially they were not keen on this, but after discussions with the hospital social worker, they agreed to it in the hope that the findings might assist other patients with HIV. There was another child with similar symptoms to John and they hoped to help this child. Six months later Christine and her husband went to Ruchill Hospital for the post mortem results. They were told that the post mortem report had been mislaid. They returned at least two further times to obtain the result, but each time they were again told it was mislaid. After Christine gave evidence the Inquiry investigated this matter further. In September 2011 the Inquiry obtained a copy of the post mortem result for John, and it was then forwarded on to Christine. The post mortem concluded that John died as a result of pneumococcal pneumonia and bronchiectasis.<sup>122</sup>

**5.56** John's funeral was attended by family, friends and representatives of the Scout Association. Nobody at the funeral knew that he had died of AIDS. They understood that he had died of pneumonia. In 1996 both Christine and her husband were tested for HIV, and were found to be negative. A few times Christine had received a needle stick injury whilst giving John his medication.

---

<sup>117</sup> Excerpts from medical records recovered in respect of John

<sup>118</sup> Post mortem report for John

<sup>119</sup> Day 28, pages 102–103; Excerpts from medical records recovered in respect of John

<sup>120</sup> Day 28, pages 103–104

<sup>121</sup> Ibid, page 105

<sup>122</sup> Post mortem report for John

**5.57** Christine and her husband were offered counselling by the MacFarlane Trust but she stated, 'it is not easy to talk to a stranger in a hotel'.<sup>123</sup> Their GP told them that they were the best counsellors for each other, but Christine feels that that advice perpetuated the secrecy. With the benefit of hindsight Christine feels that they were wrong not to accept counselling; especially in respect of their younger son. She stated that they had 'guilt trips' about how they had handled things.<sup>124</sup> She stated, 'Even now I burst into tears, when I think about the past, which may not have happened if we'd had someone to talk to at the time for advice'.<sup>125</sup> Christine and her husband subsequently attended five bereavement weekends organised by the MacFarlane Trust. Christine described these as weekends 'without any secrecy'.<sup>126</sup> She found it very helpful to meet others in the same situation, and to speak openly.

**5.58** At the time of John's death, his brother was 14 years old. He was unaware that his older brother had HIV, and when John died, he was told that he had died of pneumonia. Christine and her husband told their younger son when he was in his 20s that his older brother had died as a result of HIV. With hindsight, Christine believes that they should have told him the truth sooner. Their younger son has been deeply affected by his brother's death and has been troubled ever since. He suffered from acute depression during his teenage years. He continues to grieve for his brother. He is now an alcoholic.<sup>127</sup>

**5.59** In 1997 when Christine's younger son joined the Army, Christine and her husband were unable to envisage their future in a house without children and so they became foster parents. Since then they have fostered three children long term for about six or seven years, and cared for other children in between at weekends and overnight.<sup>128</sup>

**5.60** About a week before John died, Christine and her husband discovered that a girlfriend of John was pregnant. Christine's husband had spoken to John about this and he told his father that he had had a sexual relationship with her, but that he had practised safe sex. This girlfriend came to John's funeral. She later had a son. Christine and her husband built up a relationship with her. She had an HIV test which was negative. Eventually Christine and her husband started to see their grandson and he started to visit them regularly. He is now a teenager. He has his own room in their home and comes on holiday with them. He has the same mannerisms as John. Christine stated, 'He is a great wee lad and it makes my day when I see him'.<sup>129</sup> She believes that he and their foster children have helped them cope with their immense grief at the loss of John.

### *Financial impacts of John's infection with HIV*

**5.61** In the early 1990s Christine 'tried to top up my life insurance policy'. Her GP refused to sign the application form to enable her to do this. She believes that the GP was concerned that she too had acquired HIV. Eventually the matter was cleared up but it was 'a very long, drawn-out affair'.<sup>130</sup>

**5.62** John received two payments from the MacFarlane Trust. He received the first payment of £20,000 in 1990 when he was 15 years old and the second payment of £20,000 in

---

<sup>123</sup> Christine's Witness Statement

<sup>124</sup> Ibid

<sup>125</sup> Ibid

<sup>126</sup> Day 28, page 116

<sup>127</sup> Ibid, pages 116–117; Christine's witness statement

<sup>128</sup> Day 28, pages 117–118; Christine's witness statement

<sup>129</sup> Day 28, pages 118–119; Christine's witness statement

<sup>130</sup> Day 28, pages 106–107; Christine's witness statement

1991. In order to receive the money, John had to sign a waiver saying that he would not take any further action against the UK Government in respect of contracting HIV. He had to sign this form at a solicitor's office and neither Christine nor her husband was allowed to be present when he signed the waiver. The money was to be used to buy him a car. The rest of the money was put aside for John and was used to buy something that he wanted or needed. John wanted his parents to use the money. John also received monthly payments from the MacFarlane Trust while he was alive. Christine cannot remember how much they were. Christine's grandson now receives £250 a month from the MacFarlane Trust and will continue to do so while he is in full-time education.<sup>131</sup>

## Amy

**5.63** Amy was 49 years old when she gave evidence to the Inquiry. Amy is separated and has two sons. She gave evidence about her elder son's infection with HIV from a blood transfusion. For the purposes of this chapter Amy's elder son will be referred to as 'Luke'.

### *Luke's blood transfusion*

**5.64** Luke was born in Ninewells Hospital, Dundee in the mid-1980s. He was born at 42 weeks' gestation by emergency caesarean section due to foetal distress. At section, the fluid was blood stained which was suggestive of possible placental abruption (condition in which the placenta partially or completely separates from the lining of the uterus). At birth, Luke was seriously ill. He was 'rather flat with an Apgar score of 1 at one minute'.<sup>132</sup> He was ventilated and admitted to the Special Baby Unit. In the Unit he was noted to have signs suggestive of cerebral irritation and convulsions. An ultrasound of the skull suggested cerebral oedema (excessive accumulation of fluid in the brain). He was managed with ventilation, fluid restriction and medication. He was given a loading dose of Phenobarbitone, an anticonvulsant medication. Due to low blood pressure, he received a transfusion of plasma protein solution. He was also given fresh frozen plasma. He developed a bacterial infection and then renal failure. During this time, Amy and her husband were aware how seriously ill Luke was. They were told that he was living only on a 'day-to-day' basis.<sup>133</sup> His condition improved with treatment and, 16 days after he was born, he was discharged home on medication. He was provided with a heart monitor for use when he slept or was in the pram at home.<sup>134</sup>

**5.65** Luke continued to recover at home. At a review appointment in November 1985, he was noted to be making excellent progress and Amy had no concerns about him. He was smiling, laughing, gurgling normally and was alert and lively.<sup>135</sup>

### *Luke's diagnosis with HIV*

**5.66** Some months after Luke's birth, his GP arrived unexpectedly at their home. Amy was there with her mother and Luke. The GP explained to Amy that Luke had been infected with HIV from the blood he had received at birth.<sup>136</sup> Amy was numb with shock and she

<sup>131</sup> Day 28, pages 110–111

<sup>132</sup> Day 29, pages 6–7; Excerpts from medical records recovered in respect of Luke; the Apgar test is a test to measure the vital signs of a baby at birth. Out of a potential score of 10, 7–10 is a normal score.

<sup>133</sup> Day 29, page 10

<sup>134</sup> *Ibid*, page 8

<sup>135</sup> *Ibid*, page 9; Excerpts from medical records recovered in respect of Luke

<sup>136</sup> The donor of the FFP which Luke had received was found to be infected when he subsequently donated blood again in 1986. Retrospective testing then showed that his previous donation was infected too. Excerpts from medical records recovered in respect of Luke; Day 29, pages 13–14

could not believe what she was hearing.<sup>137</sup> She found the news 'really devastating'.<sup>138</sup> At that time the fact that Rock Hudson had AIDS was a big news story and that was what Amy knew about HIV. Her GP did give her some information about HIV but Amy cannot now remember what he told her. She remembers that he told her that Luke should attend hospital appointments. The GP then left the house, and Amy had to tell her husband when he came home from work. The news was particularly devastating for them given all they had been through since Luke's birth. She stated that, having watched their son improve after his difficult birth, they reverted to being concerned for his future. They were aware that medications for HIV were not good at that time.<sup>139</sup>

**5.67** Luke's GP referred him to a Consultant Paediatrician at Ninewells Hospital. In his letter of referral he wrote that Amy and her husband were 'naturally ... upset and anxious about the future'.<sup>140</sup> At Luke's first appointment with the Consultant Paediatrician on 1 April 1986 he was tested for HIV and found to be positive.<sup>141</sup> Amy and her husband were told the result of this test at the next hospital appointment in May. The doctor had the impression that they had accepted Luke's diagnosis 'extremely well' and had 'a realistic understanding of the problems'.<sup>142</sup> Amy remembers that, around this time, they were advised to be careful to avoid secondary infection. They were told to use gloves and bleach.<sup>143</sup>

### *Luke's early childhood*

**5.68** From May 1986 onwards Luke attended regular appointments at the hospital. These were between three to six months apart depending on his state of health.<sup>144</sup> At each appointment, Luke underwent blood tests and his glands and general welfare were checked. Amy usually took him to these appointments by bus. She had to take time off work to do so.<sup>145</sup>

**5.69** When Luke was between two and three years of age he was diagnosed with a hearing impairment affecting both ears. Before this, he had become increasingly frustrated and had difficulty with his speech. When he was about three years old, Luke had grommets inserted. He was put to the end of the operation list due to being HIV-positive. When he was five years old he was given hearing aids. Amy was told that these hearing problems were a result of the difficulties he experienced immediately after his birth.<sup>146</sup>

**5.70** Amy remembers that, in the early days after Luke's diagnosis with HIV, when they attended hospital they were sometimes put in a room on their own. This made her feel isolated. On one occasion, a doctor blamed Amy for having given HIV to her elder son as he had assumed that Luke had acquired the virus from Amy's breast milk.<sup>147</sup>

**5.71** When Luke was three years old, he frequently woke up during the night and often at that time was found to be sweating excessively. Amy stated that when her elder son

---

<sup>137</sup> Amy's Witness Statement

<sup>138</sup> Day 29, page 10

<sup>139</sup> Ibid, pages 9–11

<sup>140</sup> Ibid, page 12; Excerpts from medical records recovered in respect of Luke

<sup>141</sup> Day 29, page 15

<sup>142</sup> Ibid, page 16; Excerpts from medical records recovered in respect of Luke

<sup>143</sup> Day 29, pages 15–16; Amy's Witness Statement

<sup>144</sup> Day 29, page 15

<sup>145</sup> Ibid, page 17

<sup>146</sup> Ibid, pages 17–20; Amy's Witness Statement

<sup>147</sup> Day 29, page 19

sweated 'his blankets and everything would be absolutely soaking'.<sup>148</sup> He had swollen lymph nodes on his neck and in his armpits and was thrombocytopenic (abnormally low number of platelets). As a result of this he bruised easily. At a clinic appointment in July 1988 the possibility of Luke being treated with Zidovudine, were his condition to deteriorate, was discussed with Amy.<sup>149</sup> She was told that Zidovudine had already been introduced as treatment for a few children, and was well tolerated by them. Amy was aware that Zidovudine was a new treatment for HIV and so the side-effects of it were unknown. She thought that the doctors would effectively be testing the treatment on Luke. Notwithstanding this, she was keen to try whatever might help him.<sup>150</sup>

**5.72** In July 1989 Luke's care was transferred to Dr Tarnow-Mordi, a Consultant Paediatrician. At that time he continued to suffer from thrombocytopenia, swollen glands in his neck and armpit and enlarged lymph nodes in the groin area. In about August 1989 Luke started nursery. Amy was advised by the hospital that there was no need to inform the nursery of his HIV status, since any bleeding accident should be treated uniformly for all children.<sup>151</sup>

### *Luke's treatment with Zidovudine and immunoglobulin*

**5.73** Towards the end of 1989, when Luke was four years old, he started treatment with Zidovudine. Luke had been keeping well. Amy stated that he started treatment to sustain a better chance of living, and to improve his immune system. After starting treatment his night sweats improved slightly, and occurred only once or twice a week. He was noted to have new enlarged submandibular glands (salivary glands situated beneath the floor of the mouth).<sup>152</sup>

**5.74** Luke did not like the taste of Zidovudine and he started refusing to take it. Three months after he had started the treatment, he had lost weight. His appetite was poor and he continued to have night sweats. His submandibular lymphadenopathy (swollen lymph nodes beneath floor of the mouth) was a little more marked.<sup>153</sup> With the encouragement of a star chart, Luke was persuaded to keep taking his medication and a month later he had regained some weight, and his lymph nodes remained unchanged.<sup>154</sup>

**5.75** About this time, Dr Tarnow-Mordi put Amy in touch with another family with a similarly affected child as he thought that it would be helpful for them to speak to someone in a similar situation. Amy spoke to the mother in this family. Due to the stigma attached to the virus, Amy and her husband only told their siblings and their parents of Luke's diagnosis with HIV. They did not tell any of their friends or their aunts and uncles. They did not wish their elder son to be isolated. To this day only their immediate family know that he is HIV-positive. Amy felt that the only people she could speak to about Luke's condition were her mother and her sisters. If she spoke to them about it, she felt she placed a burden on them as they were unable to speak to anyone about it. Amy found this 'hard'.<sup>155</sup>

<sup>148</sup> Ibid, page 20

<sup>149</sup> Ibid, pages 20–21; Excerpts from medical records recovered in respect of Luke

<sup>150</sup> Day 29, page 22

<sup>151</sup> Excerpts from medical records recovered in respect of Luke

<sup>152</sup> Day 29, pages 23–24; Excerpts from medical records recovered in respect of Luke

<sup>153</sup> Day 29, pages 24–25; Excerpts from medical records recovered in respect of Luke

<sup>154</sup> Day 29, page 26; Excerpts from medical records recovered in respect of Luke

<sup>155</sup> Day 29, page 26; Amy's Witness Statement



**5.76** When Luke was four years old he sustained a laceration to his forehead, and it bled profusely. Amy took him to the Accident and Emergency Department of Ninewells Hospital. The nurse treating him did not wear gloves so Amy had to divulge that he was HIV-positive, so that the staff would protect themselves. She found this experience distressing. Had the nurse taken the appropriate precautions, she would have been spared having to explain Luke's HIV status.<sup>156</sup>

**5.77** In early 1991, when Luke was five years old, he started taking nightly Co-trimoxazole as prophylaxis against PCP.<sup>157</sup>

**5.78** Amy struggled to cope with the implications of Luke's diagnosis with HIV. She stated that she tried to put his diagnosis behind her, but every hospital visit, which she attended alone with him, was a constant reminder of his condition. She said, '[T]here would be times I would be going up there on my own and I would have [Luke] in my arms ... and I would just be crying on the bus coming home'.<sup>158</sup> 'I was hurting inside, unhappy, bitter and angry at all that has happened'.<sup>159</sup> Amy was referred for counselling in 1987 but, at that time, she was not ready for 'anything like that'.<sup>160</sup> So, in the early days of Luke's diagnosis with HIV, the only support she received was when she spoke to the doctor at his hospital appointments. When Luke was about five years old, Amy became unhappy in her marriage. She did not see the point in carrying on and tried taking her own life 'as I had just had enough .... Looking back I know it was the wrong thing to do but then it was like I had just given up'.<sup>161</sup>

**5.79** In July 1991, Luke was prescribed immunoglobulin. The immunoglobulin was administered to him at the hospital by a drip and each treatment would take about two hours.<sup>162</sup> Initially Luke was prescribed this once a month but in 1996, as he had remained so healthy with a steady CD4 count, it was reduced to once every three months.<sup>163</sup> The doctors advised Amy that they wanted Luke to have this treatment as prophylaxis against bacterial infections. Intravenous immunoglobulin was widely used to treat idiopathic thrombocytopenia purpura (an autoimmune disorder causing a reduction in platelets) in the general population, as well as in those who are HIV-infected. In children there were some positive experiences with using immunoglobulin treatment. Current practice does not include the use of intravenous immunoglobulin in HIV infection, except for severe parvovirus infection (a common infection also known as 'slapped cheek disease') and, rarely, intractable thrombocytopenia.<sup>164</sup> Luke continued to receive infusions of immunoglobulin until 1997.<sup>165</sup>

### *Luke at school*

**5.80** When Luke was five years old he started school. Only the headteacher at the school knew about his infection with HIV. The school had policies and procedures in place which meant that all blood spillages were dealt with in the same way. Luke's headteacher was told about his infection for two reasons: first, to explain why he was often absent from

<sup>156</sup> Day 29, page 27; Excerpts from medical records recovered in respect of Luke

<sup>157</sup> Day 29, pages 27–28; Excerpts from medical records recovered in respect of Luke

<sup>158</sup> Day 29, page 29

<sup>159</sup> Amy's Witness Statement

<sup>160</sup> Day 29, page 29

<sup>161</sup> Amy's Witness Statement

<sup>162</sup> Day 29, pages 31–32

<sup>163</sup> Excerpts from medical records recovered in respect of Luke

<sup>164</sup> Professor Leen – Day 33, page 28 and his Report [PEN.012.1044] at 1050; Statement of Clinical Specialist Nurse

<sup>165</sup> Day 29, page 35; Statement of Clinical Specialist Nurse

school to attend hospital appointments and, secondly, so that she could warn the family if there was an outbreak of chickenpox in the school. Chickenpox can be severe in patients with HIV so any time there was an outbreak of chickenpox at the school, Amy had to take Luke immediately to the hospital. There he was treated with Zoster Immunoglobulin injections, which he received in the top of his legs, and he was prescribed a five-day course of oral Acyclovir (a drug used to treat infections caused by viruses, including chickenpox).<sup>166</sup>

**5.81** Luke enjoyed school and ‘sailed through’ despite his hearing difficulties.<sup>167</sup> When he was seven and a half years old, a specialist nurse joined the local HIV multidisciplinary service as part of a community nursing team. Her remit was to provide information, care and support for HIV-positive patients and their families. She used to arrange Luke’s monthly appointments for his treatment with immunoglobulin. She also saw both of them at his hospital appointments and was always contactable, even outwith normal working hours. She has been, and remains, a good support to both Amy and Luke.<sup>168</sup>

**5.82** During his childhood, Luke suffered from polyps in his nose. Amy described the effects of this as ‘it was always like he was choked up’.<sup>169</sup> He was referred to an Otolaryngologist when he was young for adenoidectomy but, due to his low platelet count, the Otolaryngologist was unwilling to operate. When Luke was older he underwent surgery to cauterise the polyps.<sup>170</sup>

**5.83** In about 1996 Amy and her husband separated. Amy stated that she and her husband ‘drifted apart’.<sup>171</sup> She believes that Luke contracting HIV was a major factor in their separation. Since their separation, Amy and her husband have maintained a good relationship for the sake of their children and the children remain close to their father and his family.

### *Luke’s treatment with antiretroviral medication*

**5.84** In October 1997, Luke’s immunoglobulin treatment was stopped and he was prescribed dual antiretroviral therapy of Zidovudine and Lamivudine. Lamivudine was similar to Zidovudine, in that it was another NRTI.<sup>172</sup> It was introduced as treatment for HIV in about 1995.<sup>173</sup> Luke continued to suffer from enlarged lymph nodes under his arms and in his groin but was otherwise well.<sup>174</sup>

**5.85** In September 1998, when Luke was 13 years old, Dr Tarnow-Mordi and Luke’s parents decided that he should be told that he was HIV-positive. They agreed that it would be better if Dr Tarnow-Mordi explained this to him at the family home.<sup>175</sup> In October 1998, Dr Tarnow-Mordi and the specialist nurse visited Amy, her husband and their sons at home. In his letter to Luke’s GP about this visit, Dr Tarnow-Mordi wrote:

I saw [Luke] recently at home .... We went over the reasons for [Luke’s] regular attendances at the hospital and his frequent medicines and in particular I

<sup>166</sup> Day 29, pages 34–35; Statement of Clinical Specialist Nurse

<sup>167</sup> Day 29, page 32

<sup>168</sup> Ibid, page 33 and page 37; Statement of Clinical Specialist Nurse

<sup>169</sup> Day 29, page 45

<sup>170</sup> Ibid, page 45

<sup>171</sup> Amy’s Witness Statement

<sup>172</sup> NRTI – Nucleoside Reverse Transcriptase Inhibitor, one of six classes of antiretroviral drugs now used to treat HIV. See Chapter 8, *Knowledge of HIV/AIDS Now*, para 8.35

<sup>173</sup> Professor Leen’s Report [PEN.012.1044] at 1055

<sup>174</sup> Excerpts from medical records recovered in respect of Luke

<sup>175</sup> Ibid

explained the HIV virus which is inside his white cells and that the drugs he is taking is helping to control this virus and prevent it from damaging his white cells further. We emphasised the need for secrecy about his diagnosis outside the family because people have been and still are sometimes very cruel about this condition because of their own fear of catching it. [Luke] seemed to understand what was said and to accept it very well and his parents seemed satisfied that he had made a good start in understanding his diagnosis. They feel prepared to build on this beginning and answering any question he may have in the future with further assistance from ourselves and yourself whenever appropriate.<sup>176</sup>

**5.86** Amy and the doctors felt the need to emphasise keeping Luke's diagnosis a secret due to the stigma about HIV. Amy has always told Luke that, if the fact he has the virus should become known to others, he should never feel guilty as it was not his fault that he became HIV-positive.<sup>177</sup> It was apparent, as Amy gave her evidence on this matter, that the stigma surrounding the virus and the need to protect her elder son from this has affected her greatly.

#### *Luke's treatment with triple therapy*

**5.87** In November 1998, Luke's viral load showed an increasing level. Dr Tarnow-Mordi decided that it was appropriate to change his treatment from dual therapy to triple therapy, namely Stavudine, Didanosine and Nelfinavir.<sup>178</sup> It was arranged that he start this treatment in the near future. Stavudine and Didanosine are NRTIs. Nelfinavir is a protease inhibitor. Protease inhibitors became available to treat HIV in about 1995, and more generally in 1996, and were usually added to whatever treatment a patient was receiving. The era of Highly Active Antiretroviral Therapy (HAART), involving treatment with up to three drugs, arrived in the second half of the 1990s.<sup>179</sup> Around this time, a new laboratory technique was able to measure the viral load of an HIV patient, and this confirmed the extent of the replication of the viral particles of HIV.<sup>180</sup> The arrival of protease inhibitors heralded a marked improvement in the treatment of HIV. Professor Leen stated that, at the time, some patients were so ill that clinicians thought they would not survive. Some got married in the hospital as they thought they were going to die. They now have children and grandchildren. Professor Leen described it as 'an amazing time' which changed the face of HIV and AIDS completely.<sup>181</sup>

**5.88** In December 1998 Luke contracted a chickenpox-type rash. He was admitted to the hospital for a week's treatment with Acyclovir, and was then discharged home where he took oral Famciclovir (another medication used to treat viral infections, such as chickenpox) for a further seven days. During his admission Luke remained well and his rash resolved uneventfully. While he was an in-patient, Dr Tarnow-Mordi took the opportunity to change Luke's antiretroviral therapy to the new triple regime of Stavudine, Didanosine and Nelfinavir and to increase his dose of Co-trimoxazole. Initially, Luke vomited the Nelfinavir due to its unpleasant taste, but he started taking it with milk which helped. Having told Luke about his HIV status the previous week, Dr Tarnow-Mordi found it helpful to explain to him why he was changing his medication in terms of his underlying

<sup>176</sup> Day 29, pages 40–41; Excerpts from medical records recovered in respect of Luke

<sup>177</sup> Day 29, page 42

<sup>178</sup> Excerpts from medical records recovered in respect of Luke

<sup>179</sup> HAART – Highly Active Anti-Retroviral Treatment. See Chapter 8, *Knowledge of HIV/AIDS Now*, paras 8.43–8.44, where this triple therapy is described

<sup>180</sup> Professor Leen – Day 33, pages 40–41; and his Report [PEN.012.1044] at 1051 and 1052

<sup>181</sup> Professor Leen – Day 33, page 45

virus condition. In his letter to Luke's GP about this admission Dr Tarnow-Mordi wrote 'I don't think he understands the full implications, but he does know that he has HIV and that we are giving him life long drug medicines to keep the virus under control'.<sup>182</sup>

**5.89** Three weeks after starting the triple therapy, Luke's viral load showed a significant reduction, and his CD4 count had increased.<sup>183</sup> In September 2000, his dose of Co-trimoxazole was stopped as there was concern that this was the cause of his low neutrophil count.<sup>184</sup> Luke kept well and continued to attend three-monthly review appointments.<sup>185</sup>

**5.90** Luke left school after fifth year and went to college to complete a one-year computer studies course.<sup>186</sup>

**5.91** In January 2002, Luke attended his first appointment with a new Consultant at the Adults' Infectious Disease Clinic. He was always accompanied to these appointments by one of his parents.<sup>187</sup> Having had such a good relationship with Dr Tarnow-Mordi, Luke's relationship with this new Consultant was not good. Neither he nor Amy liked this new Doctor. They did not like 'his bedside manner'.<sup>188</sup> At this appointment Luke's blood test results were noted to be very encouraging, with a CD4 count of 682 and an undetectable viral load.<sup>189</sup>

### *Luke's non-adherence to his treatment and the subsequent deterioration in his condition*

**5.92** Amy stated that it was always 'a struggle' to encourage Luke to keep taking his medication.<sup>190</sup> She and her husband used to try to encourage and advise him to take his medication but, when he became a teenager, Amy felt that it was his choice and she could only advise him.<sup>191</sup> In the mid-1990s clinicians received frequent complaints from patients about the number of tablets they had to swallow and the large size of them. Nelfinavir was particularly difficult to take.<sup>192</sup> Some tablets could be crushed but this depended on the bioavailability of each type. Others could be dissolved in a liquid, but this would involve extra time and effort, and might not mask the bad taste.

**5.93** In November 2004 Luke stopped taking his antiviral medication. He found the tablets difficult to swallow, did not like the taste of them, and, at one point, told his mother that he did not see the point in taking them.<sup>193</sup> Luke started to miss clinic appointments. He often made up excuses to not attend.<sup>194</sup> In November 2005 Luke attended a clinic appointment accompanied by his father. His CD4 cell count in September 2005 was 323 cells/mm<sup>3</sup> compared to 724 cells/mm<sup>3</sup> measured in August 2004. His viral load in September 2005 was 15,000 copies per ml. 'Viral load' in this context, is a test that measures the amount of HIV virus in the bloodstream. The result is measured in copies (of the virus) per millilitre of blood and it can range from over 1,000,000 copies/ml to fewer than 50 copies/ml. The latter measurement is classed as undetectable. Luke did not appear to be suffering from

<sup>182</sup> Day 29, pages 43–44; Excerpts from medical records recovered in respect of Luke

<sup>183</sup> Day 29, page 45; Excerpts from medical records recovered in respect of Luke

<sup>184</sup> Day 29, page 46; Excerpts from medical records recovered in respect of Luke

<sup>185</sup> Day 29, page 47

<sup>186</sup> Ibid, page 48

<sup>187</sup> Ibid, page 47

<sup>188</sup> Ibid, page 55

<sup>189</sup> Ibid, page 47; Excerpts from medical records recovered in respect of Luke

<sup>190</sup> Day 29, page 44

<sup>191</sup> Ibid, page 50

<sup>192</sup> Professor Leen – Day 33, page 49

<sup>193</sup> Day 29, page 48

<sup>194</sup> Ibid, page 55

any symptoms at that time. He was told that his immune system could deteriorate again to a level requiring antiviral treatment.<sup>195</sup>

**5.94** In June 2006 Amy's younger son developed chickenpox. Luke felt well but in hospital received a seven-day course of Varicella Zoster Immunoglobulin and Valacyclovir (an antiviral drug used to treat infections caused by two common viruses).<sup>196</sup>

**5.95** At a clinic appointment in December 2006, Luke told his Consultant that he was considering restarting his antiviral medication as he had suffered a few infections. At that time he had a mild seborrhoeic dermatitis on his face.<sup>197</sup> In January 2007, Luke's viral load was only 4100 copies/ml, indicating only fairly low replication of the virus. Luke was still keen to restart treatment and so was prescribed Truvada, one tablet daily, and Efavirenz, one tablet daily. Truvada contains a combination of tenofovir and emtricitabine, and both are NRTIs. Efavirenz is an NNRTI.<sup>198</sup> The principal side-effects of these medications were disturbance of renal function, and vivid dreams or even nightmares.<sup>199</sup> Luke had difficulty swallowing these tablets due to their size so he did not take them. In April 2007, the Consultant wrote to Luke advising him that the Truvada tablets could be dissolved in water, but the solution they made had a slightly bitter taste. The Consultant also wrote that he was trying to obtain Efavirenz as a liquid solution.<sup>200</sup> It seems that this did not help Luke, and he did not take these medicines.

**5.96** Between April and June 2007, Luke was prescribed Kaletra (a drug used to treat HIV containing two different protease inhibitors, lopinavir and ritonavir). When Luke attended a clinic appointment with the Consultant on 19 June, Luke told him that he had not taken any of his antiretroviral medication because he could not eat meals on a regular basis and Kaletra was required to be taken on a full stomach.<sup>201</sup> In his letter to Luke's GP about this appointment, the Consultant wrote:

Overall, I was left with the distinct impression that he is seeking excuses for not being on treatment. This is obviously a pointer to non-adherence to prescribed therapy. In such a setting, he can only breed resistance to the drugs and this would leave him in a worse position than no therapy at all.<sup>202</sup>

The Consultant advised Luke to reorganise his meal times.

**5.97** Luke attended for review by the Consultant on 6 November 2007. By this time his CD4 count had dropped to 87 and he remained underweight at 53 kilogrammes. The Consultant wrote, 'things are not going terribly well'.<sup>203</sup> He had a frank discussion with Luke. He wrote:

I have never been fully convinced that [Luke] fully understands the stark choices he faces at present. I pointed out that, in the absence of treatment, HIV could kill him in the relatively near future. However, specific treatments for HIV could prolong his life very significantly and improve his overall wellbeing. I have left him to go away and think about this.<sup>204</sup>

---

<sup>195</sup> Ibid, pages 49–50; Excerpts from medical records recovered in respect of Luke

<sup>196</sup> Excerpts from medical records recovered in respect of Luke

<sup>197</sup> Day 29, page 51

<sup>198</sup> Non-Nucleoside Reverse Transcriptase Inhibitor – the second class of antiretroviral drugs developed to combat HIV

<sup>199</sup> Day 29, page 53

<sup>200</sup> Excerpts from medical records recovered in respect of Luke

<sup>201</sup> Day 29, pages 53–54; Excerpts from medical records recovered in respect of Luke

<sup>202</sup> Day 29, page 54; Excerpts from medical records recovered in respect of Luke

<sup>203</sup> Day 29, pages 54–55; Excerpts from medical records recovered in respect of Luke

<sup>204</sup> Day 29, page 56; Excerpts from medical records recovered in respect of Luke

**5.98** The Consultant asked Luke's GP to prescribe Co-trimoxazole on a regular basis as a prophylaxis against opportunistic infections. He arranged to review Luke in January 2008 to consider a once daily single pill therapy for HIV.

**5.99** On 23 November 2007, Luke was admitted to Ninewells Hospital with breathing difficulties. He was placed in an oxygenated room and was treated with IV medication. His treatment with Co-trimoxazole was stopped on admission due to him having an adverse reaction to it. Luke was discharged home on 29 November. He was prescribed Dapsone as a prophylaxis against PCP.<sup>205</sup>

**5.100** By January 2008, Luke had gained about 2kgs in weight. Luke reported that he was able to swallow tablets and so the Consultant prescribed him Truvada, one tablet daily and Kaletra, two tablets daily.<sup>206</sup> At the next clinic appointment that February, Luke told the Consultant that he had been unable to swallow any of his antiretroviral medicines. He took a couple of the tablets to the appointment to show the Consultant how big they were. He agreed that they were 'a significant size' but commented that most of his other patients were able to swallow them without difficulty.<sup>207</sup> The Consultant suspected that Luke simply did not wish to take the tablets, and so was coming up with a variety of excuses as to why he was unable to persevere with them. The Consultant agreed to speak to the pharmacist to find out whether the pills could be crushed.

**5.101** After a clinic appointment in May 2008, the Consultant wrote that no further progress had been made. He believed that Luke had come up with a variety of excuses as to why he could not start taking the antiretroviral medication. He considered that they were all part of 'an avoidance strategy' but the underlying problem was that Luke did not wish to take the pills. Obviously, this was the Consultant's understanding of the position. Amy stated that Luke did not discuss these matters with her, and so she was unable to shed light on his thinking about this matter. The poor relationship between this Consultant and Luke will not have assisted, and the Consultant wrote:

I managed to get him to admit that in the absence of treatment he will almost certainly die fairly soon. I explained to him that taking the treatments in a half hearted manner would rapidly breed resistance to the drugs which would never work again. I told him that there was no point in us seeing him again until he is prepared to take the treatments as prescribed. I have left him with an open appointment at the clinic.<sup>208</sup>

**5.102** After this appointment the Consultant wrote to the HIV clinical nurse specialist stating that Luke was continuing to make excuses as to why he could not take his treatment. He stated, 'I think we will all have to take a step back now and let him think it over himself without any prompting or encouragement from ourselves. I suspect we may have had too much intervention and support in the past'.<sup>209</sup> He advised her to wait for Luke to make an approach to them for a clinic appointment.

**5.103** On 7 October 2008, Luke attended an appointment with the Consultant. Luke advised him that he wanted to recommence antiretroviral therapy, and that his mother would help supervise the first couple of weeks of treatment. When the Consultant asked

---

<sup>205</sup> Amy's Witness statement; Excerpts from medical records recovered in respect of Luke

<sup>206</sup> Excerpts from medical records recovered in respect of Luke

<sup>207</sup> Ibid

<sup>208</sup> Day 29, page 56; Excerpts from medical records recovered in respect of Luke

<sup>209</sup> Excerpts from medical records recovered in respect of Luke

Luke why he wished to restart therapy, Luke apparently stated that he had felt 'a bit poorly' a couple of weeks before.<sup>210</sup> The Consultant undertook to find out if Luke could crush the Truvada tablets before taking them.

**5.104** In November that year, Amy asked the Consultant if Luke could be prescribed some antidepressant medication as he was feeling low. The Consultant referred Luke to a psychiatrist for assessment for a possible depressive illness.<sup>211</sup> In his letter he wrote of Amy's 'great frustration and anger about the transfusion in 1985 and the subsequent stress amongst the entire family'.<sup>212</sup> He wondered about the cause of Luke's reluctance to take treatment. As a result of the referral letter, the local Community Mental Health Services wrote to Luke twice asking him to contact the service to make an appointment. Luke failed to do so and so he had no contact with these services.<sup>213</sup>

**5.105** Due to his failure to take his antiretroviral treatment, Luke's condition deteriorated. On 17 January 2009, he was admitted to Ninewells Hospital with a four-week history of shortness of breath. He had a cough productive of green sputum, and he became breathless on limited effort. A chest x-ray showed lingula shadowing (shadowing of a segment of the left lung). Luke admitted that he was having occasional night-time sweats. He had left-thigh paresthesia (tingling sensations). On examination he was found to be extensively cyanosed (having a bluish colouring due to lack of oxygen) in his nail beds with cold hands. A few crackling sounds were heard in the base of his right lung. An initial diagnosis of PCP pneumonia or atypical pneumonia was made and Luke was started on treatment with Co-trimoxazole at 60% oxygen and IV steroids. Luke was subsequently found not to have PCP and no cause of his chest infection was found. His treatment with Co-trimoxazole was continued and his IV steroids were changed to an oral steroid, Prednisolone. Luke was discharged home on 23 January to continue taking both these medications.<sup>214</sup>

**5.106** During this admission, Luke sent a letter to one of the doctors treating his respiratory problems. It read:

I'm writing to you as regards myself being under [the Consultant]. I feel communication has broken down between us. I feel it hard to open up and express my feelings. I'm starting to have negative thoughts about the outcome of my visit before I've even seen [the Consultant]. I feel a change could do me good.<sup>215</sup>

**5.107** As a result of this letter, Professor Nathwani, a Consultant Physician, started treating Luke in respect of his HIV in place of the previous consultant.<sup>216</sup>

**5.108** In early February 2009, Luke was admitted to hospital again due to a flu-like illness.<sup>217</sup> His symptoms were arthralgia (severe pain in a joint or joints), fevers and feeling 'non-specifically unwell'. During this admission, Luke's liver function tests were noted to be abnormal, but they recovered. He underwent extensive investigations including tests for Cytomegalovirus, Epstein-Barr virus (both part of the herpes family of viruses), adenovirus (a

---

<sup>210</sup> Day 29, page 56; Excerpts from medical records recovered in respect of Luke

<sup>211</sup> Day 29, pages 57–58; Excerpts from medical records recovered in respect of Luke

<sup>212</sup> Excerpts from medical records recovered in respect of Luke

<sup>213</sup> Day 29, page 58; Excerpts from medical records recovered in respect of Luke

<sup>214</sup> Day 29, pages 58–60; Excerpts from medical records recovered in respect of Luke

<sup>215</sup> Day 29, page 60; Excerpts from medical records recovered in respect of Luke

<sup>216</sup> Day 29, page 60

<sup>217</sup> Day 29, pages 60–61; Excerpts from medical records recovered in respect of Luke

cause of respiratory illness) and a respiratory tract infection, all of which proved inconclusive. Luke was diagnosed as having a viral infection which resolved without treatment.

### *Luke resumes taking antiretroviral medication*

**5.109** On 11 February, Luke attended a clinic appointment. He was noted to be feeling well and had almost finished his course of Co-trimoxazole. He continued to take Prednisolone. It was planned for him to attend a further clinic two or three weeks later with a view to possibly starting antiretroviral treatment.<sup>218</sup> On 19 March, Luke attended a clinic appointment with Professor Nathwani. At this time Luke had completed his therapeutic course of Co-trimoxazole, but he continued to take one tablet of it daily as prophylaxis against PCP. Luke also started reducing his course of oral Prednisolone with a view to stopping it. Professor Nathwani prescribed Truvada and Nevirapine. Nevirapine is an NNRTI. Luke was prescribed these particular drugs as they were the only antiretrovirals Professor Nathwani could find which could be taken in a liquid preparation.<sup>219</sup>

**5.110** Luke managed to take this medication and has continued to do so. There was a marked improvement in his condition soon after starting the treatment. At a clinic appointment in April, the doctor 'was amazed at how well he [was] looking'.<sup>220</sup> He had gained 9kgs in weight and told her that he was 'feeling really well'.<sup>221</sup> He was noted to be eating well, and Amy's husband reported that he was much more talkative and outgoing. He had finished his course of steroids but continued to take Co-trimoxazole prophylaxis as his CD4 count remained below 200.

**5.111** In July 2009, Luke was suffering from a widespread rash which worsened particularly over his upper anterior chest, back and shins. It was thought to be seborrhoeic dermatitis. Luke was prescribed Itraconazole liquid preparation, Nizoral shampoo and Canesten HC (all antifungal medications).<sup>222</sup> His CD4 count remained low.<sup>223</sup>

**5.112** At a clinic appointment on 8 July 2010, Professor Nathwani thought that Luke was looking the best he had seen him look for a considerable length of time. Once again, Luke had gained weight and was generally feeling very well. He was tolerant of his medication, his last viral load was completely suppressed and his CD4 count was stable at 141. Professor Nathwani noted that there was a family history of cardiovascular disease. HIV treatment, particularly treatment with protease inhibitors, is associated with an increased risk of cardiovascular disease. This risk is increased by about 70% compared to patients in the same age and lifestyle group not receiving treatment.<sup>224</sup> Professor Nathwani asked Luke to pay particular attention to his diet and planned to monitor him from a cardiovascular point of view particularly because of his young age.<sup>225</sup> Professor Nathwani informed Luke that his care was being transferred to a new Consultant in Infectious Diseases.

**5.113** His viral load increased to 160 in September 2010, and his CD4 count was 204 at that time. In November, once again, Luke's rash worsened over his neck, his wrists and his abdomen. It also affected his eyes. The doctor was concerned that this rash was more than seborrhoeic dermatitis. One possibility was that the rash was caused by one of his

<sup>218</sup> Day 29, pages 60–61; Excerpts from medical records recovered in respect of Luke

<sup>219</sup> Day 29, pages 61–62; Excerpts from medical records recovered in respect of Luke

<sup>220</sup> Day 29, page 62; Excerpts from medical records recovered in respect of Luke

<sup>221</sup> Excerpts from medical records recovered in respect of Luke

<sup>222</sup> Ibid

<sup>223</sup> Ibid

<sup>224</sup> Professor Leen – Day 33, pages 64–65

<sup>225</sup> Day 29, page 63; Excerpts from medical records recovered in respect of Luke



medications each of which was known to sometimes cause this side-effect. The difficulty was in establishing which medication might be causing it. Luke was prescribed Daktacort cream (a hydrocortisone cream) and was told to continue using the Nizoral shampoo. As his CD4 count had been greater than 200 on two occasions, the doctor thought that it would be safe for Luke to stop taking Co-trimoxazole in the hope that this would improve his rash. He was referred to the dermatologists at the hospital for further advice.<sup>226</sup>

**5.114** When Luke was reviewed in the clinic on 15 December, his skin seemed 'to be a lot improved'.<sup>227</sup> The doctor hoped that this was due to the withdrawal of Co-trimoxazole and diagnosed Luke as being allergic to this drug. In March 2011, Luke's rash looked 'much improved' but flared up when he stopped using the Daktacort cream.<sup>228</sup> Luke's HIV viral load was noted to have fallen below 20 units in December 2010 and his CD4 count had reduced to 195. The new Consultant, Dr Evans, was a little disappointed that the CD4 count was so low. He suspected that the seborrhoeic dermatitis would not completely resolve unless Luke's immune system improved over the next couple of years.

### *The present position*

**5.115** Luke continues to attend clinic appointments every four months. When asked how her elder son is now, Amy said, 'He seems to be doing fine. He has put on weight, he is eating better. I think he appears happier within himself now'.<sup>229</sup> Generally he keeps good health.

**5.116** Luke lives with his brother. He does not work. At one time, when he received benefits, he obtained gardening work through Jobseekers. The work involved carrying heavy loads on his back. Due to his low bodyweight, Luke found this work difficult and was absent for a week. On his return to work, Amy believes that he was picked on by the person in charge and so he stopped work. Luke sometimes looks on the internet for employment, but Amy does not think that he has any plans to find work.<sup>230</sup> She believes that Luke does not want other people to see him taking medication and then ask questions about it. Luke receives a monthly allowance from the Eileen Trust. When asked how Luke spends his time Amy stated:

He doesn't really do a lot at all. He is in the house quite a lot. If he is not with me, he will maybe be with his dad or his granddad but he doesn't go out drinking or pubs or anything like that. And he has never had a girlfriend. He just sort of keeps himself to himself.<sup>231</sup>

**5.117** Amy worries about Luke because he does not have a job and has not been in a relationship. He once told her that he would never be able to have a girlfriend because he has HIV. He is concerned about being in a relationship as he feels that he would have to be open with the person about the fact that he has HIV.<sup>232</sup>

**5.118** Amy stated that she is very bitter and angry about what has happened. She feels that it should not have happened. She stated that she tries to put it behind her but that her elder son's infection with HIV has affected them all. She feels guilty that she moved

---

<sup>226</sup> Day 29, page 64; Excerpts from medical records recovered in respect of Luke

<sup>227</sup> Day 29, page 65; Excerpts from medical records recovered in respect of Luke

<sup>228</sup> Ibid

<sup>229</sup> Day 29, pages 65–66

<sup>230</sup> Ibid, page 67

<sup>231</sup> Ibid, page 67

<sup>232</sup> Amy's Witness Statement

out of the family home and left Luke living there with his brother. She would like him to try to become independent, but Luke continues to ask her to accompany him to medical appointments, and when he has to do anything in town. She stated that Luke is very quiet and reserved: 'He is in the house all the time more or less'.<sup>233</sup>

## Frances

**5.119** Frances gave evidence about her father's infection with HIV and Hepatitis C from treatment he received for Haemophilia A. For the purposes of this chapter Frances' father will be referred to as 'James'. James was born in the 1940s. At the time she gave evidence, Frances was 41 years old. She has two younger brothers.<sup>234</sup> Her father died in 1990.

### *James' diagnosis with Haemophilia A and his treatment*

**5.120** James suffered from severe haemophilia, having less than 1% clotting factor. There was no family history of haemophilia and it is thought that his development of the condition was as a result of a genetic mutation. James' mother was told that it was unlikely that James would live to beyond two years of age.<sup>235</sup> James was always treated for his haemophilia at the Royal Infirmary of Edinburgh (RIE). Initially, he was treated with snake venom (a strange but not uncommon treatment for haemophilia in the 1940s and the 1950s), then cryoprecipitate and Factor VIII when these products became available. He needed treatment at least weekly, and often several times a week. James did not have home treatment for his haemophilia until Frances was about nine years old, early treatments having been administered in hospital.<sup>236</sup>

**5.121** Due to his haemophilia, James was unable to attend school. At that time, schools were unwilling to accept children with severe haemophilia. He was home tutored for a while but he received no proper teaching and unsurprisingly he gained no formal qualifications.<sup>237</sup> His lack of schooling deprived James of the opportunity of meeting other children. He had an older sister and there were local children he knew. Despite this, James was a sociable person.<sup>238</sup> He was very active and had a real zest for life. He did not let his haemophilia hold him back.<sup>239</sup> Frances wished her father's occupation to remain confidential. Despite his lack of qualifications, James managed to teach himself a skill and use this to build up his own, successful business.

**5.122** In order to try to avoid having to go into the hospital for treatment, James used to try and treat his bleeds with rest at home. In 1971, James asked his then consultant, Dr Davies, if it would be possible for him to receive prophylactic weekly injections of cryoprecipitate to see if this would mitigate the number of spontaneous bleeds from which he suffered. Dr Davies was willing to try this on an experimental basis with a dose of six packs of cryoprecipitate weekly. In his letter to James' GP about this, Dr Davies stated that James appreciated that there was a small risk of serum hepatitis or even developing an antibody to Factor VIII from the transfusions of blood products, but he thought that this would not be greater than the risk James had, at that time, from the frequent transfusions on admission following bleeds.<sup>240</sup>

<sup>233</sup> Day 29, page 68

<sup>234</sup> Day 30, pages 3–4

<sup>235</sup> Ibid, page 11; Frances' Witness Statement

<sup>236</sup> Day 30, pages 6–7 and page 9; Excerpts from medical records recovered in respect of James

<sup>237</sup> Day 30, pages 4–5

<sup>238</sup> Ibid, pages 7–8

<sup>239</sup> Ibid, page 4

<sup>240</sup> Ibid, pages 8–10; Excerpts from medical records recovered in respect of James

**5.123** By 1975, James was able to self-administer Factor VIII concentrate in the hospital. In a report to a life assurance company, Dr Davies reported that James was in good health except for his haemophilia. He wrote, 'Apart from his haemophilia he is very fit. Nonetheless this disorder constitutes a definite morbidity and mortality risk increase even with modern therapy'.<sup>241</sup> He noted that James had moderate joint deformity from bleeds, mainly of his knees and elbows and less so of other joints. Frances stated that her father's bleeds used to slow him down and they caused him pain. He did not complain of pain but he looked drawn. After he started home treatment, he would inject himself with Factor VIII and then rest. As a result of the frequent bleeds into his joints, James developed arthritis. Frances remembers that he always had slightly bent and swollen joints, especially in his knees and elbows. James received physiotherapy for his joint problems and often wore splints, including at night. He also attended orthopaedic surgeons for treatment and was offered surgical options to treat his left elbow. James was not keen to undergo surgery and so did not pursue that option.<sup>242</sup>

**5.124** Initially, when James started home treatment, in about 1976, he treated bleeds when they occurred. Assisted by his wife, he kept a detailed record of each treatment he took.<sup>243</sup> Frances used to help him make the factor treatment up 'as it took ages to dissolve'.<sup>244</sup> James taught her how to give him an injection and, at the age of 10 years, Frances gave her first IV injection. In 1980, James had prophylactic cryoprecipitate three times a week for three weeks to try to settle a bleed in his left elbow.<sup>245</sup>

**5.125** Frances was unable to say whether James was specifically warned of any risks associated with his treatment for haemophilia but thought that he would have asked about this. She said, 'He was big on being fully informed and wasn't afraid to ask questions. So I expect that he knew whatever risks were known at the time'.<sup>246</sup> It is clear from the medical records that James took an active interest in his therapy. For example, he explored the possibility of prophylactic weekly injections of cryoprecipitate in 1971, and discussed the risk of acquiring 'serum hepatitis' or developing an antibody to the Factor VIII blood products.<sup>247</sup> At this time it is likely that Hepatitis B was the candidate virus.

**5.126** In 1980, Professor Ludlam replaced Dr Davies as the Consultant Haematologist treating James. Frances stated that her father was very happy with the care he received from Professor Ludlam and 'he had a lot of time for [Professor Ludlam]'.<sup>248</sup> In 1982, the family went on holiday to the United States. Professor Ludlam provided James with some Factor VIII to take with him. He advised James to try to avoid the commercial Factor VIII concentrates as 'they may well give you hepatitis'.<sup>249</sup> He suggested that James try to obtain cryoprecipitate for minor bleeds.

### *James' diagnosis with HIV*

**5.127** In about December 1984 Professor Ludlam told James that he had HIV.<sup>250</sup> Subsequent tests on stored samples of James' blood showed that his first positive HIV sample was on

<sup>241</sup> Day 30, pages 11–12; Excerpts from medical records recovered in respect of James

<sup>242</sup> Day 30, pages 11–15; Excerpts from medical records recovered in respect of James

<sup>243</sup> Day 30, pages 18–19

<sup>244</sup> Ibid, page 19

<sup>245</sup> Excerpts from medical records recovered in respect of James

<sup>246</sup> Day 30, page 21

<sup>247</sup> Excerpts from medical records recovered in respect of James

<sup>248</sup> Day 30, pages 16–17; Frances' Witness Statement

<sup>249</sup> Day 30, pages 20–22; Excerpts from medical records recovered in respect of James

<sup>250</sup> Day 30, page 23

20 June 1984. James had received treatment with 50 bottles of the HIV-infected batch number 0090 of Factor VIII.<sup>251</sup> Having looked at her old diary, Frances remembers that her father told her on 21 December 1984 that he was HIV-positive.<sup>252</sup> She believes that he would have told her 'very soon' after he was informed. Frances was a teenager.<sup>253</sup> At that time, James was running his own business. He had two business premises in Edinburgh and employed staff. Frances' mother did not work. About two weeks before her father told her that he had HIV, Frances heard a news item on the radio about people with haemophilia being affected by HIV in blood products. This meant that the news that her father had HIV did not come as a complete shock to Frances. James was 'quite matter of fact' about his diagnosis with HIV.<sup>254</sup> He told her the result of his HIV test, and what it meant as far as he understood it. He told her that the family would need to be tested for HIV. The risk to them all was low but there was a higher risk to Frances' mother and a risk to Frances as she had helped her father with his haemophilia treatment. He told Frances that he had to avoid blood contact with others. Because of this he moved into the spare bedroom as he used to have frequent nosebleeds. He knew that HIV would shorten his life, but was unsure about the progress of the disease. Frances recorded in her diary that her father told her that he could have five years left. James stressed to Frances that she was not to tell anyone ever about his diagnosis with HIV. He was a very private person.<sup>255</sup> She said, 'The main thing was the stress for secrecy. That seemed to be the only thing that was stressing him out'.<sup>256</sup> The family was subsequently tested for HIV at the haemophilia ward of the RIE and were all negative for the virus.<sup>257</sup>

**5.128** Initially, James only told Frances and her mother about his diagnosis with HIV. Her two younger brothers were not told. Other family members were told later. Frances described this as 'a difficult time emotionally'.<sup>258</sup> Frances' mother was upset. She 'stuck her head down and didn't talk about it at all. My mum ... wasn't much of a talker...'.<sup>259</sup> Like her husband, she was a very private person.<sup>260</sup> Sometime after James' diagnosis with HIV, he and the family were offered counselling by Billie Reynolds, the Haemophilia Sister at the RIE. James refused counselling on behalf of them all. He thought that counselling was 'a waste of time and for people who were weak ...'.<sup>261</sup>

**5.129** Frances stated that, from the time of her father's diagnosis, '[T]here was the beginning of a strange sort of role reversal'.<sup>262</sup> James was very protective of his wife, and there was a shift to the position where he and Frances protected her 'from the harsh reality of life'.<sup>263</sup> Frances used to join her father in his room in the evenings and they would talk. 'He needed someone to speak to and he spoke to me'.<sup>264</sup> She said, 'it was almost like I became my Dad's counsellor, I was the person he spoke to and made plans with. So it changed the dynamic'.<sup>265</sup> Understandably these talks took their toll on Frances. She stated:

<sup>251</sup> Excerpts from medical records recovered in respect of James; James was a member of the 'Edinburgh Cohort' – See Chapter 10, *Knowledge of the Geographical Spread and Prevalence of HIV/AIDS 2*, paras 10.16 onwards

<sup>252</sup> Day 30, page 23

<sup>253</sup> Ibid, page 22; Frances' Witness Statement

<sup>254</sup> Day 30, page 27

<sup>255</sup> Frances' Witness Statement

<sup>256</sup> Day 30, pages 23 and 27

<sup>257</sup> Ibid, page 29; Excerpts from medical records recovered in respect of James

<sup>258</sup> Frances' Witness Statement

<sup>259</sup> Day 30, page 28

<sup>260</sup> Ibid, page 32

<sup>261</sup> Ibid, page 32

<sup>262</sup> Ibid, pages 33–34

<sup>263</sup> Ibid, page 34

<sup>264</sup> Ibid, page 34; Frances' Witness Statement

<sup>265</sup> Day 30, page 34

It was very difficult because I couldn't talk to anybody about it. So ... I didn't know how to support him. I didn't know what to do. So I had this overwhelming feeling of responsibility but I didn't know how to meet it ... and I had nobody to ask.<sup>266</sup>

**5.130** Frances' schooling was affected by this too. She had always enjoyed learning but she went from being top of the class at school to struggling academically.

### *James' symptoms of HIV*

**5.131** In about 1986 James became noticeably unwell. He lost weight and his hair thinned. On 7 September 1986 he was admitted to the Royal Infirmary in Glasgow as he had blood in his urine and left-sided ureteric colic (severe pain in the region of the left ureter). He passed some blood clots and the pain settled. He was discharged the following day and attended the Haemophilia Centre at the RIE. He gave a three-week history of feeling generally unwell with malaise and tiredness. He had intermittent sweats but no real drenching night sweats. He had shortness of breath on exertion and while climbing stairs. James continued to suffer from blood in his urine and from left flank pain. On 11 September he was admitted to the RIE for treatment with bed rest, Factor VIII and Pethidine (an opioid painkiller). He recovered with this treatment and was discharged home on 13 September.<sup>267</sup>

**5.132** Three weeks later, on 3 October, James was readmitted to the RIE with recurrence of malaise and night sweats. He was also suffering from nausea, vomiting and intermittent shortness of breath. He looked generally unwell and had a mild temperature. He had palpable cervical and axillary lymphadenopathy (swollen lymph nodes in the armpit). His symptoms settled over 48 hours and he was discharged on 5 October. A provisional diagnosis of AIDS-related complex (ARC) was made.<sup>268</sup>

**5.133** In about December 1986, James was referred to the Wart Clinic at the RIE for treatment of a stubborn wart on the sole of his foot. He received regular treatment with liquid nitrogen and occasionally the wart was pared. He used salicylic acid plasters at home. Despite this treatment, by March 1987 the wart had grown larger and he had developed a new wart on the sole of his foot. The fact that he had haemophilia and was HIV-positive limited the therapeutic options available. The dermatologist treating James asked Professor Ludlam if he had any other suggestion about therapy and whether surgical treatment would be an option.<sup>269</sup> In June 1987 James was discharged from the dermatology clinic, having failed to attend his last two appointments. The doctor noted that when he had last seen James, the warts were improving and he assumed that the warts had resolved.<sup>270</sup>

**5.134** Between the autumn of 1986 and the summer of 1987, James suffered from intermittent bouts of malaise and night sweats. In June and July 1987 he suffered from persistent diarrhoea, night sweats, malaise, some weight loss and shortness of breath on exertion. Between July and October that year he continued to suffer from malaise, night sweats and occasional diarrhoea.<sup>271</sup>

---

<sup>266</sup> Ibid, page 35

<sup>267</sup> Ibid, pages 36–37; Excerpts from medical records recovered in respect of James

<sup>268</sup> Day 30, page 37; Excerpts from medical records recovered in respect of James

<sup>269</sup> Day 30, pages 37–38; Excerpts from medical records recovered in respect of James

<sup>270</sup> Excerpts from medical records recovered in respect of James

<sup>271</sup> Ibid

### *James' treatment with Zidovudine*

**5.135** By letter dated 1 October 1987, Professor Ludlam wrote to James advising him that Zidovudine was available as a treatment and that it might be of benefit to him. He asked James to attend an appointment with him on 14 October to discuss this potential treatment.<sup>272</sup> James told Frances about the possibility of treatment. She stated, 'He absolutely wanted to try whatever was going'.<sup>273</sup> At the appointment it was noted that James had had 'longstanding liver enzyme disturbances since 1983'.<sup>274</sup> Non-A non-B Hepatitis and alcohol are noted as being possible causes for this. It was noted that the three indications for James starting treatment were the fact that he had developed ARC, the fact his T4 cell count was progressively declining and HIV antigenemia (the presence of HIV antigen in the blood). On 21 October 1987, James started treatment with Zidovudine, 200 mg every four hours with a double dose at bedtime, presumably so that he could sleep undisturbed for eight hours. During the first week of treatment James experienced a metallic taste in his mouth, but appeared not to suffer from any other side-effects of the medication. James continued to suffer from occasional night sweats and fatigue.

**5.136** At the beginning of June 1988 James suffered from increasing breathlessness on exertion with occasional bouts of breathlessness whilst at rest. He had a dry cough. On 14 June he was seen by a Senior Lecturer in the Department of Respiratory Medicine at the City Hospital, Edinburgh. As well as describing the symptoms of breathlessness, James also told him that he had been suffering from lethargy for six months. James was investigated for pneumonia, particularly PCP, but these tests were negative. He was found to have mild airways obstruction and was prescribed an inhaler of Beta 2 agonist (a drug used to treat asthma). After taking this treatment for a week or so, James was 'slightly better'.<sup>275</sup> Towards the end of June 1988, he developed an upper respiratory tract infection and was prescribed Flucloxacillin for this.<sup>276</sup>

### *James' diagnosis with non-A, non-B Hepatitis*

**5.137** On 28 June 1988 James saw Dr Finlayson, a Consultant Physician at the Gastrointestinal and Liver Service at the RIE, having been referred to him by Professor Ludlam. Dr Finlayson noted that James was mildly jaundiced, his liver was 'very considerably enlarged' and his spleen was palpable. Dr Finlayson considered that James' symptoms were consistent with a diagnosis of chronic liver disease and he thought it was 'probably the consequence of a chronic non-A, non-B Hepatitis virus infection acquired from his blood product therapy'.<sup>277</sup> This was consistent with the state of knowledge about non-A, non-B Hepatitis at the time. He also considered two other possible causes of his liver disease: first, that James was developing AIDS in light of his recent respiratory illnesses and, second, that he was developing a lymphoma in relation to his HIV infection. Dr Finlayson arranged for James to undergo an ultrasound of his abdomen to look at his liver and his spleen and also to see if there were any detectable lymph nodes there. The ultrasound appearances were of diffuse liver disease but no evidence of any enlarged nodes in the upper abdomen. Dr Finlayson then wanted James to undergo a liver biopsy but he was not at all keen on this. He was aware of the risks of a liver biopsy to him, as a

---

<sup>272</sup> Day 30, page 38; Excerpts from medical records recovered in respect of James

<sup>273</sup> Day 30, page 38

<sup>274</sup> Day 30, page 39; Excerpts from medical records recovered in respect of James

<sup>275</sup> Day 30, pages 40–41; Excerpts from medical records recovered in respect of James

<sup>276</sup> Day 30, page 43; Excerpts from medical records recovered in respect of James

<sup>277</sup> Day 30, pages 44–45; Excerpts from medical records recovered in respect of James

person with haemophilia, and could not understand what the benefits would be. In the event he did not undergo a liver biopsy until the day he died.<sup>278</sup>

**5.138** In July 1988, James developed pain in the left side of his mouth. The floor of his mouth was tender and he had an ulcer of about 0.5 cm in diameter on the surface of his tongue. He was treated with Flucloxacillin and then Penicillin but neither had any effect. He was referred to the Department of Oral Medicine at the Dental Hospital in Edinburgh for advice about treatment.<sup>279</sup> He saw a consultant there. The consultant noted, on examination, that James had 'a major recurrent aphthous ulcer<sup>280</sup> which is one of the more common manifestations associated with HIV infection'.<sup>281</sup> He also noted that James showed signs of early periodontal disease which needed to be treated aggressively from a preventative point of view as it was likely to become an aggressive form of the disease. The doctor arranged for James to have routine oral hygiene care. He prescribed Corsodyl mouthwash for symptomatic relief of his mouth ulcer, which had started to heal.

### *James' treatment with Interferon*

**5.139** Without carrying out a liver biopsy, Dr Finlayson and Professor Ludlam were unable to make a definitive diagnosis of the cause of James' liver disease. They both agreed that a liver biopsy 'would not be without hazard' due to James' severe haemophilia, his prolonged prothrombin time (a measure of the time blood takes to clot) and his propensity to allergic reactions to Factor VIII. Accordingly, they decided to treat him for non-A non-B Hepatitis. In about October 1988, James started a trial of three million units of Interferon treatment, three times a week. Professor Ludlam advised James' GP that it was possible that James might 'be a little upset by the treatment and develop flu-like symptoms'.<sup>282</sup> He planned to reduce the treatment if these side-effects were troublesome. Frances remembers her father taking the Interferon treatment. She said, 'it made him feel quite ill and he had flu-like symptoms. He was very tired and had dreadful diarrhoea'.<sup>283</sup> He continued to work throughout the treatment. Frances stated that her father had a very strong work ethic and 'if he could stand up he went to work'.<sup>284</sup>

**5.140** In about January 1989, James suffered from a bad head cold. He was prescribed Ampicillin (an antibiotic used to treat bacterial infections) for this and the cold resolved. Professor Ludlam saw James in January 1989, and noted that he had made no improvement after the trial of Interferon and so Professor Ludlam stopped this treatment.<sup>285</sup>

### *The deterioration in James' condition*

**5.141** In 1989 James' breathlessness, from which he had suffered since about September of the year before, started to worsen. He remained tired and lost a lot of weight.<sup>286</sup> He was referred to the Department of Respiratory Medicine Clinic at the RIE and underwent a number of investigations there, including a chest x-ray, blood tests and measuring of his transfer factor for carbon dioxide. In May 1989, tests revealed that James was anaemic and this was thought to be the cause of his breathlessness at that time. James was reassured

---

<sup>278</sup> Day 30, pages 43–45; Excerpts from medical records recovered in respect of James

<sup>279</sup> Excerpts from medical records recovered in respect of James

<sup>280</sup> An aphthous ulcer is also known as a canker sore. It is a type of mouth ulcer and presents as a painful open sore

<sup>281</sup> Excerpts from medical records recovered in respect of James

<sup>282</sup> Day 30, pages 46–47

<sup>283</sup> Ibid, pages 47; Excerpts from medical records recovered in respect of James

<sup>284</sup> Day 30, page 47

<sup>285</sup> Ibid, pages 47–48; Excerpts from medical records recovered in respect of James

<sup>286</sup> Excerpts from medical records recovered in respect of James

that he did not have any chronic infection in his lungs, although he was warned that this remained a possibility.<sup>287</sup>

**5.142** Around this time, James also suffered from a sore throat and a cough. He was tired and his cervical glands were swollen. A throat swab was taken and he was prescribed Cephalexin (a drug used to treat bacterial infections). On 2 June 1989 James discussed an impending family holiday with the doctor he saw at a clinic appointment. He told the doctor that he was very keen to go to Spain with his family; he considered that it might be the last holiday he would have with them. He realised that the trip would curtail investigations into his condition and that he might develop other infections or medical problems.<sup>288</sup> The day after this discussion James was admitted to the RIE with a 24-hour history of non-productive cough, increased breathlessness, several episodes of vomiting and a macular rash (a rash characterised by small flat spots). On admission his temperature was 40°C. James underwent a number of investigations. Bronchoscopy confirmed a diagnosis of PCP. He was treated with high doses of intravenous Co-trimoxazole. This was discontinued on 12 June following which James received a week's course of high dose oral Co-trimoxazole. In addition he was transfused with two units of red cells. He underwent a marrow aspirate and trephine (a biopsy of bone marrow sample) which revealed moderately hypocellular (containing fewer than the normal number of cells) marrow. This is a known side-effect of treatment with Zidovudine. James' treatment with Zidovudine was stopped. He was discharged home on 13 June and at that time was prescribed oral Co-trimoxazole, Flucloxacillin, Lactulose (a medication used to treat constipation) and Bisacodyl (a laxative drug). It was planned that James be prescribed a Pentamidine nebuliser as prophylactic treatment for PCP as soon as the equipment for it became available.<sup>289</sup>

**5.143** While he was an in-patient being treated for PCP, Frances' two brothers and her mother left to go on holiday to Spain. James did not disclose to them how seriously unwell he was. A day or two after his discharge he flew out to Spain to join them. Frances remembers driving him to the airport. She did not go on this holiday as she had to sit exams.

**5.144** Frances stated that she was getting on 'badly' in her courses due to her father's illness. During his admission to hospital, James told one of the doctors that Frances was sitting exams at that time. This doctor wrote a letter addressed 'To whom it may concern' at the place where Frances was studying explaining that James was an in-patient in the hospital and that Frances was under external pressure. He asked that, with this in mind, 'a compassionate attitude' be taken to her exam results.<sup>290</sup> Frances also spoke to her tutor about the pressure she was under. She failed the four exams she sat that year.<sup>291</sup>

**5.145** Frances 'really struggled' with her courses.<sup>292</sup> She just managed to pass the exams at the end of first year, but she failed her second year exams twice. She considers that, as a result of her father's illness, she had quite a different student experience to that of her peers, and she did not lead a normal student life. She used to return home a lot. She felt separate from her peers as they seemed to be out having fun, drinking and partying while she felt 'distracted' and was trying to deal with her father's illness.<sup>293</sup>

<sup>287</sup> Ibid

<sup>288</sup> Day 30, page 48; Excerpts from medical records recovered in respect of James

<sup>289</sup> Day 30, pages 49–50; Excerpts from medical records recovered in respect of James

<sup>290</sup> Excerpts from medical records recovered in respect of James

<sup>291</sup> Day 30, pages 50–51

<sup>292</sup> Ibid, page 51

<sup>293</sup> Ibid, pages 51–52



**5.146** In July 1989 James suffered from abdominal distension, constipation and nausea. He looked anaemic and slightly jaundiced. He developed a small abscess at the site of the bone marrow biopsy procedure. He was prescribed antibiotics for this and it improved. On 23 July, James was given nebulised Pentamidine with no ill effects. His oral Co-trimoxazole was stopped and he continued to receive doses of Pentamidine instead. He continued to suffer from abdominal distension, constipation and tiredness. He developed a further rash. It was suggested that he see Dr Finlayson again, but James was not keen to do so as he did not wish to have a liver biopsy.<sup>294</sup>

**5.147** On 30 August 1989 James met with Billie Reynolds, the Haemophilia Sister. She recorded their discussion in the clinical notes:

Spoke with [James] today. He expressed some wishes regarding his impending demise. He does not want an autopsy, and doesn't wish his wife to be approached on this subject. He is concerned about the writing on the death certificate. Was re-assured about wording on the death certificate.

[Frances] would like a screen placed over the door of the cubicle to ensure privacy when he is very ill.

He has given his consent for us to tell any patient that enquires about him, what is wrong, when he is very ill.<sup>295</sup>

**5.148** James continued to attend the hospital regularly for review as his condition deteriorated. On 3 October he reported that he was 'feeling terrible'.<sup>296</sup> He was tired and sleepy. His abdomen was more distended and uncomfortable. He developed bleeding from his rectum. He asked about re-starting Zidovudine or another 'new American drug'.<sup>297</sup> On 11 October he restarted treatment with Zidovudine. He asked about treatment with Didanosine, but he was told that this was not available. At the end of October James developed itchy skin and eyes; problems which were particularly marked at night.<sup>298</sup> He was referred for a dermatology opinion. The dermatologist considered that the rash was most likely related to his jaundice, or the Zidovudine treatment. She recommended emollient cream.<sup>299</sup>

**5.149** In November 1989 James was admitted to the RIE for review by Dr Finlayson. His main symptoms at this time were hepatomegaly (enlarged liver), jaundice, itch and fatigue.<sup>300</sup> He was diagnosed with cholestatic jaundice (jaundice resulting from inability of bile to flow from the liver to the duodenum). It was suggested that James undergo an ultrasound and CT scan. He was prescribed Questran (a type of medicine called a bile acid sequestrant which works in the intestine where it binds to bile acids).<sup>301</sup> This improved his itch for a while.

**5.150** On 27 January 1990 he was admitted to hospital with a temperature, shortness of breath and coughing. His temperature returned to normal and investigations of his chest were normal. He was discharged home the following day.<sup>302</sup> He continued to suffer

---

<sup>294</sup> Excerpts from medical records recovered in respect of James

<sup>295</sup> Day 30, page 52; Excerpts from medical records recovered in respect of James

<sup>296</sup> Excerpts from medical records recovered in respect of James

<sup>297</sup> Ibid

<sup>298</sup> Ibid

<sup>299</sup> Ibid

<sup>300</sup> Ibid

<sup>301</sup> Ibid

<sup>302</sup> Ibid

from intermittent breathlessness.<sup>303</sup> On 6 June James was again admitted to hospital after suffering a reaction to the factor treatment he had received for persistently bleeding gums. While an in-patient, he had a temperature and he was started on broad spectrum antibiotics. He recovered quickly. His treatment with Zidovudine was discontinued and it was planned that he would start treatment with Didanosine.<sup>304</sup> In July, James developed bloating of his abdomen, and there was concern that this was caused by ascitic fluid (fluid which accumulated in the abdominal cavity).<sup>305</sup>

**5.151** Some weeks after this, James woke one morning suffering from a bleed in his abdomen. He said to Frances' mother 'this is it'.<sup>306</sup> He was admitted to hospital that day. He underwent a laparotomy<sup>307</sup> at which the possibility of bleeding from his spleen was raised. A splenectomy was performed but no other source for the bleeding was identified. After this procedure he remained hypotensive (with low blood pressure) and it became clear that the intra-abdominal bleeding was continuing. He was treated with 20 units of blood, fresh frozen plasma, platelets, Factor VIII, antibiotics, adrenaline and dopamine. Sadly, the bleeding persisted and James died later that night.<sup>308</sup>

**5.152** On the day James died, a Friday, Frances was preparing to sit exams on the following Monday. This was her 'last shot' at the exams. Having failed the exams a number of times before, she had been expelled. She successfully appealed her expulsion and was given one last chance to pass the exams.<sup>309</sup> James was aware of this and was keen that Frances sit her exams. When he developed abdominal bleeding he asked his wife not to tell Frances. However, Frances' brother telephoned her and Frances was able to reach the hospital before her father died. When she arrived her father was on a ventilator. Frances' mother asked her 'How will I know when he's gone?' and Frances said that she would tell her. Frances arranged his funeral.<sup>310</sup>

**5.153** James' request for AIDS not being recorded on his death certificate was adhered to and no autopsy was undertaken. His death was reported to the Procurator Fiscal's office due to the fact that he was HIV-positive.<sup>311</sup> A liver biopsy taken at the time of the splenectomy revealed that he had established cirrhosis.<sup>312</sup> A retrospective test carried out on 13 January 1992 on a blood sample dated 5 January 1988 confirmed that James was positive for the antibody to the Hepatitis C virus.<sup>313</sup>

### *Specific impacts of James' infection with HIV*

**5.154** Frances stated that finding out he had HIV had 'a massive impact' on her father.<sup>314</sup> She stated that, when he was younger, her father knew he would not live a long life as a result of his haemophilia, but his life expectations changed when treatment with cryoprecipitate and factor concentrate became available.<sup>315</sup> Knowing that he had HIV curtailed his greatest hobby (which Frances wishes to remain confidential). It also had

<sup>303</sup> Ibid

<sup>304</sup> Ibid. Didanosine was approved in 1991, but was available on a named patient basis in 1990

<sup>305</sup> Excerpts from medical records recovered in respect of James

<sup>306</sup> Day 30, page 53; Frances' Witness Statement

<sup>307</sup> Surgical incision into the abdominal cavity

<sup>308</sup> Excerpts from medical records recovered in respect of James

<sup>309</sup> Day 30, pages 53 and 54

<sup>310</sup> Frances' Witness Statement

<sup>311</sup> Excerpts from medical records recovered in respect of James

<sup>312</sup> Ibid

<sup>313</sup> Day 30, page 55; Excerpts from medical records recovered in respect of James

<sup>314</sup> Frances' Witness Statement

<sup>315</sup> Ibid

'a huge impact' on his relationship with his wife.<sup>316</sup> Frances stated that her father was a very tactile man and not being able to share a bed with his wife would have been 'a real trauma' for him.<sup>317</sup> It also took his focus away from his children, and he was unable to father them as well as he had done before his diagnosis with HIV.

**5.155** James was a successful businessman and was fairly comfortably off. As he had to reduce work due to his illness, there was less income for the family. When he died his business was still operational. After he was diagnosed with HIV, James took out some life assurance. He managed to find some policies which did not exclude paying out even if the death was attributable to HIV. On his death, the MacFarlane Trust made a payment of £60,000 to the family. This money, together with the rental from the shops which James had owned, and the 'money from insurance' supported Frances' mother and Frances' younger brother.<sup>318</sup> James had arranged everything for his wife. After his death, Frances' mother did not know how to pay the gas bill.

**5.156** Frances' mother was devastated by her husband's death, she 'fell apart'.<sup>319</sup> She had 'totally devoted herself to [James]. Her family and her husband were her whole life'.<sup>320</sup> After James was diagnosed with HIV, both her father and mother started drinking. After his death, Frances' mother continued drinking and she eventually became an alcoholic. She also increased her smoking habit from about 20 cigarettes a day to 60. Latterly she drank coffee and vodka and did not eat. In 2000 she died weighing just five stone.<sup>321</sup> Frances was 30 years old when her mother died. At this time her younger brother was in higher education so Frances and her other brother supported him through this.<sup>322</sup>

**5.157** The elder of Frances' two brothers was not told about his father's illness until a few months before his father died, when he was 18 years old. Up until this time, her father's illness had been downplayed. The family was used to him going to the hospital. The elder of the two brothers was unaware how unwell his father was. Frances remembers persuading her father to tell this brother about his infection because she believed that it was important that he have some warning about his father's condition. After the elder brother was told about his father's illness, he had only a short period of time to come to terms with this before his father died. He became very angry.<sup>323</sup> Frances believes that this brother was a little resentful of her as she knew more about her father's illness than he did. After her father died, he felt that he needed to be the man of the family but did not know how to be that man. Frances stated that he is similar to his parents in that 'he is not a talker, so we never really discussed how it affected him because he doesn't want to talk about it; but his life became smaller'.<sup>324</sup> Frances' brother had a road traffic accident which affected his ability to continue working in his job. Frances believes that it is likely that he is fit for other types of work but he has not worked since the accident. Frances believes that he is 'emotionally damaged. It's too big a thing to retrain. Whereas if my dad had been around, he would have had more of a push, more support'.<sup>325</sup>

---

<sup>316</sup> Ibid

<sup>317</sup> Ibid

<sup>318</sup> Day 30, pages 55–56

<sup>319</sup> Frances' Witness Statement

<sup>320</sup> Ibid

<sup>321</sup> Day 30, pages 56–57; Frances' Witness statement

<sup>322</sup> Frances' Witness Statement

<sup>323</sup> Day 30, page 57

<sup>324</sup> Ibid, page 58

<sup>325</sup> Ibid, pages 58–59

**5.158** The younger of Frances' two brothers provided the Inquiry with a statement. He recalled, when he was five years old, being taken to the blood transfusion centre for a blood test. He did not know why. When he was 18 or 19 years old he discussed the blood test with his mother and was shocked to learn that the blood test was to determine if he had been infected with HIV. He remembered that his father was often in hospital but he did not know the reason for this. His parents slept in separate beds for as long as he could remember. He thought that this was normal because he slept in a separate bedroom from Frances. He stated that once when a friend came to the house, he showed him around. His friend was amazed when he saw that his parents slept in separate beds.<sup>326</sup>

**5.159** He stated that his father could be an angry, irritable man who, occasionally, was very mean to him. When he was about seven years old, his father threatened to throw out all his toys as he had not tidied his bedroom in the allocated time. He thought that his mother was the voice of reason.<sup>327</sup>

**5.160** He was 10 years old when his father died. Frances was away continuing her studies and his older brother seemed 'a very angry person' at this time.<sup>328</sup> The older brother remained at home until he attended higher education about two years later. Frances' youngest brother considered that all his father's friends disappeared after his father died. He felt angry with them for not supporting his mother. When he was older he learned that some of the friends had tried to support her. They had tried to introduce her to other men but she was not interested. After his father died, he stated that he did all the gardening and as he got older he did more of the housework.<sup>329</sup>

**5.161** When he was 16 years old, his mother said to him that she was proud that she had seen all her children grow up, and that she could die now. By that time, she had no appetite and was very frail. He did not recall her drinking excessively during his school days. When he returned home from school she was always interested in his day, and was not drunk. She smoked a lot. By the time he was 18 years old, his mother was drinking more. She would get up during the night and fall over. He got up then to help her back to bed. When he was 20 years old, his mother fell during the night and broke her hip. She was admitted to hospital where she died three weeks later from liver failure.<sup>330</sup>

**5.162** After her father's death, Frances did better academically and obtained a professional qualification. She has become prone to anxiety and depression. Her father's infection with HIV and her mother's subsequent problems have played a significant role in her development of these symptoms. In April 1997 Frances attended her GP with stress, low mood and anxiety symptoms. Frances believes that this was a delayed reaction to the stress she was under as a result of her father's illness. Frances was initially prescribed Fluoxetine (an antidepressant medication). This was changed to Paroxetine (another antidepressant medication) in August 1997, and she continued to take this until the following December. In January 1998 she again attended her GP with recurrent low mood and anxiety. This did not improve by February and so, once again, she was prescribed Paroxetine. Initially Frances responded well to this, but she became of low mood and anxious again in late 1998. In January 1999 her dose of Paroxetine was increased. She was signed off work

---

<sup>326</sup> Ibid, pages 59–60; Statement of Frances' youngest brother

<sup>327</sup> Day 30, page 60; Statement of Frances' youngest brother

<sup>328</sup> Ibid

<sup>329</sup> Day 30, pages 60–61; Statement of Frances' youngest brother

<sup>330</sup> Day 30, page 61; Statement of Frances' youngest brother

from February until September 1999. She attended a psychiatrist for treatment, and he prescribed her with Venlafaxine (a different antidepressant medication) with good effect. She continued to take Venlafaxine until October 2001.<sup>331</sup>

**5.163** Frances' GP provided the Inquiry with a brief medical report. In it she stated:

Over the years Frances has demonstrated a very resourceful personality, coping incredibly well ... as well as dealing with her family issues. I have no doubt that her father's illness and in turn the effects that this had on her family have had an immense role to play in [these problems].<sup>332</sup>

**5.164** Frances stated that it is hard for her to imagine what her life would have been like had her father not been infected with HIV. She believes that, had she had some support at the time 'it possibly wouldn't have had quite such an ongoing effect'.<sup>333</sup> She stated:

I think one of the difficult things is a sense of shame ... and I know there is not real shame but they are not neat, tidy acceptable deaths. It subsequently means that I don't feel able to talk about them. My dad had AIDS and my mum was an alcoholic. It's not, you know, 'My dad had a heart attack'. It has contributed to quite a private personality. This is – this has been quite a difficult process for me because I'm talking about things that I don't talk about. And I have done the work, you know, I have had some counselling myself, I don't share my parents' views on counselling.

I have done the work and I have dealt with it, but it's just utterly changed my life. It has affected how I relate to people. It has no doubt affected my choice of [work], it has affected my relationships. It has influenced my choices in – whether or not to have a family. I don't have children. It was just too difficult to think about, because my dad is a haemophiliac, I'm a carrier. It was too difficult to think about having a child but it was bad enough going through it with my dad. With the possibility of going through it with a son was just too hard. That makes me sad.<sup>334</sup>

## David

**5.165** At the time he gave evidence to the Inquiry, David was 44 years old. He is married and has a daughter. David was unemployed when he gave evidence, and he wished his previous occupation to remain confidential. David has Haemophilia B. He acquired both HIV and Hepatitis C from his treatment with blood products.<sup>335</sup>

### *David's diagnosis with Haemophilia B and his treatment*

**5.166** David was diagnosed with Haemophilia B when he was three years old. He has a family history of haemophilia. Five of his cousins have Haemophilia B. His clotting factor is about 13% of normal, and his haemophilia is classified as moderate.<sup>336</sup>

---

<sup>331</sup> Day 30, page 62; Statement of Frances' GP

<sup>332</sup> Day 30, pages 62–63; Statement of Frances' GP

<sup>333</sup> Day 30, page 63

<sup>334</sup> Ibid, pages 63–64

<sup>335</sup> Ibid, pages 80–81

<sup>336</sup> Ibid, pages 81–82

**5.167** As a child David was treated at Yorkhill Hospital in Glasgow, and this is where, in October 1970, when he was four years old, he received his first treatment with blood products. After a fall, he sustained bruising of his face and a bleed in his left knee. He was treated with a rapid intravenous injection of fresh frozen plasma.<sup>337</sup>

**5.168** David only needed treatment for his haemophilia if he had an accident, or received dental treatment. He estimated that he had such treatment about once a year. As a child his treatment for bleeds usually involved an admission to hospital for about a week. In addition to treatment with blood products, he was also treated with physiotherapy, splints and bed rest. He often used a wheelchair while he was in hospital.<sup>338</sup>

**5.169** David recalled that, in about 1977, treatment for his haemophilia became easier. This is likely to have been when he started treatment, in hospital, with Factor IX concentrate. It reduced the time taken to receive treatment, and it seemed to be effective more quickly. As a result he spent less time in hospital.<sup>339</sup>

**5.170** David was aware that it was not normal to need treatment after a fall so he came to understand that he was different from his friends. At school he was wary of contact sports. He would have liked to play rugby but was unable to do so. Instead he played football and sometimes sustained injuries as a result. In 1979, when David was 13 years old, he sustained a bump to his right knee while playing football. He was treated with bed rest, Factor IX, a splint, a cast and then a walking support. He missed about three months of school due to this injury. His school was very supportive of him. When he was discharged from hospital some of the teachers came to his home and taught him there. They sent him homework. David believes that his haemophilia did not have a detrimental affect on his schoolwork, or the qualifications he obtained at school.<sup>340</sup>

**5.171** In 1981, when David was about 15 years old, his haemophilia care was transferred from Yorkhill Hospital to the Glasgow Royal Infirmary (GRI), under the care of Professor Forbes.<sup>341</sup> In 1982, when David was 16 years old, he started to administer Factor IX concentrate at home. At that time David had marked synovitis (inflammation of the synovial membrane) of both knees. He was instructed to give himself two vials of Factor IX concentrate weekly. He was also told to take Factor IX concentrate at the first sign of a bleed. David had a good response to the regular treatment with Factor IX and the pain and stiffness in his knees improved. In 1983 blood tests showed that David had raised serum transaminases (enzymes in the blood). Professor Lowe, a Senior Registrar at the time, noted that such results were commonly found in people with haemophilia who were on regular treatment. In keeping with the clinicians' state of knowledge at the time, it appears that non-A non-B Hepatitis was considered as a cause for this. David has no recollection of these blood test results being mentioned to him.<sup>342</sup> In 1984, during routine screening for Hepatitis A, David was warned of the risk of infection with this virus from his treatment. He was not warned of the risk of being infected with any other virus as a result of his haemophilia treatment.<sup>343</sup>

---

<sup>337</sup> Ibid, pages 84–85; Excerpts from medical records recovered in respect of David

<sup>338</sup> Day 30, page 85

<sup>339</sup> Ibid, pages 85 and 88

<sup>340</sup> Ibid, pages 89–90; Excerpts from medical records recovered in respect of David

<sup>341</sup> Day 30, pages 90–91; Excerpts from medical records recovered in respect of David

<sup>342</sup> Day 30, page 94; Excerpts from medical records recovered in respect of David

<sup>343</sup> Day 30, pages 102–103

**5.172** On 25 January 1985 David attended a clinic appointment at the GRI.<sup>344</sup> As usual he gave a blood sample. This was tested for HIV and was reported on 28 January to be negative. David told the Inquiry that at that time he was unaware that he was being tested for HIV, although he did understand that various tests were undertaken as part of routine screening at clinic appointments. David continued to take prophylactic Factor IX until about July or August 1985. By then David's knee problems had settled. He kept a record of each treatment he gave himself. This record detailed the date he administered the treatment, and the serial numbers of the bottles of factor concentrate that he used. David handed these records into the hospital at the time of further treatment.<sup>345</sup>

### *David's diagnosis with HIV*

**5.173** On 8 November 1985, David attended one of his routine haemophilia clinic appointments. At this time, David was 19 years old and he was working. He has worked in the same industry throughout his working life. The notes of this appointment record that David was feeling well. They also record that he was HIV-negative as at 25 January 1985 and that he was given a Haemophilia Society booklet.<sup>346</sup> David had no recollection of being told that a test had been negative for HIV. He gave a blood sample at this appointment which was tested on 12 November and found to be HIV-positive.<sup>347</sup> When David gave blood samples at his clinic appointments, he understood that these samples were being tested to monitor his haemophilia and to check for Hepatitis A and Hepatitis B. He did not know that his blood sample would be tested for HIV.<sup>348</sup>

**5.174** About a week after the appointment on 8 November 1985 David received a telephone call from the Haemophilia Department asking him to come in to the hospital to meet with Professor Lowe. He was not given any explanation for this. Having just attended a clinic appointment, David was unsure of the purpose of the meeting. He had heard of HIV from articles in the press. He was worried about it as he knew of the risk of transmission of the virus by blood products but, as stated above, he did not know that he had been tested for it.<sup>349</sup>

**5.175** On 2 December, David attended the arranged appointment with Professor Lowe. David was alone when he went to this appointment. He felt that, while having someone to 'lean on' would have been helpful, it would not have changed the fact of his infection.<sup>350</sup> Professor Lowe explained to David that he had been infected with HIV from blood products, and that he was now HIV-positive. David formed the impression that Professor Lowe was not 'entirely comfortable' speaking one-to-one with him about this and it felt to David as if Professor Lowe wished to convey the news to him and then move on. He thought that Professor Lowe spoke to him in a very matter of fact way.<sup>351</sup> Professor Lowe told David that the doctors did not know much about the virus, and gave David some leaflets about general wellbeing and what was known about the virus at the time. He warned him of the risks of secondary infection. He told him about the dangers of cuts, blood spills and unprotected sex. David was told that his girlfriend would need to be tested for HIV. Professor Lowe told him

---

<sup>344</sup> Excerpts from medical records recovered in respect of David

<sup>345</sup> Day 30, pages 96–98

<sup>346</sup> Ibid, page 104; Excerpts from medical records recovered in respect of David

<sup>347</sup> Excerpts from medical records recovered in respect of David

<sup>348</sup> David's witness statement

<sup>349</sup> Day 30, pages 103–104 and 106

<sup>350</sup> Ibid, page 114

<sup>351</sup> David's witness statement. The manner in which David was told of his diagnosis with HIV, including Professor Lowe's comments on this, is discussed in more detail in Chapter 33, *An Investigation into the Systems in Place for Informing the Patients about the Risks – HIV/AIDS*, para 33.325

to lead a healthy lifestyle. He told David that he would continue to monitor his condition by the usual routine checks and that they would give him further information about the virus as it became available. As David recalled, apart from this general information, no advice, counselling or support was offered then or subsequently.<sup>352</sup> The notes of this appointment suggest that David was also told that he had non-A non-B Hepatitis, although he does not remember being told that at the time.<sup>353</sup>

**5.176** It was put to David in oral evidence, that Professor Lowe's position in response to David's characterisation of his manner, was that telling him about his infection was very difficult, because of the uncertainty about the virus and its prognosis, and that he, Professor Lowe, had tried his best.<sup>354</sup> David made no significant comment.<sup>355</sup> It was also suggested that he had been offered counselling, after his diagnosis, from Dr Wilkie and/or Miriam Guthrie, a social worker at the GRI. David said that he was aware that there was a social worker, but that he had never spoken to her.<sup>356</sup>

**5.177** David felt numb immediately after being told that he was infected with HIV. He stated that he then felt a number of emotions. He thought, 'Well, what does this mean and what does the future look like or lack of it?'<sup>357</sup> From what he had read in the newspapers, he thought that the prognosis for him was a life expectancy of eight to 10 years.<sup>358</sup> David also felt angry that he had been tested for the virus without his knowledge, and without his consent.<sup>359</sup> Questions of practice, in 1985, in relation to the testing of blood samples without a patient's consent are discussed in detail in Chapters 33 and 34. David was still living with his parents and after this appointment he returned home and told them about his diagnosis. They were shocked, and wanted to speak to someone at the hospital to understand the implications of this diagnosis for David. On 4 December, David and his mother saw Professor Lowe at the hospital. David's recollection is that their discussion then was very similar to the discussion he had had with Professor Lowe two days before.<sup>360</sup> David's girlfriend was tested for HIV. She and David attended an appointment with Professor Lowe later in December. She was advised that the result of the test was negative, but that she should undergo repeat tests.<sup>361</sup>

**5.178** Following the appointment on 2 December, Professor Lowe advised David's GP that if David needed any blood tests, they should be carried out by the Haemophilia Unit at the GRI. He also arranged for David's dental care to be transferred from his normal dentist to the hospital dentist, so that all appropriate precautions could be taken.<sup>362</sup>

**5.179** After his diagnosis with HIV David felt 'huge uncertainty'.<sup>363</sup> He stated:

[A]t that point it was a case of almost living from day-to-day, every indication at that point was you could expect a life expectancy of eight to ten years and each time you attend the unit, you are wondering 'What are my results going to be now? Is it getting any better? Is it worse? Is it stable?' You just don't know.

---

<sup>352</sup> David's witness statement

<sup>353</sup> Day 30, pages 108–109

<sup>354</sup> Comments on David's witness statement made by Professor Lowe dated May 2011

<sup>355</sup> Day 30, pages 118–119

<sup>356</sup> *Ibid*, page 119

<sup>357</sup> *Ibid*, page 114

<sup>358</sup> *Ibid*, page 109

<sup>359</sup> *Ibid*, pages 155–156

<sup>360</sup> Day 30, page 114

<sup>361</sup> *Ibid*, page 115

<sup>362</sup> *Ibid*, page 112; Excerpts from medical records recovered in respect of David

<sup>363</sup> Day 30, page 119



So there was always the anxiety and a general feeling of anxiety, just simply because you had no idea what the future would be like, and I guess being guarded as well in your relationships with people.<sup>364</sup>

**5.180** Due to the ‘huge stigma’ surrounding HIV, David did not tell anyone other than his parents and his girlfriend about diagnosis with it. He did not tell his brother, sister or any of his friends.<sup>365</sup> His siblings still do not know that he is HIV-positive.<sup>366</sup>

### *David’s symptoms of HIV*

**5.181** At the time David was diagnosed with the virus in December 1985, he had some ‘small enlarged lymph nodes in the neck and somewhat larger lymph nodes in both [armpits]’.<sup>367</sup> He carried on attending three-monthly clinic appointments at the Haemophilia Unit. He often saw a junior doctor and gave blood samples. He assumed that the doctors monitored his HIV status, but this was not discussed with him.<sup>368</sup> In June 1986 David had a palpable lymph node on the left submandibular region (situated under the jaw bone), but was otherwise well.<sup>369</sup> In April 1987 he had swollen lymph nodes in the left supraclavicular (neck) and right axillary (armpit) regions.<sup>370</sup> In February 1988 he had no swollen lymph nodes.<sup>371</sup>

**5.182** In November 1988, David was admitted to the GRI due to bleeding gums. He was treated with IV antibiotics and made excellent progress. A swab of his gums was taken and showed evidence of a heavy mixed growth of mouth flora. The report of the sample noted that the significance of the result was doubtful as little was known about the microbiology of dental plaque in HIV-positive individuals.<sup>372</sup>

**5.183** Additionally, in 1988, David developed sinusitis and persistent warts on his hands. He had swollen lymph nodes under his armpits. His CD4 count remained normal. Liver function tests showed continued elevation in transaminases. In August 1989 David’s general health was good. He had no swollen lymph nodes. He suffered from bleeding gums and once again this was thought to be due to a bacterial infection. He was treated with IV antibiotics followed by oral antibiotics.<sup>373</sup> At a review appointment in March 1990, David was found to have developed swelling of lymph nodes in both armpits. His serum transaminases remained raised.<sup>374</sup>

**5.184** David was encouraged to attend his three-monthly clinic appointments. It was quite a challenge for him to do so as his employers were unaware of his condition. The hospital was 10 miles from his place of work. He stated that he was always vague with his employers about why he needed to go to the hospital. Also, he tried to fit his clinic appointments around a time when he would be on annual leave, or when there was an easy way to attend the hospital without having to explain why he was absent from work.<sup>375</sup>

---

<sup>364</sup> Ibid, pages 119–120

<sup>365</sup> Ibid, page 120

<sup>366</sup> David’s Witness Statement

<sup>367</sup> Day 30, page 111; Excerpts from medical records recovered in respect of David

<sup>368</sup> Day 30, pages 120–121

<sup>369</sup> Excerpts from medical records recovered in respect of David

<sup>370</sup> Ibid

<sup>371</sup> Ibid

<sup>372</sup> Day 30, pages 121–122; Excerpts from medical records recovered in respect of David

<sup>373</sup> Day 30, pages 122–123; Excerpts from medical records recovered in respect of David

<sup>374</sup> Excerpts from medical records recovered in respect of David

<sup>375</sup> Day 30, page 124

**5.185** In May 1990, David had persistent soft enlargement of his cervical and axillary lymph nodes which meant that he fell into the category of persistent generalised lymphadenopathy as regards his HIV infection. His CD4 count had fallen slightly to 429 cells/mm<sup>3</sup>; this was at the lower end of the normal range. He continued to have elevated serum transaminases. Professor Lowe mentioned the possibility of treatment with Zidovudine. As he felt well, David was resistant to the idea of treatment.<sup>376</sup>

**5.186** In July 1990 David got married. Before their wedding David told Professor Lowe that he and his fiancée had a full discussion about the risk of transmission of HIV infection. They used condoms and took precautions with blood. Professor Lowe offered David's fiancée the opportunity to meet with the Haemophilia Unit social worker, or a consultant gynaecologist, but David's fiancée declined this.<sup>377</sup> Professor Lowe also gave David advice about holiday insurance for his honeymoon.<sup>378</sup> David was aware that if he declared that he was HIV-positive he would be declined cover and so he did not declare this and bought travel insurance to cover other risks.<sup>379</sup>

**5.187** David remained well. In October that year the possibility of treatment with Pentamidine (a medication given to prevent PCP) and Zidovudine was raised with David. He remained reluctant to have treatment unless it was necessary.<sup>380</sup>

#### *David's diagnosis with Hepatitis C*

**5.188** In April 1991 David tested positive for the antibody to the Hepatitis C virus.<sup>381</sup> Around this time Professor Lowe informed him that he had been infected with Hepatitis C from blood products.<sup>382</sup> David stated,

It felt exactly the same as when he told me I had got HIV. He was very matter of fact about it. He did not tell me much about the severity of the virus, the health implications of it or the risk of secondary infection. He told me that they would continue to monitor my liver function tests at my routine haemophilia clinic appointments.<sup>383</sup>

**5.189** Between 1991 and 1997 David's CD4 count fluctuated between about 270 cells/mm<sup>3</sup> and 370 cells/mm<sup>3</sup>.<sup>384</sup> Other than swollen lymph nodes, David remained asymptomatic in respect of both HIV and Hepatitis C. He continued to attend the GRI for monitoring of his condition. In November 1995 the responsibility for the HIV monitoring and managing of haemophilia patients at the GRI was transferred to a consultant specialising in infectious diseases.<sup>385</sup> Towards the end of 1997 David developed a facial rash. He was prescribed Tetracycline (an antibiotic cream) for this.<sup>386</sup> In May 1999, David's CD4 count was noted to have shown a very slow decline. The doctor considered that he was at risk of opportunistic infections and so prescribed him Co-trimoxazole indefinitely. David was warned of a 5–10% risk of hypersensitivity reaction to this medication. His viral load of HIV was also

---

<sup>376</sup> Ibid, pages 125–126; Excerpts from medical records recovered in respect of David

<sup>377</sup> Day 30, pages 123–124; Excerpts from medical records recovered in respect of David

<sup>378</sup> Day 30, page 125; Excerpts from medical records recovered in respect of David

<sup>379</sup> Day 30, page 125

<sup>380</sup> Ibid, pages 126–127; Excerpts from medical records recovered in respect of David

<sup>381</sup> Excerpts from medical records recovered in respect of David

<sup>382</sup> Day 30, pages 129–130

<sup>383</sup> David's Witness Statement

<sup>384</sup> Excerpts from medical records recovered in respect of David

<sup>385</sup> Letter from David's consultant

<sup>386</sup> Excerpts from medical records recovered in respect of David

noted to have increased 'modestly', but David remained reluctant to start antiretroviral therapy.<sup>387</sup>

**5.190** David was aware that once he started taking the treatment he would have to continue to do so, and it would then become part of his daily life. He felt that once he started taking medication he would be 'on a downward spiral'.<sup>388</sup> Instead, David did what he could to stay healthy. He took exercise, watched his diet, did not smoke and did not drink to any great extent.<sup>389</sup>

### *Family planning advice*

**5.191** In 1992, Professor Lowe referred David and his wife to a Senior Lecturer in Women's Reproductive Health at the Glasgow Royal Maternity Hospital to discuss the possibility of having a family.<sup>390</sup> David and his wife wanted to obtain more information about the options available to them at that time. David stated, 'We wanted to have a family as naturally as possible and really risk-free'.<sup>391</sup> David was unwilling to put his wife at any risk of acquiring HIV.<sup>392</sup> Having had an initial discussion with the doctor about their options, they were re-referred to her in October 1994.<sup>393</sup> David found seeing the doctor very helpful. She told him a lot about HIV with regard to looking after himself, the precautions he should take, the health implications of the virus and the risk of secondary infection.<sup>394</sup> In 1996 the doctor contacted a colleague in London to explore the possibility of sperm washing, followed by artificial insemination. She was told that, at that time, the service was not yet available in the UK and that the limited tests of the procedure in Italy had not provided proof that there was no risk of infection to the woman.<sup>395</sup> Having considered the options open to them, David and his wife decided that the best option was donor insemination. They attended the Assisted Conception Service at the GRI and their daughter was born as a result of this procedure.<sup>396</sup>

**5.192** Over the years and due to his fluctuating CD4 count and viral load, there were frequent discussions about treatment. In 2000, David was found to have Genotype 3 of Hepatitis C which was known to be 'relatively favourable' to treatment with Pegylated Interferon.<sup>397</sup> David was given some written information about Pegylated Interferon and asked to consider it.

**5.193** In April 2001, David and his wife were again referred to the doctor at the Glasgow Royal Maternity Hospital for advice about having a second child. They were interested in discussing the possibility of sperm washing and artificial insemination. By this time Dr Seaton, an Infectious Disease Consultant had taken over from the previous consultant. Dr Seaton was planning to treat David with Pegylated Interferon and Ribavirin. David was told that conception was contraindicated while taking this treatment, because of the unknown risks of congenital abnormalities.<sup>398</sup>

<sup>387</sup> Day 30, page 135; Excerpts from medical records recovered in respect of David

<sup>388</sup> Day 30, page 136

<sup>389</sup> Ibid, page 137

<sup>390</sup> Ibid, page 130; Excerpts from medical records recovered in respect of David

<sup>391</sup> Day 30, page 130

<sup>392</sup> Ibid, page 128

<sup>393</sup> Excerpts from medical records recovered in respect of David

<sup>394</sup> David's Witness Statement

<sup>395</sup> Day 30, page 131; Excerpts from medical records recovered in respect of David

<sup>396</sup> Day 30, pages 132–133; Excerpts from medical records recovered in respect of David

<sup>397</sup> Day 30, page 139; Excerpts from medical records recovered in respect of David

<sup>398</sup> Excerpts from medical records recovered in respect of David

*David's treatment for HIV*

**5.194** In July 2002, David's CD4 count 'dropped substantially' to 198 cells/mm<sup>3</sup>.<sup>399</sup> Dr Seaton noted that David had 'a lot of minor symptoms' but, other than a facial rash, David could not remember what these symptoms were.<sup>400</sup> As a result of this change in David's condition, Dr Seaton decided that treatment for HIV was more appropriate than treatment for Hepatitis C and he discussed this with David and his wife. In August 2002 David's CD4 count had risen to 319 cells/mm<sup>3</sup>. He had seborrhoeic dermatitis. Dr Seaton remained concerned that, despite this increase in David's CD4 count, starting treatment for Hepatitis C would lead to further drops in his CD4 count. David and his wife agreed that he should start treatment for HIV on their return from holiday at the end of September 2002. David was prescribed Daktacort (hydrocortisone) cream for the dermatitis.<sup>401</sup>

**5.195** In the following September David started treatment for HIV with Efavirenz (an NNRTI), and Combivir (a combination of Zidovudine and Lamivudine, both NNRTIs). David took the Efavirenz at night time and the Combivir twice a day, one tablet in the morning and one at night time. David tolerated the treatment very well. Initially, he noticed some vivid dreams as a result of Efavirenz. He also experienced some episodes of dizziness if he got out of bed during the night.<sup>402</sup>

**5.196** In January 2003 David's viral load of HIV had dropped to below 50 copies/ml, compared to 77,000 copies/ml in October 2002.<sup>403</sup> His CD4 count was 392 cells/mm<sup>3</sup>. He continued to tolerate the treatment well. He asked to defer starting treatment for Hepatitis C for a further three to six months. In October, despite excellent compliance with the medication, David's viral load increased briefly to 330 copies/ml. It then returned to below 50 copies/ml.

*David's treatment for Hepatitis C*

**5.197** In January 2004 David started treatment for Hepatitis C. He was prescribed Pegylated Interferon and Ribavirin which he took in addition to the Efavirenz and Combivir. David found the side-effects of the treatment for Hepatitis C 'draining'.<sup>404</sup> In March 2004, Dr Seaton noted that David was suffering 'substantial symptoms' from the treatment. He suffered flu-like symptoms over the weekend, having taken the injection of Interferon on the Friday of each week. He deliberately took the injection on a Friday so that he could recover over the weekend and be able to work the following Monday. In the first six weeks of treatment his haemoglobin dropped by four grams; a very significant drop. He attended the ward each week for treatment with an injection of Erythropoietin (a hormone that controls red blood cell production).<sup>405</sup> David suffered from exhaustion, depression, nausea, loss of appetite, weight loss and fatigue. He felt like he had flu for a year. To his credit, David managed to keep working for the first eight months of this treatment, but had to stop during the last four months of his treatment due to the side-effects. In January 2005, David's GP wrote that he was full of admiration for David having persevered at work for as long as he had. David stated that the treatment is 'not something I ever wish to have to repeat'.<sup>406</sup> While taking this treatment, David was concerned about the effect it would

<sup>399</sup> Day 30, page 140; Excerpts from medical records recovered in respect of David

<sup>400</sup> Day 30, page 140; Excerpts from medical records recovered in respect of David

<sup>401</sup> Day 30, page 141; Excerpts from medical records recovered in respect of David

<sup>402</sup> Day 30, page 142; Excerpts from medical records recovered in respect of David

<sup>403</sup> Day 30, page 143; Excerpts from medical records recovered in respect of David

<sup>404</sup> Day 30, page 143

<sup>405</sup> Excerpts from medical records recovered in respect of David

<sup>406</sup> Day 30, page 144

have on the HIV virus. As the treatment affected him so badly, he thought that it could well be affecting the HIV virus. In fact, David sustained a good CD4 count throughout the treatment.<sup>407</sup>

**5.198** Two months after starting treatment with Pegylated Interferon and Ribavirin, David's liver function test results started to improve. This improvement encouraged David to keep taking the treatment despite the side-effects. When he finished this treatment he was told that the Hepatitis C virus was undetectable. David was told that if the virus remained undetectable for two years, he would be deemed to be cured of the Hepatitis C virus. He spent the next two years hoping that this would be the case. Two years after completing his treatment with Pegylated Interferon and Ribavirin, David remained Hepatitis C PCR negative and he was told that he was cured of the virus.<sup>408</sup>

**5.199** In October 2008 David's antiretroviral therapy was changed from Combivir to Kivexa (a combination of Abacavir and Lamivudine). This change was to reduce the risk of therapy-related lipodystrophy (fat loss, often from the face) which had been found to be associated with Zidovudine.<sup>409</sup>

**5.200** David had continued to attend regularly at his HIV clinic appointments. He has remained relatively asymptomatic, and has tolerated his antiretroviral treatment to date.<sup>410</sup>

### *Specific impacts of David's infection with HIV and Hepatitis C*

**5.201** David stated that his infection with HIV has 'hugely' impacted on his family life. He and his wife were unable to conceive children naturally. David's daughter is not yet aware of how she was conceived. This is something David and his wife will have to speak to her about when she has the maturity to understand it. Understandably, David is concerned about the impact this will have on his daughter and how she will react to this. David has asked the hospital, and the MacFarlane Trust, for advice on how and when to explain this to a child but he has been advised that there is no specific information tailored for children.<sup>411</sup>

**5.202** David and his wife's attempts to have a second child failed. David's wife suffered a number of ectopic pregnancies and a miscarriage. They were advised by a doctor at the Assisted Conception Service that assisted conception itself increases the likelihood of ectopic pregnancies. Had David and his wife been able to follow the natural course of having a family, they would have done so, and hopefully they would have had more children. His wife might not have suffered these failed pregnancies or their physical and emotional consequences.<sup>412</sup>

**5.203** When asked about the effect of being infected with HIV on him and his family David stated:

[I]t's just the huge uncertainty with regard to the future and it's something that, other than taking the medication, you really have no control over and you feel that there is a lack of empowerment there because it's not something I can control, as I say, other than taking the medication, and there is the anxiety

---

<sup>407</sup> Ibid, page 145

<sup>408</sup> Ibid, pages 145–146

<sup>409</sup> Day 30, page 147; Letter from David's consultant

<sup>410</sup> Day 30, page 148

<sup>411</sup> Ibid, pages 148–150

<sup>412</sup> Ibid, pages 133–134; David's Witness Statement

every time you attend the appointments of: am I still stable; I feel – well, I don't feel any different but I'm aware that there could be a lead-in time before any symptoms start to show. For as long as I feel well, there is always the hope that treatments are continuing to evolve and ... the carrot out there, that one day they will find a cure for it.<sup>413</sup>

**5.204** Since his diagnosis with HIV, David has only told a couple of friends about it. As a result he and his wife always have a 'feeling of holding back with family and friends'.<sup>414</sup> He stated that living with a secret like that is 'not a way you would choose to lead your life'.<sup>415</sup>

**5.205** David and his wife would be wary about moving away from the area where they live because they have such good support there. It has helped them to have their family close by. David has found the Brownlee Centre at the Gartnavel Hospital in Glasgow, where he is now treated, to be excellent and he has built up a trust with the people there. He is sure that other centres will also be very capable but he is more comfortable dealing with the people he knows. 'I have got to know them and they have got to know me'. This inability to move has affected David's employment prospects. There are more job opportunities in England in the industry in which David works, and it will take longer for him to find suitable employment in Scotland.<sup>416</sup>

**5.206** David has not lost any earnings as a result of his infection with HIV and Hepatitis C. David and his wife funded two attempts at donor insemination, but their daughter's conception was funded by the NHS. Their attempts to have a second child were funded by a combination of David and his wife, the NHS and the MacFarlane Trust. Since 2007 David has received a monthly payment from the MacFarlane Trust. David and his wife have a mortgage, but the life assurance for it is in his wife's name. David has never tried to obtain life assurance as he did not think that it would be an option for him. He is aware that the position with life assurance has altered over the years, and so it is something he may look at in the future. His pension has not been affected by having HIV and Hepatitis C. David stated that it has only been in the last three years that insurance companies have been willing to provide travel insurance to people with HIV. Even then, the insurance premiums are double what they would otherwise be.<sup>417</sup>

**5.207** Dr Seaton provided a written report to the Inquiry. In it, he stated that he was of the view that David's infection with HIV and Hepatitis C had 'hugely affected and impacted on David's family life' as David had described in his witness statement.<sup>418</sup> He further stated:

[H]aving known David since 2000, I have been hugely impressed by his stoical nature, his resolve and his determination to live a fulfilling and normal family life despite the physical and psychological burden of haemophilia and the complicating infections and treatment.<sup>419</sup>

---

<sup>413</sup> Day 30, pages 152–153

<sup>414</sup> Ibid, page 149

<sup>415</sup> Ibid, page 150

<sup>416</sup> Ibid, page 150 and 153–154

<sup>417</sup> Ibid, pages 150–152

<sup>418</sup> Ibid, page 148; Letter from David's consultant

<sup>419</sup> Day 30, page 148; Letter from David's Consultant

## Elaine

**5.208** Elaine was 66 years old when she gave evidence to the Inquiry. She lives in Fife. Elaine's husband had Haemophilia A. He and Elaine were married in 1964.<sup>420</sup> They have a son.<sup>421</sup> Elaine's husband acquired HIV from his treatment with blood products and died from AIDS, aged 47 years, in 1992.<sup>422</sup> For the purposes of this chapter, Elaine's husband will be referred to as 'Brian'.

### *Brian's haemophilia and his treatment*

**5.209** Brian was the third of four brothers, all of whom had Haemophilia A. There was no family history of haemophilia. The only surviving brother, who was the youngest of the four, also provided a statement to the Inquiry.<sup>423</sup> One brother died, aged 21 years, as a result of a motorcycle accident in the 1960s. The other brother died of AIDS, aged about 52 years, having also been infected with HIV from blood products.<sup>424</sup>

**5.210** Brian's haemophilia was classed as moderate to severe. Hardly a week went by when he did not need treatment for a bleed. The severity of his haemophilia, and the treatment he received for it, were very similar to that of his surviving brother. This brother's haemophilia is also classified as moderate.<sup>425</sup> As a child Brian was treated for bleeds mainly with bed rest, often in hospital. He was also treated with plaster casts. There were times when three of the brothers were being treated for bleeds, each in different hospitals in Edinburgh. Their parents would have to take a taxi to try to visit each of them for 10 minutes during visiting hours.<sup>426</sup> Brian's oldest brother was once in hospital for about six years due to a bleed.<sup>427</sup>

**5.211** Unsurprisingly, due to the disruption caused by his treatment, Brian only managed to attend primary school for a few years. He was then home tutored with his youngest brother instead. He did not attend secondary school.<sup>428</sup> The fact that he was unable to go to school did not bother him. He told Elaine that he thought that he learned more in the hour or two with the tutor, than he would have learned in the classroom. Brian loved being in the fresh air and occasionally swimming. He liked animals.<sup>429</sup>

**5.212** Elaine remembers that, at the time when she and her husband were married (in 1964), most of her husband's treatment for bleeds was bed rest. Sometimes he stayed in bed for four to six weeks. Due to the pain of the bleed, often Brian was unable to bear the weight of the blankets on the area where the bleed was, or even the vibration caused when someone walked across the room. He was provided with a wire cage to take the weight of the blankets. Most of Brian's bleeds were in his knees.<sup>430</sup>

**5.213** In about 1969 Brian's brother received his first treatment with factor concentrate, and it is likely that Brian received this treatment around then too. Brian and his brother thought that this treatment was a miracle cure as it shortened the time a bleed lasted. Also, Brian could often sense when a bleed was starting. When this happened, he either

---

<sup>420</sup> Day 31, page 114

<sup>421</sup> Ibid, page 141

<sup>422</sup> Ibid, page 117

<sup>423</sup> Statement of Elaine's brother in law

<sup>424</sup> Day 31, page 118; Statement of Elaine's brother in law

<sup>425</sup> Day 31, page 117

<sup>426</sup> Ibid, pages 117–118

<sup>427</sup> Ibid, page 121

<sup>428</sup> Ibid, page 122; Elaine's Witness Statement

<sup>429</sup> Day 31, page 125

<sup>430</sup> Ibid, pages 119–120

rested, or obtained treatment with factor concentrate as quickly as possible to keep the bleed and its effects to a minimum.<sup>431</sup> As the factor concentrate worked so well, Brian started going to the hospital more often to receive treatment for a bleed.<sup>432</sup>

**5.214** During the 1970s and the early 1980s Brian's treatment for bleeds consisted of a mixture of both cryoprecipitate and Factor VIII. He also received blood products when he underwent dental treatment. He was treated at the Royal Infirmary of Edinburgh (RIE). The amount of treatment he needed varied from year to year, but it was usually at least twice a month.<sup>433</sup> At some time Brian started home treatment. Elaine could not remember when this was but it seems likely it was around the early 1980s.<sup>434</sup> Brian was warned, in general terms, about the risk of a hepatitis virus.<sup>435</sup> Between 7 March and 19 August 1984, Brian was treated on 11 occasions with the HIV-infected batch number 0090 of Factor VIII.<sup>436</sup>

### *Brian's diagnosis with HIV*

**5.215** In the summer of 1984, Elaine went on a trip to Canada. While she was there she read an article in a newspaper about a person with haemophilia having contracted HIV as a result of receiving contaminated blood products. Elaine had already heard through the media about HIV, but this was the first time she had heard of a person with haemophilia contracting the virus. Elaine cut the article out of the newspaper and brought it home to show her husband. When he saw it on her return in July 1984, Brian 'completely dismissed it'. He told Elaine that that could not happen in Scotland as Scotland produced its own blood products. He was sure that the blood product, which the person described in the article had received, was commercial blood from either drug addicts or prisoners.<sup>437</sup> At this point, unknown to himself, Brian was already infected with HIV. He was later found to have been HIV-positive on 29 May 1984.<sup>438</sup>

**5.216** In late 1984 Brian received word from the Haemophilia Society about practising safe sex. He and Elaine were unsure why they were being told about this, particularly as they had been married 20 years by then. Towards the end of 1984, Brian, by himself, attended a meeting of other haemophilia patients and Professor Ludlam at the RIE. He later told Elaine what had happened at the meeting 'word for word'. Elaine told the Inquiry that the doctors at the meeting were asked by those present if HIV could be transmitted through blood products. The doctors told everyone there not to worry. 'They were still maintaining that it was coming through the gay community. The doctors said 'We are only telling you about this virus but it won't affect you.' Brian stood up at the meeting and said, 'Of course it won't affect us. Scotland makes its own.' One of the doctors told him that they had been given 'not home grown stuff'. Brian was very angry when he heard this and told the doctors 'they had no business giving them stuff from abroad'. He asked the doctors why they had not been told about this. The doctors told them that Scotland was running low and they had to give the patients something.<sup>439</sup>

<sup>431</sup> Ibid, pages 123–124

<sup>432</sup> Ibid, page 127

<sup>433</sup> Ibid, pages 128–129

<sup>434</sup> Ibid, page 130; Statement of Elaine's brother in law – Brian's older brother started home treatment in the late 1970s.

<sup>435</sup> Day 31, page 20

<sup>436</sup> Ibid, page 129; Excerpts from medical records recovered in respect of Elaine's husband; Thus Brian was a member of the 'Edinburgh Cohort' – See Chapter 10, *Knowledge of the Geographical Spread and Prevalence of HIV/AIDS 2*, paragraphs 10.16 onwards

<sup>437</sup> Day 31, pages 132–134

<sup>438</sup> Letter from Brian's consultant. Early kits that tested for antibodies to HIV became available on an experimental basis in October 1984, and Brian's blood sample given in May was retrospectively found to be positive.

<sup>439</sup> Day 31, pages 134–137; Although this may have been Brian's understanding of what was said at the meeting, this was not what patients were told at this meeting. The details of this meeting are narrated in Chapter 33, *An Investigation into the Systems in Place for Informing the Patients about the Risks – HIV/AIDS*, paragraphs 33.221–33.252



**5.217** In December 1986 Brian arranged an appointment with the Haematology Department so that he, Elaine and their son could be tested for HIV. Elaine thought that he arranged the appointment as more and more information was coming out in the press, and from the Haemophilia Society, about people with haemophilia being infected with HIV. As a result, Brian became increasingly concerned about the virus. Elaine stated that her husband was not worried about himself, only about her and their son. At the appointment in December 1986 the doctor advised them that there was no need for their son to be tested, but Brian insisted that they were all tested. About a week or two later Brian returned alone for the results of the blood tests. The doctor told him that his family was 'okay'.<sup>440</sup> Brian took this to mean that all their results were negative, but the doctor said to him 'You are not asking about yourself'. The doctor then told Brian that he was HIV-positive.

**5.218** The doctor told Brian that the virus might not develop into AIDS.<sup>441</sup> When Brian returned home after being diagnosed with HIV, he was upset, but relieved for Elaine and their son. Neither Brian nor Elaine knew much about HIV. Elaine commented, 'We had no idea what we were in for'.<sup>442</sup>

**5.219** Brian realised that the doctors had known that he was HIV-positive before he had asked to be tested for it. This made him angry; he realised that he could have transmitted the virus to Elaine while the doctors were aware that he had been infected. When Brian asked a doctor (Elaine was unsure who the doctor was) why he had not been told sooner that he was HIV-positive, he was told that Professor Ludlam did not like telling people that they were infected and patients would be told that they were HIV-positive only if they asked about it.<sup>443</sup>

**5.220** After his diagnosis with HIV, Brian and Elaine continued to live life as before. Brian very rarely managed to work due to his haemophilia. He was classed as disabled and had a 'green card'. They lived in a small community which meant that most people knew him. He used to try to persuade potential employers that he was fit for work, but most employers were unwilling to employ someone with haemophilia. He sometimes managed to obtain labouring work which was not recommended. Elaine did not work either, but their son, who was still living at home at the time, did work.<sup>444</sup>

**5.221** In the late 1980s Brian was referred by Professor Ludlam to Dr Alison Richardson, a Clinical Psychologist, for counselling in respect of his diagnosis with HIV. Initially he was reluctant to meet with her, but eventually he did so. He found his meetings with her helpful. She was able to tell Brian and Elaine what his symptoms of HIV might be. Until she did so, Elaine stated, 'we were just in the dark'.<sup>445</sup> At one point Brian spoke to Dr Richardson about suicide. Dr Richardson was very supportive to both him and Elaine and continued to see Elaine after her husband died.

**5.222** In her evidence to the Inquiry, Dr Richardson stated that during the group counselling sessions of the patients with haemophilia and HIV, a number of topics were discussed. These included anger against the Blood Transfusion Service and Professor Ludlam, suicide,

---

<sup>440</sup> Day 31, pages 138–142

<sup>441</sup> *Ibid*, page 145

<sup>442</sup> *Ibid*, page 146

<sup>443</sup> *Ibid*, pages 145

<sup>444</sup> *Ibid*, pages 146–148; Elaine's Witness Statement

<sup>445</sup> Day 31, pages 148–149

wills, funerals, loved ones watching them all the time for symptoms, being irritable with family, sexual anxieties and alcohol problems.<sup>446</sup> She stated these patients, 'were understandably very anxious about what was going to happen to them, and of course at that time it was very, very unclear what might happen'.<sup>447</sup>

**5.223** Elaine is unsure what her husband was told about the risk of transmission of HIV. After he was diagnosed with HIV, they stopped having a sexual relationship. She tried to reassure him, but he was so 'paranoid and petrified of infecting [her] that [that] side of [their] marriage was over forever'.<sup>448</sup>

**5.224** A further impact of Brian's diagnosis with HIV was that, for a period of about six months, he started to drink more. Before he did not drink much alcohol, having only a whisky or a stout if they went out at the weekend. Brian used to prefer being outside and being with his animals which Elaine thought stemmed from being ill so much.<sup>449</sup> After his diagnosis with HIV, Brian started drinking more whisky when they went out and then 'his personality changed altogether'.<sup>450</sup> He became very argumentative. Elaine and their son bore the brunt of this, and Elaine found it very difficult to cope with. She realised that the excessive drinking was her husband's way of coping with his diagnosis and the fear and frustration it caused him. She stated that it was terrible to see her husband's personality change in this way, and she repeatedly reminded herself that this was not her husband. Their son also suffered as a result of this. He was still living at home at the time. He tried to be understanding of his father, but he did not wish to see his mother or his father hurt.<sup>451</sup>

**5.225** Brian and Elaine did not know how to tell people about his diagnosis with HIV, and they told very few. Brian told one good friend that he was HIV-positive. A couple of weeks later at New Year, Brian gave the friend's grandchild a kiss. The friend told Brian never to kiss his grandchild again. Brian was very distressed by this. Elaine stated that he 'completely broke down'.<sup>452</sup> Brian was also concerned for his son. He worried about how his girlfriend at the time would react. Brian did not want 'anything coming back on [his son]'.<sup>453</sup> They spoke to Dr Richardson about this; she told them that as they lived in a small community she did not know if that would work for them or against them. After the reaction of his friend, Brian did not want to tell anyone else that he was HIV-positive.

### *Brian's symptoms of HIV*

**5.226** The Inquiry tried to recover Brian's medical records to assist Elaine's evidence, but unfortunately NHS Lothian was unable to locate them.<sup>454</sup> Instead, it provided two pages of data stored on a historical database.<sup>455</sup> Elaine and Professor Ludlam were able to provide copies of some excerpts from Brian's medical records which assisted the Inquiry. It was explained to the Inquiry that the copy records provided by Professor Ludlam came from a separate filing system, in which blood treatment records at the RIE were maintained.<sup>456</sup>

<sup>446</sup> Day 29, pages 9–11

<sup>447</sup> Ibid, page 11

<sup>448</sup> Day 31, page 150

<sup>449</sup> Ibid, pages 150–151; Elaine's Witness Statement

<sup>450</sup> Day 31, page 152

<sup>451</sup> Ibid, pages 151–153

<sup>452</sup> Ibid, page 164; Elaine's Witness Statement

<sup>453</sup> Day 31, page 165

<sup>454</sup> Letter from NHS Lothian to Central Legal Office dated 9 February 2001

<sup>455</sup> Excerpts from data received from NHS Lothian in respect of Brian

<sup>456</sup> Email from Central Legal Office to the Inquiry dated 7 June 2011

**5.227** Elaine stated that her husband's first symptoms of HIV were loss of appetite and weight-loss. She thought that he had these symptoms for a couple of years before he was diagnosed with the virus.<sup>457</sup> It is possible, having seen the limited medical records available for Brian, that he may have been found to have persistent generalised lymphadenopathy in August 1985.<sup>458</sup> Elaine remembered that his lymph nodes were checked. As this was before Brian discovered that he was HIV-positive, it seems likely that he was not told about this. In April 1989, Brian was prescribed 'irregular' Pentamidine, suggesting that he may also have suffered from some symptoms of pneumonia.

**5.228** In June 1990 Brian developed PCP. He and Elaine were supposed to be going to Ireland to stay in a caravan owned by the Haemophilia Society, but Brian had to be admitted to hospital instead. Elaine remembers he had chest problems, such as breathlessness, and that he was quite 'chesty'.<sup>459</sup> Brian was treated in hospital and recovered from PCP. Elaine remembers that he was told that he was lucky to recover as, a few years before, HIV patients usually died soon after developing PCP. At this time Brian started treatment with Zidovudine and prophylactic treatment for PCP.<sup>460</sup> Elaine was unsure if he suffered from any side-effect of these medications.<sup>461</sup>

**5.229** Despite this prophylactic treatment, Brian developed PCP again in January 1991. He was admitted to hospital for treatment. His dose of Zidovudine was increased and he was prescribed Pentamidine. Elaine stated that while her husband was in hospital the consultant haematologist treating Brian tested him for PCP, and told him that if the result was positive he had developed AIDS. At Brian's request this doctor agreed to tell him the result of the test that night. Elaine stated that her husband 'was in pieces'.<sup>462</sup> Instead of the same doctor returning with the result, a younger doctor came. This doctor told Brian that he had developed AIDS and walked out of the room. Brian was very upset to be told that he had AIDS by a doctor he did not know, and in what he considered to be such a callous manner. Later the consultant haematologist apologised to Brian for not having given him the result himself.<sup>463</sup>

**5.230** After this, Brian's condition deteriorated, and 'his body started to give out'.<sup>464</sup> He became very tired. He developed a rash on his face. He suffered from diarrhoea.<sup>465</sup> In April 1991 he was diagnosed as having HIV-wasting. In July he developed oesophageal candidiasis (a fungal infection of the oesophagus). His treatment with Zidovudine was stopped in November 1991 due to cytopenia (a deficiency of cellular elements of the blood), a known side-effect of Zidovudine. His treatment with Zidovudine was restarted in December that year.<sup>466</sup>

**5.231** Brian developed a lot of infections. He had to have a nasogastric tube inserted for feeding. Elaine became his carer, and did everything for him. Brian preferred only Elaine to care for him. He used to say, 'I don't need help, my wife will do it'.<sup>467</sup> Occasionally Brian's

---

<sup>457</sup> Day 31, page 153; Elaine's Witness Statement

<sup>458</sup> Day 31, page 154; Excerpts from data received from NHS Lothian in respect of Brian

<sup>459</sup> Day 31, pages 158–159; Elaine's Witness Statement

<sup>460</sup> Day 31, page 158; Excerpts from data received from NHS Lothian in respect of Brian – the record does not disclose what prophylactic medication he was prescribed

<sup>461</sup> Day 31, page 161

<sup>462</sup> Elaine's Witness Statement

<sup>463</sup> Day 31, pages 160–161

<sup>464</sup> Elaine's Witness Statement

<sup>465</sup> Day 31, page 161

<sup>466</sup> Ibid, page 162; Excerpts from data received from NHS Lothian in respect of Brian

<sup>467</sup> Day 31, pages 162–163

GP came out to visit him, and the local nurse came every Monday. Dr Richardson used to visit them and give them advice. Initially their home did not have a shower, and a bath-chair was installed so that Brian could have a bath. He needed Elaine's help with bathing, and once joked to her that he would die of pneumonia not HIV, due to the length of time she took helping him into the bath.<sup>468</sup>

**5.232** Brian became good friends with a 30-year-old man with haemophilia who had acquired HIV, and who lived quite close to him. This friend died a couple of months before Brian, and Elaine said 'his death broke Brian's heart'.<sup>469</sup> In January 1992 Brian returned from a hospital appointment and broke down. He told Elaine that he had been told that he only had six weeks to live. In fact he had not been told this, but he was very upset about his friend's death. He had told the nurses at the hospital that he would die next, and that he had only about six weeks to live. The nurses told him that he had at least another year. Elaine reminded her husband that he had promised her that he would keep fighting. He replied, 'I'm not giving in ... I'm tired'.<sup>470</sup>

**5.233** Brian died at home about five weeks later on 8 February 1992. Before his death, he asked Elaine that his body be kept in the house before it was cremated. When the undertaker came to the house, Elaine felt she had to tell him that her husband was HIV-positive. At that point the undertaker said that he was unable to prepare her husband's body himself, and that his body would need to be taken away. Their son and Brian's brother put Brian's body into a body-bag and it was taken out of the house. Elaine did not know where her husband had been taken. She wished to visit him but the undertaker would not tell her where he was. Elaine stated that 'to this day nobody has told me where my husband went to'.<sup>471</sup> She stated:

I always have felt, and always will feel, that I broke my promise to [my husband]. [He] never asked for much – just to be with his family – and they even took that away and put him in a strange place completely on his own. It was bad enough for him to die like that but to be treated like a leper and without any dignity, he certainly didn't deserve that.<sup>472</sup>

**5.234** After Elaine gave evidence the Inquiry carried out some investigations to ascertain where her husband was taken after he died. The Inquiry found out the details and passed this information to Elaine.

**5.235** Brian had asked the doctors not to put AIDS on his death certificate and so the cause of his death was listed as septicaemia, pneumonia, immunosuppression and haemophilia.

**5.236** About a year after Brian's death, Elaine asked to be tested again for HIV before she was admitted to hospital for a minor operation. The result of this test was negative.<sup>473</sup> Elaine felt guilty that she was not HIV-positive, 'why did [he] have it and why did I escape?'.<sup>474</sup>

**5.237** In late 2002 Elaine heard from the Haemophilia Society that haemophilia patients who were HIV-positive were very likely also to be infected with Hepatitis C. Elaine asked her GP to test her for Hepatitis C. The result of this test was negative. At a meeting with

---

<sup>468</sup> Ibid, pages 163–164

<sup>469</sup> Ibid, pages 165–166

<sup>470</sup> Ibid, pages 166–167

<sup>471</sup> Ibid, pages 168–169;

<sup>472</sup> Elaine's Witness Statement

<sup>473</sup> Day 31, page 167

<sup>474</sup> Ibid, page 170

Professor Ludlam in January 2003, Elaine was told by him that her husband had also been infected from blood products with the virus that causes Hepatitis C. A blood test result, dated 13 January 1992, had confirmed that he was positive for the antibody to HCV. Elaine is sure that her husband did not know that he had been infected with Hepatitis C; if he had known he would have told her.<sup>475</sup> By mid-January 1992, Brian was a very sick man and he died less than a month later from a different infectious disease. His condition at that time may explain why Brian was not informed of the test result by those then treating him. At that meeting she expressed concern that she had been at risk of acquiring the virus from her husband, and no-one had warned her or advised her of the measures she could take to avoid infection. Professor Ludlam indicated that the risk of transmitting the virus through sexual contact was low.<sup>476</sup> Nevertheless, Elaine felt that she should have been informed in 1992 of her husband's hepatitis diagnosis as she might herself, by that time, or before, have contracted the virus from her husband. If she had done so, she would, without her knowledge, have suffered the effects of the virus until 2002 when she went to her GP for Hepatitis C testing in consequence of the information she had received from the Haemophilia Society.

**5.238** Elaine has suffered from anxiety and depression since the 1980s. Following her husband's death, in March 1992 Elaine was diagnosed with reactive depression. This persisted and she was deemed unfit for work until at least 1998. During 1992, Elaine attended counselling but she did not wish to take medication. Since then Elaine has been seen by her GP on a fairly regular basis. On occasion she has been prescribed various different antidepressants which Elaine has taken for a while, and then discontinued. Elaine stated that she did not want to become dependent on pills, and so she tried to work through her mental health problems herself. In August 1998 Elaine was noted to be 'verging on panic attacks'. In 2000, Elaine was noted to be concerned that she was infected with Hepatitis C, but she was found to be negative for this. She was prescribed a further dose of antidepressant therapy in 2002, on the tenth anniversary of her husband's death, and has been prescribed such therapy intermittently since then. She was last prescribed antidepressant therapy in September 2009.<sup>477</sup>

**5.239** Elaine stated that her son is 'a very deep person'.<sup>478</sup> She believes that he has been very affected by having to assist with putting his father into a body-bag. After his father died, he told Elaine that he was going to do what his father had asked of him before he died and marry his girlfriend. They married soon after. A year or so after Brian's death, her son's wife came to Elaine and told her that her son was not speaking to her. Elaine believed that her son's behaviour was due to his father's death. When her son heard that Elaine had made contact with the Inquiry, he advised her to 'forget it all'<sup>479</sup> but before she came to give evidence he offered her any help she needed.

**5.240** In October 1990 Brian's GP told him that he should make a claim for Special Attendance Allowance. The GP told him that he would state on the appropriate form that he expected Brian to die within six months. It proved very difficult for Brian to be awarded this benefit, but finally, in August 1991, after Brian underwent a medical examination while he was an in-patient in hospital, he was awarded the higher rate for day and night

---

<sup>475</sup> Ibid, pages 171–172; Elaine's Witness Statement; Excerpts from data received from NHS Lothian in respect of Brian

<sup>476</sup> Day 31, pages 172–173; Elaine's Witness Statement

<sup>477</sup> Day 31, pages 170–173

<sup>478</sup> Ibid, page 182

<sup>479</sup> Ibid, pages 183–184

care instead of the allowance awarded to those who are terminally ill. While Brian was alive he received money from the MacFarlane Trust. When he died, Elaine was paid £1000. She was also paid a widow's allowance of about £100 a month which she still receives.<sup>480</sup>

## Mark

**5.241** Mark was 41 years old when he gave evidence. Mark used to work as a cabinet maker. He was medically retired in 1997. Mark has Haemophilia A and contracted both HIV and Hepatitis C from blood products.<sup>481</sup>

### *Mark's diagnosis with haemophilia and his treatment*

**5.242** In 1970, when Mark was a baby, he fell and cut his lip. His lip continued to bleed and 10 days later he was admitted to the local hospital in England, where the family then lived. On examination Mark was very pale. Tests revealed that he had mild Haemophilia A. He was treated with blood, fresh frozen plasma and cryoprecipitate and discharged home after two days in hospital.<sup>482</sup>

**5.243** In 1972, Mark and his family moved permanently to Scotland, and thereafter lived at various locations. Mark was treated with cryoprecipitate when he was two and a half years old when he bit his tongue, again when he was seven years old for a bleed in his right elbow secondary to trauma, when he was eight years old due to a bleed in his right knee and when he was nine years old due to a further bleed in his right knee.<sup>483</sup>

**5.244** In 1979, Mark and his family moved to an address in the countryside. Mark was referred to a consultant haematologist at the Royal Infirmary of Edinburgh (RIE), in respect of his haemophilia. Further investigations at the RIE revealed that Mark's Factor VIII level was only 2.2% which meant that his haemophilia was, in fact, moderately severe. His mother's Factor VIII level was found to be 34% which meant that she was likely to be a carrier of haemophilia. It was noted that Mark's right knee was swollen with a small degree of fixed flexion. Mark's right knee became one of his target joints (a joint where there is regular bleeding).<sup>484</sup>

**5.245** Mark received treatment for his haemophilia at his local hospital as it was too far for him to travel to Edinburgh on a regular basis. The amount of treatment Mark received increased substantially. He stated, 'Now that they knew what was wrong with me, it was not a case of just rest and relax, it was off to the hospital for assessment'.<sup>485</sup> Between 18 April and 5 June 1980 he was treated with cryoprecipitate on three separate occasions, each occasion involving treatment in the local hospital over a number of days. Mark's mother started administering his treatment herself.<sup>486</sup> Between 5 June and 4 August 1980 Mark was treated with cryoprecipitate on six separate occasions.<sup>487</sup> As well as attending his local hospital for treatment, Mark also attended the Haematology Department of the RIE every three months for review.<sup>488</sup>

---

<sup>480</sup> Ibid, pages 174–175; Elaine's Witness Statement

<sup>481</sup> Day 32, pages 93–95

<sup>482</sup> Day 32, pages 95–98; Excerpts from medical records recovered in respect of Mark

<sup>483</sup> Day 32, pages 98–99; Excerpts from medical records recovered in respect of Mark

<sup>484</sup> Day 32, pages 100–102; Excerpts from medical records recovered in respect of Mark

<sup>485</sup> Day 32, page 103

<sup>486</sup> Excerpts from medical records recovered in respect of Mark

<sup>487</sup> Day 32, pages 101–102; Excerpts from medical records recovered in respect of Mark

<sup>488</sup> Day 32, pages 103–104

**5.246** In 1981 Mark's mother was taught how to administer Factor VIII. Mark was treated with Factor VIII at home when he had a bleed or after a severe bleed to prevent it recurring. In about 1983, when Mark was 14 years old, he began treating himself with Factor VIII. He stated that this did not make the treatment hurt any less, but concentrating on what he was doing served as a distraction. Mark and his mother used to keep detailed records of the treatment he took at home. These were handed back to the hospital. A record of treatment Mark took in 1984 showed that he was treated with the HIV-infected batch of Factor VIII numbered 0090 between 25 March and 27 April 1984.<sup>489</sup>

**5.247** Mark's haemophilia had a significant effect on his childhood. Living in the country he enjoyed the outdoor life. He used to help his parents. He developed a bleed after cutting nettles with a small scythe, and chopping logs with a full-sized axe. He was advised by his local doctor that it was unwise for him to use such instruments, and so he had to stop these activities.<sup>490</sup> Mark did not enjoy primary school and it seems that his haemophilia was a major factor in this. He stated that after it was 'announced' that he had a bleeding disorder, the other children used to push or shove him and ask him why he was not bleeding.<sup>491</sup> In secondary school, he was singled out as being 'rather weak and feeble'.<sup>492</sup> He was not allowed to take part in games and used to have to go to the library instead. He stated 'for certainly the first year, there was an element of being pushed around and bullied'.<sup>493</sup> This stopped when Mark stood up for himself in a fight with another pupil. Mark missed a lot of school due to bleeds. Soon after starting secondary school, he developed further bleeds in his right knee. He spent a lot of time in hospital before his O-grade exams. His teachers told him that, as a result of this, he did not need to sit his prelims or the O-grades. Mark thought that he should sit the prelims and so he did. He 'failed everything quite spectacularly'.<sup>494</sup> After this, he worked harder and passed all his O-grade exams except one. He left school with six O-grades and one Higher grade. He believed that his exam results were also affected by teachers' strikes which happened around the time of some of his exams.<sup>495</sup>

**5.248** In about 1983 or 1984, Mark watched a television programme with his family which talked about the spread of a 'horrific virus that was going to wipe out a quarter of the world's population', HIV.<sup>496</sup> The programme stated that the virus had infected drug users and homosexuals. It also mentioned that another category of people at risk was those who used blood products and those at the highest risk were people with haemophilia. On hearing this, Mark panicked and found himself unable to breathe properly. He had to leave the house.<sup>497</sup>

**5.249** Mark continued to attend clinic appointments at the Haemophilia Centre at the RIE. He was accustomed to regularly giving blood samples at these appointments.<sup>498</sup> His mother accompanied Mark to these appointments until about 1986.<sup>499</sup> Mark and his parents were warned of the risk of infection from blood products, including the risk of HIV and the risk

<sup>489</sup> Ibid, page 107; Excerpts from medical records recovered in respect of Mark; thus Mark was a member of the 'Edinburgh Cohort' – See Chapter 10, *Knowledge of the Geographical Spread and Prevalence of HIV/AIDS 2*, paragraphs 10.16 onwards

<sup>490</sup> Day 32, pages 104–105; Excerpts from medical records recovered in respect of Mark

<sup>491</sup> Day 32, page 110

<sup>492</sup> Ibid, page 110

<sup>493</sup> Ibid, page 110

<sup>494</sup> Ibid, pages 111–112

<sup>495</sup> Ibid, pages 112–113

<sup>496</sup> Ibid, page 113

<sup>497</sup> Ibid, pages 113–114

<sup>498</sup> Ibid, page 128

<sup>499</sup> Ibid, pages 114 and 116

of NANB Hepatitis. It was emphasised to them that Mark was being treated with blood products 'from Edinburgh' and not commercial blood products. The fact that the treatment he was receiving was produced locally was emphasised to a high degree. He said that doctors always stressed that he was being treated with factor concentrate manufactured in Edinburgh, not with commercial factor of foreign origin, and that continuing to take local factor was the safest option and reduced the risks.<sup>500</sup> Mark and his parents felt reassured by this.<sup>501</sup> Mark described going down to England to stay with his grandparents and being given letters stating that he was only to be treated with local Factor VIII, which he could hand over in the event that he had to attend a hospital.<sup>502</sup> Mark did not know whether his parents went to the meeting about HIV infection held at the RIE in December 1984.<sup>503</sup>

**5.250** After leaving school, despite being advised to find an office-based job, Mark started training in joinery and cabinet making. With help from a Government enterprise allowance scheme, he set up his own cabinet-making business. He continued to attend the Haemophilia Centre at the RIE for monitoring and treatment of his haemophilia.<sup>504</sup> Mark said that, after 1986, when he attended for his three-monthly clinic appointments the doctor would want to discuss his blood test results. It was either Professor Ludlam or Dr Dennis he saw at the clinic appointments.<sup>505</sup> He said that there would be discussions, often using technical terms such as red blood cells and white blood cells, which did not mean anything to him at his age.<sup>506</sup> He knew at the time that they were testing for things like HIV and hepatitis. He knew that there was a small risk of infection and assumed that the doctors would keep an eye on things to see if he had caught anything. He did not know about HIV infection in other patients.<sup>507</sup> He continued to rely on his doctors, upon whom he had relied for years, and assumed that they would tell him if there was anything amiss.<sup>508</sup> He would be asked whether he wanted to know the results of his tests and said that he would reply, 'Tell me if there's anything wrong.' The doctor would then close the file and say, 'See you in three months.'<sup>509</sup>

**5.251** Before giving evidence, Mark had been made aware that Dr Bernadette Auger had noted in his RIE records for 20 March 1989 that he was: 'Aware we have been doing HIV tests – DOES NOT WANT TO KNOW THE RESULT.'<sup>510</sup> The latter part of this quote had a star in the margin next to it. The full note described his examination results, including observations of swelling in his left elbow and small nodes in both armpits, and continued:

I have told him that if he ever wants to discuss his HIV results, he can contact one of the doctors in the centre and arrange to see them at any time. I have advised him to assume that he is at risk of passing on HIV infection and therefore should use protection for intercourse and be especially careful with the disposal of needles and blood spillages.<sup>511</sup>

<sup>500</sup> Ibid, pages 107–108

<sup>501</sup> Ibid, pages 107–109

<sup>502</sup> Ibid, pages 108–109

<sup>503</sup> See Chapter 33, *An Investigation into the Systems in Place for Informing the Patients about the Risks – HIV/AIDS*, paragraphs 33.221 onwards; Day 32, pages 115–116

<sup>504</sup> Day 32, page 120

<sup>505</sup> Mark's witness statement

<sup>506</sup> Day 32, page 117

<sup>507</sup> Ibid, pages 117–120

<sup>508</sup> Ibid, page 117

<sup>509</sup> This does not accord with the evidence of the doctors. It is discussed in more detail in paras 33.304–33.307 and 33.401–33.404 of Chapter 33, *An Investigation into the Systems in Place for Informing the Patients about the Risks – HIV/AIDS*; Mark's witness statement

<sup>510</sup> Mark's witness statement; Excerpts from Mark's OP clinical notes

<sup>511</sup> Excerpts from Mark's OP clinical notes



**5.252** The note continued that he was referred to the Haemophilia Society for the most recent information concerning possible loans for house purchases, in which he was interested. Mark's response to the note in oral evidence was:

Well, yes. I knew I was being tested for HIV but I would have expected a doctor to have actually informed me if there is anything wrong. So when they say, "Do you want to know the results of your tests," I was expecting it to be a whole list of information that ... didn't really mean very much to me. So again, knowing that HIV was a risk, I would have automatically assumed, for the medical practitioners that I trusted and relied on, they would tell me if anything as monumentally wrong as being infected with HIV – I would be automatically informed.

So, as I say, my assumption is the blood test results would be red blood cells, white blood cells and the levels of what is in my blood, not a virus

....

The other thing ... about looking at buying a house. If I had any inkling of what was wrong with me, why would I be buying a house? So does that not indicate that I had no idea that anything was wrong with me? If I'm discussing the possibility of buying a house or a flat, if I was HIV positive, knowing that HIV in those days was classified as a fatal condition, that if you have HIV you will be dead in three or five years; if I suspected I had HIV, why on earth would I be looking at buying a flat or a house?<sup>512</sup>

**2.253** Mark was told that there were other entries in the records to the same effect as Dr Auger's and was asked whether it was possible that the doctors had formed the impression that he did not want to know, although his own recollection was evidently different. Mark simply repeated his answer that when his doctors asked whether he wanted to know the results he invariably answered: 'Tell me if there is anything wrong'.<sup>513</sup>

**5.254** Asked whether he thought, on the basis of Dr Auger's note, that the doctors and social workers at the hospital may have thought that he did not want to know the results of the test, Mark replied:

But why should I – should they not tell me? If something is seriously wrong with a patient, is it not their job as a trained practitioner to help and assist the patient? So if there is something wrong – if you went to see a GP and the doctor found you had cancer or something – "We won't tell him just now. We don't want to spoil the weekend." You wouldn't consider that fair, would you?

On that basis I would have assumed if they knew I was HIV positive but they deliberately did not tell me and as I have subsequently discovered, they didn't tell me but they were publishing it in the Lancet from 1985, I believe. So they are telling the rest of the world and the medical fraternity but they don't have the manners or conscience to tell the actual victim who is infected.<sup>514</sup>

---

<sup>512</sup> Day 32, pages 122–123

<sup>513</sup> Ibid, page 122

<sup>514</sup> Ibid, page 124

**5.255** In his statement, he said:

If at this time the doctor was trying to inform me that I had HIV I certainly did not appreciate what he was implying. It was discussed with me on more than one occasion about the risks of passing on HIV infection and to use protection for sexual intercourse. However, I took this to be more of general guidance of how things should be done.<sup>515</sup>

### ***Mark's diagnosis with HIV***

**5.256** In January 1991, when Mark was 21 years old, he was told by Professor Ludlam that he had been infected with HIV. He described the disclosure in these terms:

I saw Dr Ludlam at a regular clinic appointment in 1991 when I would have been 21 years of age. I hadn't seen him for a while as it had been Dr Dennis I had been seeing. I was having regular bleeds in my right knee and joint damage. My knee and other bleeds were discussed at this appointment. There was an awkward pause and then Dr Ludlam said to me, "It has come to my attention that you were one of the few unfortunates to be infected with HIV. You have been infected for a number of years and you will be dead within a year." I was absolutely stunned. I was aware that there was a risk of contracting HIV but had been told that blood products from Ellens Glen [ie SNBTS products] were the safest you could get. The nurses at the haemophilia centre had said this and had also discussed safe sexual intercourse with me. Dr Ludlam informed me that I was entitled to an ex-gratia payment to help me through the last few months of my life. He said to qualify for this payment all I had to do was to sign here and here. There was no one else present at this meeting other than me and Dr Ludlam. After giving me this information he then said that the offer of the ex-gratia payment would be withdrawn unless I agreed to this in the immediate future and then I would get nothing. This was the Macfarlane Trust payment. He said if I signed the money would be in my bank account within a week. He said go out and enjoy yourself. I am now aware that Dr Ludlam shouldn't have given me such news without someone of my choice accompanying me and he also should have had someone present. I was not offered any counselling.<sup>516</sup>

**5.257** In oral evidence, Mark agreed that his immediate reaction was just to 'get away':

I believe it was three lots of documents I had to sign and I believe I received counseling and there was other discussions. Again, you are in a stunned condition. Your world has just been smashed to pieces and I do remember wanting to be out of the hospital as soon as possible.<sup>517</sup>

**5.258** Professor Ludlam's notes of this appointment were read to Mark. They commented that the hospital had 'at last managed to persuade (him) to come for review'. They noted:

I have told him of his HIV status. He had not really suspected that he might be positive and he was therefore quite taken aback. Does not wish to tell anyone at present. To see Mrs Brown today. Review one week.<sup>518</sup>

---

<sup>515</sup> Mark's witness statement

<sup>516</sup> Ibid

<sup>517</sup> Day 32, page 126

<sup>518</sup> Excerpts from Mark's OP clinical notes

**5.259** Mark's final comments in oral evidence returned to this event:

I suppose the thing that I remember is how my world was smashed into a million pieces from one sentence, when Ludlam told me what the situation was; that was my world effectively over, plus the fact that the outcome of being – you know, “You have been infected for a number of years, you will be dead within a few months” is a very difficult thing to live with and seems very harsh and unfair when you have worked very hard and made a lot of effort to achieve a lot of things that I was told I wouldn't be able to do.<sup>519</sup>

**5.260** He thought that immediately after seeing Professor Ludlam he saw Mrs Geraldine Brown, the hospital social worker. He had met her on a number of occasions previously. Mark was asked whether he had seen Dr Alison Richardson. He thought that was later: she told him that she had been watching him on paper for thirteen years before they met and that there had been a lot of interest in his case.<sup>520</sup> Mark agreed to undergo further HIV tests. He then wanted to get away from the hospital as quickly as possible.<sup>521</sup> He cannot remember what he did directly after that appointment.<sup>522</sup>

**5.261** Mark had obtained his medical records some seven years before giving oral evidence.<sup>523</sup> He said that he then discovered that he had been infected with HIV in 1984, although he was part of Professor Ludlam's 'AIDS study' from 1983. He referred to a positive HIV test report in his medical records dated 18 January 1988.<sup>524</sup> Mark added:

From information I have received I am number 15 in Professor Ludlam's selection. He has published articles in the *Lancet* in 1985 and defines myself and others as his 'unique group'.<sup>525</sup>

**5.262** Due to the stigma surrounding HIV Mark told nobody, not even his parents, of his diagnosis for eight years: 'I effectively lived a lie'.<sup>526</sup> He stated:

In those days, the ... programmes on the television were gravestones falling down, and if you shake hands with somebody who is HIV positive, a quarter of the population will be dead.<sup>527</sup>

**5.263** Mark stopped buying newspapers. He stopped socialising: 'I basically stopped doing things'.<sup>528</sup>

**5.264** Professor Ludlam referred Mark to the Western General Hospital in Edinburgh for treatment of his HIV. Initially, Mark refused to attend as he did not see the point. He realised that he had been infected with the virus for a number of years. He assumed that the life expectancy of a person with HIV was three to five years and so he thought that he had only months to live.<sup>529</sup> He stated:

---

<sup>519</sup> Day 32, page 187

<sup>520</sup> Ibid, pages 128–129

<sup>521</sup> Ibid, pages 126–128

<sup>522</sup> Ibid, page 133

<sup>523</sup> Ibid, page 129

<sup>524</sup> Excerpts from Mark's medical records

<sup>525</sup> Mark's Witness Statement; Professor Ludlam's evidence in relation to this aspect of Mark's evidence is detailed in paragraphs 33.305–33.307 of Chapter 33, *An Investigation into the Systems in Place for Informing the Patients about the Risks – HIV/AIDS*; The issues raised by Mark's evidence are discussed in paragraphs 33.401–33.404

<sup>526</sup> Ibid

<sup>527</sup> Day 32, page 133

<sup>528</sup> Ibid, page 133

<sup>529</sup> Ibid, pages 133–134

I do recall being sent information which I would put in the car, drive out into the middle of the countryside, read through everything I possibly could and then, the paranoia was to the extent that I would then shred it and burn it so there was no evidence. And it was the same when they suggested medication and again, would it cure it? No. So what's the point? And I refused everything.<sup>530</sup>

**5.265** Mark carried on working as normal and spent 18 months of 'relaxation and leisure'.<sup>531</sup> He received £22,500 from the MacFarlane Trust and spent it on the biggest and fastest motorcycle he could find. He found this a good way to let off steam and 'rode it like a lunatic'.<sup>532</sup> One of his friends warned him that he would need to calm down or he would kill himself. Mark stated, 'I would have actually seen that more as a bonus than a minus because if I had died in a motorcycle accident, it may have turned out that no one would ever know what happened'.<sup>533</sup> He felt extremely stressed and also a mixture of frustration, anger and despair:

I carried on as though everything was perfectly all right until you shut the front door and then it's back to utter despair and the end of the world, and that went on for years.<sup>534</sup>

**5.266** As he shared a flat with others and worked in a workshop with three other people, Mark was very reluctant to take any medication. He did not wish anybody to find out and ask him what the medication was for. The only medication Mark took was Septrin, which is the trade name for Co-trimoxazole, as prophylactic treatment for PCP. Mark suffered diarrhoea as a result of taking this medication. In about November 1993, Mark ran out of Septrin. His diarrhoea resolved and so he stopped taking it.<sup>535</sup>

**5.267** In 1993, Mark was lodging with a couple in a small village. One evening there was a programme on television about people with haemophilia having AIDS. Mark did not watch it. Immediately after the programme finished the couple came to his room and told him what the programme had said. He described this as '[a] very awkward moment'.<sup>536</sup> Mark pointed out to them that the media were trying to horrify people, and that they should not believe everything they heard. He told them that the programme was mainly about people in England and that he had received blood products from Scotland which were considerably safer and meant that the number of people affected was fewer. This appeased one of them but the other said, 'You haven't answered the question: do you have AIDS?' Mark replied 'No, I don't have AIDS at the moment. I'll let you know if I do'.<sup>537</sup> At that point Mark did not know whether he had AIDS or not so, having been brought up not to lie, he considered he was not lying to them. A few years later he returned to visit the couple and the woman told him that a couple living down the road from her had AIDS. As a result of this she would not let their son play in the garden. Seeing how paranoid she was about HIV, Mark was very relieved that he did not tell them that he was HIV-positive. He is still friendly with this couple and they still do not know that he has HIV.<sup>538</sup>

---

<sup>530</sup> Ibid, page 134

<sup>531</sup> Ibid, page 135

<sup>532</sup> Ibid, pages 134–135

<sup>533</sup> Ibid, page 140

<sup>534</sup> Ibid, page 135

<sup>535</sup> Ibid, pages 136–137

<sup>536</sup> Ibid, pages 137–138

<sup>537</sup> Ibid, page 138

<sup>538</sup> Ibid, page 139

**5.268** Mark attended the Haemophilia Centre for review in December 1993. The records of that appointment state that Professor Ludlam's clinical assistant had a long discussion with Mark about Hepatitis C as he had been found to be antibody positive. They record that Mark was given an information leaflet on Hepatitis C and invited to attend the joint liver clinic run with a consultant hepatologist. Mark recalled discussions about different medical matters but he was unable to recall when they took place. He believed that the first time he was made aware that he had Hepatitis C was in 1997. At this appointment it was also noted that he was feeling 'very well at present, has a good appetite and no specific symptoms'.<sup>539</sup> Mark's GP was a family friend, and was also Mark's parents' GP. Mark was so concerned about confidentiality that, for a period, he stopped being registered with a GP.<sup>540</sup>

**5.269** In June 1995 Professor Ludlam wrote a letter to the Benefits Agency advising it that, as a result of many bleeds into his right knee, Mark now had very pronounced arthritis. He stated that the progressive arthritis in Mark's knee was of sufficient severity that Mark was unable to continue with his work, and that the arthritis was permanent.<sup>541</sup> Despite this, Mark continued to work. The business became less lucrative as, over the years, customers started to haggle over the cost of his work. This resulted in Mark working longer hours, sometimes working nearly 18 hours a day.<sup>542</sup>

**5.270** In November or December 1995 Mark developed a rash affecting his trunk and forearms. This was treated to good effect with Canesten cream (an antifungal treatment).<sup>543</sup>

**5.271** On 9 December 1995, while machining wood, Mark severed the end of two of his fingers. The wife of a man who worked in a nearby workshop was a district nurse. She offered to assist Mark. She tried to examine Mark's hand but, due to his concern about the risks from his blood, Mark would not allow her to do so which caused her some offence. Mark was driven by the man to a local cottage hospital. He was then transferred by blue-light ambulance to another hospital where, under general anaesthetic, the ends of his middle and ring fingers on his left hand were amputated.<sup>544</sup>

**5.272** In July 1996, Mark attended the Haemophilia Centre with a recurrence of the rash which he had at the end of the previous year. The rash was on both arms and on his left thigh. It presented as 3cm diameter circular patches with raised margin and clear centre. It was itchy. It was thought to be caused by a fungal infection. Mark was prescribed more Canesten cream.

**5.273** Mark's financial situation remained difficult. His income from the business was low. In addition to this Mark received a monthly payment of £80 from the MacFarlane Trust as well as mobility allowance. Mark remained very concerned about the stigma surrounding HIV, and still did not confide his HIV status to any family or friends. He believed that if it was known where he lived that he was HIV-positive, he would be unable to continue to run his business or to stay there. For these reasons, Mark continued to be reluctant to register with a GP and did not wish to divulge his HIV status to the Benefits Agency. In July 1996 Mark discussed his feelings of social isolation with Geraldine Brown, the social worker at the Haemophilia Centre. In his discussions with Mrs Brown, Mark mentioned

---

<sup>539</sup> Ibid, page 142; Excerpts from medical records recovered in respect of Mark

<sup>540</sup> Day 32, pages 144–145; Excerpts from medical records recovered in respect of Mark

<sup>541</sup> Excerpts from medical records recovered in respect of Mark

<sup>542</sup> Day 32, page 151

<sup>543</sup> Ibid, page 150; Excerpts from medical records recovered in respect of Mark

<sup>544</sup> Day 32, pages 146–150

that he might like to meet other HIV-positive individuals. Despite Mrs Brown offering to put him in touch with Edinburgh-based support groups or individuals, Mark did not meet other HIV-infected people.<sup>545</sup>

### ***Mark's diagnosis with Progressive Multifocal Leukoencephalopathy***

**5.274** About the beginning of July 1996 Mark suffered a rapid deterioration of his eyesight. He first noticed it when he struggled to read a tape measure at work. He went to an optician and had his eyes tested. He was advised that he needed very weak prescription spectacles but, due to the cost, Mark did not buy them. His eyesight continued to deteriorate and Mark found that he was unable to work. He could not see what he was doing. He had serious problems when riding his motorcycle as he found he could not see where he was going.<sup>546</sup> On 22 July, Mark attended the Haemophilia Centre as he was worried about these symptoms.<sup>547</sup> He was admitted for further investigation. He was found to have minor, superficial widespread lymphadenopathy. His CD4 count was 50 cells/mm<sup>3</sup>, having declined relatively slowly over the preceding 12 years. He was referred to a Consultant Ophthalmologist at the City Hospital in Edinburgh. This doctor confirmed that Mark had a reduction in visual acuity but there was no evidence of retinitis (a disease of the eye that leads to loss of vision and blindness). Mark underwent CT and MRI scans. The results of the MRI scan were suggestive of Progressive Multifocal Leukoencephalopathy (PML).<sup>548</sup> PML is a rare, and usually fatal, disorder of the brain which damages the material that covers and protects nerves in the white matter of the brain. It is a consequence of immune deficiency caused by HIV. There is no known cure for PML. The best therapy is the reversal of the immune-deficient state. In the case of HIV-associated PML, immediate treatment with HAART will benefit most patients.<sup>549</sup>

**5.275** Mark underwent a lumbar puncture and samples were sent for virological studies 'including JC the virus PCR'.<sup>550</sup> He was very uncomfortable after this procedure. 'I think I was a horrible grey colour and in a fair amount of pain'.<sup>551</sup>

**5.276** At the end of September 1996 Mark was told about his diagnosis with PML by two doctors and a nurse.<sup>552</sup> He still had not told anyone that he was HIV-positive and so he had no one with him at this time. He was told that PML was a fatal condition and that it was caused by HIV having detrimentally affected his immune system. He was informed that from the moment when the eyesight starts to fail, the condition gets dramatically worse. He stated that, initially, the doctors were rather vague but they told him that PML was very serious. Mark pressurised them into saying what was going to happen and their response was, 'It's not good, it's not good. You are very ill.'<sup>553</sup> Mark insisted that the doctors explain to him what was likely to happen. He was told that:

[M]y sight would go completely, so I would end up deaf, dumb, blind, incontinent and infirm. And the end result is ... it would only be my heart and lungs that would be working and it would be matter of whichever failed first. All this is likely to occur within three months and you are fairly well advanced already.<sup>554</sup>

<sup>545</sup> Ibid, pages 155–157

<sup>546</sup> Ibid, pages 157–158

<sup>547</sup> Excerpts from medical records recovered in respect of Mark

<sup>548</sup> Day 32, pages 159–160; Excerpts from medical records recovered in respect of Mark

<sup>549</sup> Professor Leen – Day 33, page 49

<sup>550</sup> Excerpts from medical records recovered in respect of Mark

<sup>551</sup> Day 32, page 163

<sup>552</sup> Excerpts from medical records recovered in respect of Mark

<sup>553</sup> Day 32, pages 164–165

<sup>554</sup> Ibid, pages 161–162

**5.277** On hearing this Mark 'wanted it all over'.<sup>555</sup> He stated:

[T]hey had been telling me for years that 'You are very ill, you are dying' .... Well get on with it. You know? I suppose that the anger, the frustration and the rage has faded away. You are now in such a medical mess that to die would have actually been pretty much a relief.<sup>556</sup>

**5.278** Mark was offered treatment with antiretroviral triple therapy but he did not wish to take it due to the side-effects. He decided that he would rather have a good quality of life than extended survival with significant disability.<sup>557</sup>

**5.279** Mark still did not want his parents to know that he had HIV, and that he had been diagnosed with PML. Obviously this caused the medical staff some concern. One of the social workers at the hospital asked Mark how his parents might feel if he died, and he had not warned them about his diagnosis. They both became 'really quite upset' during this discussion.<sup>558</sup>

**5.280** Following his diagnosis with PML Mark was discharged home. On 19 December 1996, Mark attended the Haemophilia Centre. He was found to have expressive dysphasia (difficulty in putting words together to make meaning). The doctors were unsure when this had developed. Their initial concern was that Mark had experienced an intracranial bleed. Mark initially declined treatment with Factor VIII, but relented after about four hours. He was found to have further visual loss in his right eye. The following day Mark had more than 80% recovered from his expressive dysphasia. Due to the sudden deterioration in his condition and his subsequent recovery, Dr Grant, Consultant Neurologist, wondered if Mark had suffered from a seizure. Mark was prescribed Sodium Valproate, an anti-convulsant medication. Mark's CD4 count was still 50 cells/mm<sup>3</sup>. Mark eventually agreed to his parents being informed of his admission to hospital. Professor Ludlam insisted that they were told that he was hepatitis-positive. Mark agreed to Professor Ludlam speaking to them regarding the risk of contact with body fluids, suggesting that they should wear gloves if they were going to come into contact with Mark's body. In view of Mark's increasing disability, this was becoming more likely. Mark's parents were not told of his HIV status, in accordance with Mark's wishes. Mark was discharged from hospital on 23 December.<sup>559</sup>

**5.281** Mark described one of his early seizures:

[I] remember one very horrific one, being woken up late at night, and it was a feeling of being squashed to the floor and I know I lost consciousness. The use of the right-hand side, the arm was then not controllable but I was having difficulty with it. It tended to go off and do its own thing, and in no time at all ... I was losing the use of it and shortly afterwards ... the right leg still worked but not very controllably but the right arm ended up completely floppy and useless.<sup>560</sup>

---

<sup>555</sup> *Ibid*, page 164

<sup>556</sup> *Ibid*, page 164

<sup>557</sup> *Ibid*, pages 163–164; Excerpts from medical records recovered in respect of Mark

<sup>558</sup> Day 32, page 165

<sup>559</sup> *Ibid*, pages 167–169; Excerpts from medical records recovered in respect of Mark

<sup>560</sup> Day 32, page 167

**5.282** He also suffered from muscle spasms on the right-hand side, often without warning. His muscles would tighten from the right groin area, his right arm would straighten and then it would twitch uncontrollably. On several occasions he bit his tongue. Mark found these episodes frightening as he often knocked things over. Occasionally he punched himself.<sup>561</sup> He was unable to control the severe seizures, but he discovered that he could control the severity of some of them by bending over, and controlling his breathing.<sup>562</sup>

**5.283** Mark stopped work and, in January 1997, he moved to a town where he was able to receive the support he needed. He was allocated a flat in supported accommodation, in the town. He found this very awkward. At this stage he could still walk although his sight had deteriorated, and he had lost some of the use of the right side of his body. The local social work team provided Mark with regular support and somebody used to visit Mark on Mondays, Wednesdays and Fridays.<sup>563</sup> Initially, Mark found it difficult to accept home help: 'I wanted to do things on my own. I didn't want other people telling me what to do and providing food that I didn't like and didn't want'. Mark also wore an alarm around his neck in case of emergencies.<sup>564</sup>

**5.284** In early February 1997, Mark registered with a GP.<sup>565</sup> One of his support workers persuaded Mark to tell his parents about his diagnosis with HIV and PML. On 19 February Mark invited his parents and his sister to his flat and, after a meal, told them about his condition. Understandably, they were very upset and shocked. Mark gave the doctors at the hospital permission to discuss his condition with his parents and also stated that his parents could make decisions for him, if he was unable to do so. After hearing of Mark's diagnosis his father spoke to the doctors about Mark's condition. Mark continued to attend the Haemophilia Centre for weekly monitoring.<sup>566</sup>

**5.285** Mark's parents became very involved in their son's care: his mother brought him meals and his father took him out for a meal and shopping. He received daily visits from his social worker.<sup>567</sup> At a clinic appointment on 26 February 1997, Mark was noted to be experiencing increasing problems with coordination and loss of power in his right arm and leg. The clinical assistant to Professor Ludlam noted that these problems had become 'considerably worse' since the previous week and that Mark was walking with a marked limp. He was almost unable to use his right arm as his coordination was poor. He had developed aching discomfort in his right shoulder. She considered that Mark was reaching the stage where he was unable to manage on his own at home. Mark told her that he wished to remain in his flat as long as possible, if necessary with 24-hour help.<sup>568</sup>

### *Mark's treatment for HIV*

**5.286** Mark continued to live at his flat with a comprehensive level of support. He often listened to talking books.<sup>569</sup> His condition remained stable. At an appointment on 9 April 1997, Mark discussed antiretroviral treatment for HIV with Professor Ludlam. Mark was given a prescription for Zidovudine and told Professor Ludlam that he would probably start this treatment after discussion with his parents. At his next appointment, on 16 April,

<sup>561</sup> Excerpts from medical records recovered in respect of Mark

<sup>562</sup> Day 32, page 168

<sup>563</sup> Ibid, pages 170–171; Excerpts from medical records recovered in respect of Mark

<sup>564</sup> Day 32, pages 171–172

<sup>565</sup> Ibid, page 171

<sup>566</sup> Ibid, pages 172–173; Mark's Witness Statement

<sup>567</sup> Day 32, page 173; Mark's Witness Statement; Excerpts from medical records recovered in respect of Mark

<sup>568</sup> Excerpts from medical records recovered in respect of Mark

<sup>569</sup> Ibid



Mark told the Registrar that he had not started the medication as he was concerned about the side-effects and did not like taking tablets. Mark also told him that his main concern was that people would know about his HIV status if they saw him taking the tablets. The Registrar discussed this with him and, after this appointment, Mark started taking Zidovudine. On 30 April, Mark was also prescribed Didanosine and he started taking this medication in addition to the Zidovudine.<sup>570</sup> In May, Professor Ludlam asked Dr Brettle, a Consultant at the Regional Infectious Diseases Unit, City Hospital in Edinburgh, to assist in the management of the treatment of Mark's HIV.<sup>571</sup> At Dr Brettle's suggestion Mark was prescribed Lamivudine (an NRTI) instead of Didanosine.<sup>572</sup> Mark stated that he suffered stomach upsets as a result of these medications but no more serious side-effects.<sup>573</sup>

**5.287** In May 1997, Mark asked if it was possible for him to obtain an exercise bicycle at his flat. He was aware that the Haemophilia Society provided some bicycles to patients.<sup>574</sup> He was keen to improve his condition by exercise.<sup>575</sup> After starting medication, Mark noticed some improvement in his right arm. He started to get a small amount of movement in the arm.<sup>576</sup> This encouraged him to keep taking medication. At a review appointment at Dr Brettle's clinic on 13 May, Mark's main problems were noted to be poor eye sight, weakness of his right arm, limited mobility, poor memory and an itchy rash. At one point Mark was unable to hold a conversation due to poor memory and poor speech.<sup>577</sup> Mark was prescribed Ketoconazole (an antifungal drug) for his rash. In May 1997 Mark's CD4 count was 40 cells/mm<sup>3</sup> and his viral load was 2000 copies/ml.<sup>578</sup>

**5.288** At an appointment on 5 August 1997, Mark agreed to start taking PCP prophylaxis and was given a supply of Co-trimoxazole.<sup>579</sup> On 25 August Mark was reviewed by Dr Grant, a Consultant Neurologist, and underwent two further MRI scans.<sup>580</sup> These demonstrated findings consistent with arrested PML.<sup>581</sup> On 17 September, at a review appointment at the Haemophilia Centre, Mark was noted to be getting on 'remarkably well'. Mark remained reluctant to start his treatment with Co-trimoxazole and Dr Dennis tried to persuade him to do so. He continued to suffer from a slight tremor in his right arm. He still had considerable difficulty walking, but could manage unaided reasonably well. His vision was no better. Mark was able to do his own washing up and domestic cleaning. Mark's parents continued to visit him regularly.<sup>582</sup>

**5.289** Mark's CD4 cell count from a sample taken in October 1997 was 17 cells/mm<sup>3</sup>. This was similar to the pre-antiretroviral treatment level. His viral load from a sample taken the previous month was 1700 copies/ml. Due to these test results, Mark's antiretroviral treatment was changed, in November 1997, to Didanosine, Stavudine and Nevirapine (an NNRTI). At that time Nevirapine was not yet licensed in the UK. It was available on a named patient basis.<sup>583</sup> Mark was warned that the main side-effect of Nevirapine was a rash. Due to the potential for increased bleeding from protease inhibitors, it was decided

<sup>570</sup> Day 32, page 174; Excerpts from medical records recovered in respect of Mark

<sup>571</sup> Excerpts from medical records recovered in respect of Mark

<sup>572</sup> Ibid

<sup>573</sup> Day 32, page 174

<sup>574</sup> Excerpts from medical records recovered in respect of Mark

<sup>575</sup> Day 32, page 175

<sup>576</sup> Ibid, page 174

<sup>577</sup> Excerpts from medical records recovered in respect of Mark

<sup>578</sup> Ibid

<sup>579</sup> Ibid

<sup>580</sup> Ibid

<sup>581</sup> Ibid

<sup>582</sup> Ibid

<sup>583</sup> See footnote 98 above on the meaning of 'named patient basis'.

that it was preferable for Mark to avoid this type of drug. Towards the end of 1997 Mark was prescribed Dapsone (to prevent PCP) instead of Co-trimoxazole.<sup>584</sup>

**5.290** In early January 1998, Mark stopped taking Dapsone due to experiencing loose stools.<sup>585</sup> Mark's liver function test results deteriorated as a result of his treatment with Nevirapine. In the middle of that month Mark was contacted by one of the Staff Grade Physicians and he was told to stop taking Nevirapine. On 26 January Mark was admitted to hospital having suffered a possible complex partial seizure. He suffered sudden onset expressive dysphasia. He became increasingly drowsy then slept. When he woke he vomited and developed a headache. His right sided weakness worsened. On admission to hospital Mark was examined and a repeat MRI scan was performed. This showed no evidence of his PML having spread. Mark was discharged from hospital the following day. Mark was prescribed Saquinavir (a protease inhibitor) instead of Nevirapine.<sup>586</sup>

**5.291** The addition of Saquinavir to Mark's HIV treatment had a good effect. In March 1998 Mark's CD4 count had increased to 74 cells/mm<sup>3</sup> and his viral load was lower than 400 copies/ml. In June Mark's dose of Didanosine was stopped as Mark had developed peripheral neuropathy (damage to the peripheral nervous system). The plan was that Mark be prescribed Abacavir (an NNRTI) instead.<sup>587</sup> Unfortunately Mark's liver function tests results remained grossly abnormal, his recent ALT being over 700. It was thought that the cause of this was the antiretroviral medication. Mark was told that it would not be safe for him to take Abacavir but that continuing with just two drugs was sub-optimal therapy. He was told that, from a liver point of view, it would be desirable to stop all medication and monitor his liver function. This ran the risk of Mark's PML progressing. Mark decided to stop the antiretroviral therapy and undergo liver function monitoring. He was told to contact the hospital immediately if there was any change in his neurological state, particularly relating to vision, speech, headaches or weakness.<sup>588</sup>

**5.292** In July 1998 Mark developed a further rash affecting his arms, back and upper thighs. He was prescribed Zirtek (allergy relief medication) and Eumovate ointment (a topical corticosteroid) and referred to the Dermatology Department.<sup>589</sup> By the time Mark saw the dermatologist his rash had improved, although he showed evidence of scalp psoriasis. He was prescribed coal tar shampoo for this.<sup>590</sup>

**5.293** When he was reviewed in September 1998, Mark's liver function tests had reverted to normal, but his HIV viral load had increased to 67,000 copies/ml. His CD4 count had dropped to 55 cells/mm<sup>3</sup>. It was decided that Mark should restart antiretroviral therapy and so he was prescribed Stavudine, Lamivudine (an NRTI) and Efavirenz (an NNRTI).<sup>591</sup>

**5.294** After starting this treatment, Mark's liver function test results deteriorated and then stabilised. He continued to suffer from occasional partial seizures and from muscle spasms mainly in his upper limbs.<sup>592</sup> Towards the end of 1999 Mark was again prescribed Dapsone as PCP prophylaxis. He stopped taking this medication in early 2000 after experiencing numbness of his hands, mood swings and tiredness which he believed were attributable

<sup>584</sup> Day 32, page 175; Excerpts from medical records recovered in respect of Mark

<sup>585</sup> Excerpts from medical records recovered in respect of Mark

<sup>586</sup> Ibid

<sup>587</sup> Ibid

<sup>588</sup> Day 32, pages 176–177; Excerpts from medical records recovered in respect of Mark

<sup>589</sup> Excerpts from medical records recovered in respect of Mark

<sup>590</sup> Ibid

<sup>591</sup> Ibid

<sup>592</sup> Ibid

to that medication. He was then prescribed nebulised Pentamidine instead.<sup>593</sup> When he started taking this medication, he received it fortnightly. He suffered from nausea and intermittent diarrhoea. At the beginning of April 2000 he started taking it monthly. This improved the side-effects and he was able to continue taking it.<sup>594</sup>

### ***Mark's symptoms and treatment during the period 2000 to 2006***

**5.295** In May, Mark developed thoracic shingles.<sup>595</sup> In the summer of that year he suffered from a spell of depression and saw Dr Alison Richardson, a Clinical Psychologist. In September he was noted to be feeling a little brighter, had gained weight and was getting out a little more.<sup>596</sup> In addition to his symptoms of HIV and PML, Mark also continued to suffer as a result of bleeds in his right knee. He received treatment for this in the form of intensive physiotherapy, traction and splints.<sup>597</sup>

**5.296** In August 2001, Mark discussed treatment of his Hepatitis C with a doctor working with Dr Brette. His liver function test results remained abnormal. His alphafetoprotein was normal (elevated or rising alphafetoprotein is a marker for the development of liver cancer). It was explained to Mark that his liver disease appeared to be stable; but that the only way to be sure that he was not developing cirrhosis was for him to undergo a liver biopsy. Mark did not want to be treated with Pegylated Interferon and Ribavirin and so he thought there was no point undergoing a laparoscopic liver biopsy. Monitoring of Mark's liver continued by way of blood tests, and regular abdominal ultrasounds.<sup>598</sup>

**5.297** In about March 2002, Mark experienced a further episode of speech disorder, shaking of his upper limbs, altered consciousness and headaches.<sup>599</sup> This was investigated by an EEG and the results were suggestive of temporal lobe seizures. Mark was advised that, if these episodes became more frequent in the future, he might need anticonvulsant therapy but it was not thought necessary at that time.<sup>600</sup> In August 2002 Mark developed mild gynaecomastia (abnormal growth of the male breast tissue) which can be caused by antiretroviral therapy.<sup>601</sup> In the following November he developed aphthous mouth ulcers and was prescribed Corlan pellets.<sup>602</sup>

**5.298** Mark continued to suffer from significant pain and disability as a result of the damage caused to his right knee by repeated bleeds. It was decided that he required a right knee replacement. Due to his HIV status, there was a greater risk of the site of the prosthetic knee becoming infected, and of such an infection being difficult to eradicate. Mark was warned that, in these circumstances, further surgery might be necessary and he could even become septicaemic and have a life-threatening systemic illness. There was also the risk of amputation if such an infection could not be eradicated. Despite these risks Mark was prepared to proceed with this surgery.<sup>603</sup> He was prescribed an additional antiretroviral medication, Tenofovir, in an attempt to reduce his viral load of HIV prior to the surgery.<sup>604</sup> On 29 January 2003 Mark underwent right knee replacement. He made

---

<sup>593</sup> Day 32, page 178; Excerpts from medical records recovered in respect of Mark

<sup>594</sup> Excerpts from medical records recovered in respect of Mark

<sup>595</sup> Ibid

<sup>596</sup> Ibid

<sup>597</sup> Ibid

<sup>598</sup> Ibid

<sup>599</sup> Ibid

<sup>600</sup> Ibid

<sup>601</sup> Ibid; Gynaecomastia is also associated with Hepatitis C.

<sup>602</sup> Excerpts from medical records recovered in respect of Mark

<sup>603</sup> Ibid

<sup>604</sup> Ibid

good progress following this surgery although his altered gait following the knee surgery caused him to have bleeds in both his ankles. By the April he walked with the aid of a walking stick.<sup>605</sup>

**5.299** Mark developed marked facial lipoatrophy (facial wasting).<sup>606</sup> He was upset about this and, in particular, the idea that it might stigmatise him as being HIV-positive. In April 2004, he was referred to a Consultant Plastic Surgeon to discuss the possibility of treatment by injection with an artificial filling agent.<sup>607</sup> Having consulted with the surgeon and weighed up the risks, which were increased due to his haemophilia, and the possible benefits of treatment, Mark decided against surgery:

I refused. What's the point? I can't see myself in a mirror. Who is going to be looking at you? .... I don't go out, I don't get about. The only people I'm seeing are friends, social workers and colleagues. So what's the point in having more medical procedures, as there is more risk?<sup>608</sup>

**5.300** In July 2004 Mark's antiretroviral treatment was reviewed. At that time he continued to take Stavudine, Lamivudine, Efavirenz and Tenofovir. His CD4 count was 243 cells/mm<sup>3</sup> and his viral load was 537 copies/ml. Resistance tests showed evidence of viral resistance to Lamivudine and Efavirenz so it was not possible to improve Mark's antiretroviral treatment without the introduction of a protease inhibitor or Fuzeon (an HIV fusion inhibitor, administered subcutaneously twice a day). Mark was not keen to change his medication.<sup>609</sup>

**5.301** Mark continued to suffer from partial seizures, including brief 'absences' during which he would stare into space or repeat the word 'yes'.<sup>610</sup> In August 2005, Mark was prescribed Carbamazepine, an anticonvulsant. This was effective in controlling his seizures. Unfortunately, there was a potential interaction between Carbamazepine and Efavirenz and so the Carbamazepine was stopped and he was prescribed Levetiracetam, another anticonvulsant, instead.<sup>611</sup> Mark suffered side-effects from this new drug and so he reduced his dose of that medication himself. In October 2005, he suffered a worsening of his seizures and was admitted to hospital for a night for observation. He was discharged home with the advice to return to his previous dose of Levetiracetam.<sup>612</sup>

### ***Mark's symptoms and treatment during the period 2006 to 2011***

**5.302** In 2005 Mark started attending the clinic of Professor Leen, a Consultant Physician at the Regional Infectious Diseases Unit at the Western General Hospital in Edinburgh. In early 2006, Mark and Professor Leen discussed changing Mark's drug treatment for HIV, and commencing treatment for Hepatitis C. Having discussed the question of treatment with other patients with haemophilia, Mark was reluctant to start treatment for Hepatitis C or to change his treatment for HIV. Professor Leen advised Mark that having his HIV better controlled would be beneficial for his Hepatitis C progression. It was agreed that Mark would consider treatment for Hepatitis C before his next review appointment.<sup>613</sup> In

---

<sup>605</sup> Ibid

<sup>606</sup> See paragraph 8.40 of Chapter 8, *Knowledge of HIV-AIDS Now*.

<sup>607</sup> Day 32, pages 179–180; Excerpts from medical records recovered in respect of Mark

<sup>608</sup> Day 32, page 180

<sup>609</sup> Excerpts from medical records recovered in respect of Mark

<sup>610</sup> Ibid

<sup>611</sup> Ibid

<sup>612</sup> Ibid

<sup>613</sup> Ibid

April 2006, Mark told Professor Leen that his main concerns were his increased spasms, his arthritis and his visual impairment. In addition, he told Professor Leen that, in light of the poor response rate of Genotype 1 of Hepatitis C to treatment, he did not want to impair his quality of life by trying treatment for Hepatitis C even for a short period. Mark asked Professor Leen instead to try to improve his quality of life by reducing the number of spasms and monitoring his visual changes. With regard to his treatment for HIV, Mark was aware that on his current treatment, the HIV virus was not fully suppressed. Professor Leen told him that there was ongoing viral replication and that he was likely to acquire new mutations in his HIV which might make future treatment more difficult. Despite this, Mark was not keen to change his HIV treatment. Professor Leen thought that Mark was 'just coping'. He planned to refer Mark back to Dr Grant due to the spasms he was having and to the Consultant Ophthalmologist for advice about his visual problems.<sup>614</sup> Mark subsequently saw Dr Grant in August 2006 who noted that Mark had a postural tremor in his right arm and some unsteadiness on his feet. He thought that Mark looked 'much better than I had seen him previously'.<sup>615</sup> He hoped that Mark would not be troubled further with spasms and neurological pain, and did not arrange any further review.

**5.303** At a review appointment at the Haemophilia Centre on 24 October 2006, Mark complained of bleeding haemorrhoids which had been a problem for a few months. Dr Dennis referred him to Professor Dunlop, Professor of Coloproctology at the Western General Hospital in Edinburgh.<sup>616</sup> At the appointment Mark also expressed some frustration at his inability to undertake everyday tasks, such as shopping. Mark's social work support had been reduced over the years and, at that time: he received three hours per week from a social worker who was unable to drive.<sup>617</sup>

**5.304** In November 2006, after discussions with Professor Leen, Mark agreed to change his treatment for HIV. He was prescribed a new combination of antiretroviral therapy, Etravirine (an NNRTI) and Kaletra (a combination of Lopinavir and Ritonavir, both protease inhibitors) with Truvada. Professor Leen was confident that these drugs would suppress Mark's HIV. Mark was warned about the risk of bleeding as a result of the protease inhibitors.<sup>618</sup> In December that year, Professor Leen noted that Mark seemed 'to have a new lease of life since starting his new medication'.<sup>619</sup> He had had no increased bleeding, and felt much less tired. In January 2007 Mark's HIV viral load was suppressed 'for the first time for a long time if ever'.<sup>620</sup> His CD4 cell count was 153 cells/mm<sup>3</sup> but Professor Leen expected his cell count to rise as his HIV was suppressed.

**5.305** Mark attended Professor Dunlop's clinic for investigation of his rectal bleeding, and initially Professor Dunlop was of the view that the bleeding was caused by an anal fissure. He prescribed Diltiazem cream (a cream used to relax the anal sphincter) for this, but the bleeding continued.<sup>621</sup> On 19 February 2007 Mark was admitted to the Colorectal Unit of the Western General Hospital, after attending the Haemophilia Unit, due to rectal bleeding and pain. The Haemophilia Unit had treated Mark with Factor VIII. Mark did not wish to remain in hospital and so, after being advised about the application of the cream,

---

<sup>614</sup> Ibid

<sup>615</sup> Ibid

<sup>616</sup> Ibid

<sup>617</sup> Ibid

<sup>618</sup> Ibid

<sup>619</sup> Ibid

<sup>620</sup> Ibid

<sup>621</sup> Ibid

was discharged home.<sup>622</sup> A week or so later Mark was admitted to the Colorectal Unit for further investigations. These investigations revealed that Mark had T3 anal squamous cell carcinoma.<sup>623</sup> Squamous cell carcinoma is the second most common cancer of the skin, and T3 means that the tumour is over 5 cm in size. The risk of anal carcinoma is increased in HIV-infected patients.

**5.306** Mark was referred to Dr McLean, a Consultant Clinical Oncologist at the Western General Hospital, for consideration of radiotherapy and chemotherapy. On 13 March, Mark saw Dr Horn, a Consultant Haematologist, at a review appointment. She noted that Mark might require increased prophylactic Factor VIII treatment to cope with his chemotherapy. She also noted that, due to his HIV status and his low CD4 cell count, he might be more susceptible to infection than most patients if he became myelosuppressed (suppression of the bone marrow activity) and neutropenic (abnormally low number of neutrophils, white blood cells) as a result of the chemotherapy treatment. She commented that there would need to be close liaison between Dr McLean, Professor Leen and herself during Mark's cancer treatment. She noted that Mark was continuing to struggle 'considerably' with practical aspects of his life as his partner was unwell, and was staying with him less frequently.<sup>624</sup> Many of his struggles related to his visual impairment, and he found situations like collecting his medication and dealing with his banking and mail difficult. Dr Horn was of the view that he needed support from a worker with experience of working with visually impaired individuals, particularly in light of his impending treatment. She liaised with Professor Leen about this and wrote to the community social worker on Mark's behalf. She advised Mark to cancel a holiday he had booked to Lanzarote on 27 March, in case he experienced rectal bleeding while abroad.

**5.307** On 20 March 2007 Mark underwent a staging MRI and CT scan.<sup>625</sup> In April, when he was 37 years old, Mark started radiotherapy and chemotherapy treatment at the Western General Hospital in Edinburgh. Mark was classed as 'a very high risk patient' to have treatment-related complications, including opportunistic infections, due to his low CD4 cell count. These risks were explained to Mark.<sup>626</sup> He attended the hospital six days a week for this treatment. As a result of the treatment Mark lost all of his body hair, except on his head. During the last week of treatment he was in a great deal of pain. He was prescribed Oramorph (an oral solution containing Morphine) and other painkillers.<sup>627</sup> Mark stated that after the treatment he was given the all clear.<sup>628</sup> After this treatment Mark travelled on the back of a motorcycle around Europe with some friends.<sup>629</sup>

**5.308** On 21 June 2007, four weeks after Mark had finished his radiotherapy and chemotherapy treatment, Dr Horn visited Mark at home. She wrote that she was pleased to see that he had tolerated the treatment very well.<sup>630</sup> She noted that one of Mark's main problems was reduced appetite and episodes of nausea. He had been prescribed Metoclopramide (a medication used to treat nausea) by the Oncology Unit, along with nutritional supplements.

<sup>622</sup> Ibid

<sup>623</sup> Day 32, page 180; Excerpts from medical records recovered in respect of Mark

<sup>624</sup> Excerpts from medical records recovered in respect of Mark

<sup>625</sup> Ibid

<sup>626</sup> Ibid

<sup>627</sup> Day 32, pages 180–181

<sup>628</sup> Ibid, page 181

<sup>629</sup> Ibid, page 182

<sup>630</sup> Excerpts from medical records recovered in respect of Mark

**5.309** In October that year, Mark attended an outpatient appointment with Professor Hayes, Professor of Hepatology at the RIE to discuss treatment for Hepatitis C. Professor Hayes conceded, in light of Mark's recent treatment for cancer, that the timing was not perfect for this discussion.<sup>631</sup> Mark proved himself to be very knowledgeable about the likelihood of the success of treatment. Professor Hayes was of the view that Mark was possibly at either a pre-cirrhotic or early cirrhotic stage, characterised by a slightly reduced platelet count, and a higher serum hyaluronic acid concentration.<sup>632</sup> As Mark had never undergone a liver biopsy, it was difficult to be more definite about whether he had cirrhosis or not.<sup>633</sup> He suggested that Mark continue with surveillance for hepatocellular carcinoma with six-monthly alphafetoprotein checks. He noted that Mark had previously had an endoscopy which had showed one column of grade two varices. He was being treated with Propranolol (a medicine used to treat a number of conditions, including varices).

**5.310** On 8 January 2008, Mark attended an appointment at the Haemophilia Centre. At the previous appointment in December 2007 a small lymph node was palpable in Mark's neck. When he was re-examined at his appointment in January there was no longer lymphadenopathy palpable in his neck. Dr Horn noted that Mark was under some stress due to problems with neighbours; his sleeping pattern was abnormal, and he was experiencing waking early. She also noted that Mark was still struggling with his social circumstances. A Consultant Ophthalmologist had offered Mark an appointment at the Vision Support Centre. Unfortunately this appointment did not take place as he was diagnosed with anal cancer around the same time and his oncology appointment took precedence. Dr Horn planned to write to ask for the appointment to be rescheduled.<sup>634</sup>

**5.311** About a year after Mark's diagnosis with anal cancer, he attended a review appointment with Professor Dunlop. Professor Dunlop found a lump and, after further investigation including surgery, Mark was advised that the anal cancer had recurred. He was told that the only treatment option was abdominoperineal resection (removal of the anus, the rectum and part of the sigmoid colon) with a permanent colostomy. Mark underwent this procedure on 13 August 2008. While he was an in-patient, an occupational health worker came to speak to him about the support he would need at home. The worker put on a mask, gown and gloves and stood at the far side of the room to speak to him.<sup>635</sup> Mark recovered very well from the surgery.<sup>636</sup> There was a concern that, due to Mark having undergone radiotherapy so recently, the wound would not heal properly and might remain open. However it healed well and Mark described the scars as 'impressive'.<sup>637</sup> There was concern about how Mark would cope with a colostomy in view of his visual impairment, but in fact he managed 'surprisingly well'.<sup>638</sup> In October 2008, Dr McLean noted that Mark 'really is a remarkable man, given all his adversities .... He really is quite inspirational'.<sup>639</sup>

---

<sup>631</sup> Ibid

<sup>632</sup> 'Serum hyaluronic acid' levels increase with the development of liver fibrosis in patients

<sup>633</sup> The severity of the disease is assessed by the pathologist who, having had regard to the amount of inflammation and scar tissue, grades the liver biopsy samples as mild, moderate or severe. Liver biopsy is discussed in more detail in paragraphs 13.89–13.91 of Chapter 13, *Knowledge of Viral Hepatitis Now*.

<sup>634</sup> Excerpts from medical records recovered in respect of Mark

<sup>635</sup> Mark's Witness Statement

<sup>636</sup> Day 32, page 181; Excerpts from medical records recovered in respect of Mark

<sup>637</sup> Day 32, pages 181–182; Excerpts from medical records recovered in respect of Mark

<sup>638</sup> Day 32, page 181

<sup>639</sup> Excerpts from medical records recovered in respect of Mark

**5.312** Mark has continued to experience muscle spasms and episodes of tremor, particularly affecting his right side. This has exacerbated the pain he has experienced due to bleeds, and has affected his ability to inject himself with Factor VIII. In June 2010, Mark was referred back to Dr Grant for advice about the tremor and absence seizures.<sup>640</sup> Dr Grant noted that these worsened when Mark was anxious, and he suggested that Mark's doses of Propranolol and Levetiracetam be increased and, if that did not improve his symptoms, then he be prescribed Diazepam.<sup>641</sup> In the October, Mark's CD4 count was 219 cells/mm<sup>3</sup> and his viral load was lower than 40 copies/ml.<sup>642</sup>

**5.313** In December 2010, Mark complained of poor appetite and nausea. He wondered if there might be a psychological component to these symptoms as he associated eating with his colostomy bag filling up.<sup>643</sup> These symptoms subsequently improved.

**5.314** With regard to treatment for Hepatitis C, Mark has continued to have regular discussions about this with Professor Leen and, occasionally, at his Haemophilia Clinic appointments, with Professor Hayes about this. A liver ultrasound in 2010 was 'satisfactory', with no evidence of any focal lesion.<sup>644</sup> Mark is aware of the new treatments which have been recently licensed, and are likely to benefit, in particular, those who have Genotype 1 of the virus.<sup>645</sup> It is unclear when Mark will be eligible for treatment with these new drugs.<sup>646</sup>

#### *Specific impacts of Mark's infection with HIV*

**5.315** It is apparent that the impact of all Mark's symptoms and disabilities has made, and will continue to make, life extraordinarily difficult for him. He is registered blind, and although he does have some awareness of things moving on his left-hand side, he is unable to read or recognise people.<sup>647</sup> He has advanced arthritis in his knees, both ankles and both elbows as a result of bleeds. Sometimes he is wheelchair bound when a bleed occurs. Otherwise he walks with the support of a stick or crutches.<sup>648</sup> Mark has regained strength in his right arm but has little coordination of it.<sup>649</sup>

**5.316** A very significant impact of Mark's symptoms of HIV in combination with his haemophilia is that Mark has needed, and will continue to need, support with day-to-day living. It was apparent from Mark's evidence that he has strived for his independence. He stated:

I have tried to live a lot of my life very independent and the lack of sight very much takes that away. I'm relying on other people for everything from shopping to transport and that has got to be one of the hardest things for me to deal with, you know, to take that deep breath and allow other people.<sup>650</sup>

---

<sup>640</sup> Ibid

<sup>641</sup> Ibid

<sup>642</sup> Ibid

<sup>643</sup> Ibid

<sup>644</sup> Ibid

<sup>645</sup> These new treatments are discussed in more detail in Chapter 13, *Knowledge of Viral Hepatitis Now*, paragraph 13.115.

<sup>646</sup> Excerpts from medical records recovered in respect of Mark

<sup>647</sup> Day 32, page 95

<sup>648</sup> Excerpts from medical records recovered in respect of Mark

<sup>649</sup> Mark's Witness Statement

<sup>650</sup> Day 32, page 187



**5.317** In a letter to the City of Edinburgh, Health and Social Care Department dated 18 November 2009, Dr Horn wrote:

[Mark] has coped extremely well over the years with the many difficulties that have faced him. Although he has support from a number of agencies, this is not proving sufficient to meet his very unique needs at present and there is also a lack of continuity of care for [Mark], which is having a major impact on his ability to cope with life.

He is also becoming increasingly socially isolated as a result of difficulties taking part, without support, in the activities that he enjoys.<sup>651</sup>

**5.318** Giving some insight into the type of support which Mark needs, she wrote:

[T]here seems to be a lack of continuity and there have been several instances of [Mark] not realising the timing of important appointments and missing them because he cannot read his appointment cards/letters. He is also struggling with his medication, which is very complex and although he has managed this very well over the years he feels and I agree, that he is requiring more help with this. The counsellors who have been provided to give him psychological support are increasingly inappropriately involved in doing practical tasks for him. He has difficulty with shopping and sometimes difficulty with meal preparation. His condition means that he is vulnerable to losing weight if his nutritional in-take is inadequate and he is currently having ready meals or snacks prepared for him intermittently when possible. He has lost his confidence in going out alone and is struggling with issues such as his banking. The district nurses provide support for his stoma and he is able to do some of the stoma care himself. However there are aspects of his stoma care that he cannot manage on his own and he is currently sometimes relying on his parents for this.<sup>652</sup>

**5.319** Like others needing support at home, Mark has had to cope with changes in the care he receives, and has had to argue for more support. This has taken its toll on Mark. In 2009, he was seen by a Consultant Clinical Psychologist from the Edinburgh Cancer Centre at the Western General Hospital. This psychologist believed that the low mood that Mark was experiencing at the time was 'directly related to his frustrations and anger regarding the level of social support and nursing care that he is receiving'.<sup>653</sup> She wrote:

I have the impression that he has tried on many occasions in the past to be able to effect some change, but has had little success. [Mark] has always been a man who has prided himself with being effective and competent and it is particularly difficult for him to manage his multiple health conditions while having less security in the quality of the care that is being offered to him. Although I would describe [Mark] as experiencing a moderate level of depression at present, I am concerned that his low mood may well escalate should these difficulties in his care not be resolved.<sup>654</sup>

---

<sup>651</sup> Excerpts from medical records recovered in respect of Mark

<sup>652</sup> Ibid

<sup>653</sup> Ibid

<sup>654</sup> Ibid

**5.320** Now Mark has home-help support every day of the week which, he stated, 'certainly makes a difference'. He stated that he has 'a fair degree of determination to stay in [his] own house'.<sup>655</sup>

**5.321** When asked how he spends his time, Mark stated that he has a talking computer. He has had parts of his home and garden adapted so that he is able to move around outside and go upstairs. One issue for him is that he needs to know where everything is so that he can move around safely. For example, if a home help puts a sharp knife in a different place, Mark is unable to see it and may injure himself as a result.<sup>656</sup>

**5.322** Mark owns his home and has a mortgage for this arranged through the MacFarlane Trust. He has never applied for life insurance and has no pension. Mark obtained travel insurance after his chemotherapy and radiotherapy treatment. He stated that it was more expensive as he had undergone a serious medical procedure within 12 months. Mark has received both Skipton Fund payments and recently he has applied for the increased payment.<sup>657</sup>

**5.323** Mark has some feelings of regret that he did not tell his parents sooner that he was HIV-positive: 'I feel I have let them down to some degree'.<sup>658</sup> He stated that it was awkward not telling them his diagnosis at the time. Like Mark, his father likes motorcycles too. Mark used to ride his motorcycle past their house but he did not stop and say hello because 'there was the possibility of conversation. You know, if he had asked me directly, I wouldn't have been able to deny it'.<sup>659</sup> He stated, on the other hand:

I think in the scheme of things it has probably helped my parents to some degree because they didn't know. I know the stress and concern would have been greatly increased over the years. Again, I think, if I had told them, they would have been very enthusiastic for me to start taking medication or antiretrovirals before I actually did, which in the scheme of things may not have been beneficial.<sup>660</sup>

**5.324** Mark stated, 'My parents and sister have been a fantastic help to me'.<sup>661</sup>

**5.325** When asked about the personal impact of his infection with HIV, Mark stated:

I suppose the thing that I remember is how my world was smashed into a million pieces from one sentence, when Ludlam told me what the situation was;.... So again I suppose it's the same situation. I mean, I'm in my 40s. I did not expect to get this far. Again whether I have helped myself by refusing medication and letting my body get on with things, it's difficult to say. The biggest problem I have at the moment again is my sight ... But it has – very much brought out who my proper friends are and who is on my side.<sup>662</sup>

---

<sup>655</sup> Day 32, Page 184

<sup>656</sup> Ibid, Page 184

<sup>657</sup> Ibid, page 185; Excerpts from medical records recovered in respect of Mark

<sup>658</sup> Day 32, page 186

<sup>659</sup> Ibid, Page 186

<sup>660</sup> Ibid, Page 186

<sup>661</sup> Mark's Witness Statement

<sup>662</sup> Day 32, pages 187–188



## CHAPTER 6

### AN EXAMINATION OF THE EFFECTS OF INFECTION WITH HEPATITIS C ON THE PATIENTS AND THEIR FAMILIES, INCLUDING TREATMENT

#### Introduction

**6.1** This chapter deals specifically with the effects of infection with Hepatitis C, on those who were infected by blood and blood products, and on the families of infected persons.

#### Hearings of evidence

**6.2** The hearings of evidence on this topic took place on 8, 9, 13, 14 and 15 December 2011 and on 10 January 2012. The following patients or relative witnesses<sup>1</sup> gave evidence to the Inquiry in respect of this topic:

1. Stephen
2. Bridie
3. Colin
4. Gordon
5. Laura
6. Anne
7. Alex

**6.3** Their evidence is narrated in this chapter. Another witness, Christine, who gave evidence about her son's infection with HIV also spoke about her own infection with Hepatitis C from blood products. Her evidence, insofar as it is relevant to this topic, is also included in this chapter.

**6.4** In addition, both Professor Howard Thomas and Professor Peter Hayes (Professor of Hepatology in the Liver Unit, Royal Infirmary of Edinburgh (RIE) with Honorary Consultant Physician status with Lothian Health Board), provided the Inquiry with a clinical view on the effects of infection with Hepatitis C on patients and their families. Their evidence is referred to, where appropriate, throughout this chapter.

#### Stephen

**6.5** Stephen was 44 years old when he gave evidence. He is married and has a daughter. He lives in the north of Scotland and works in the financial sector.<sup>2</sup> Stephen suffered from Haemophilia A and acquired both the HIV and Hepatitis C viruses from blood products.<sup>3</sup>

#### *Stephen's diagnosis with and treatment for Haemophilia A*

**6.6** In 1968 when he was 11 months old Stephen was diagnosed with severe Haemophilia A, having a clotting factor of less than 1%. His maternal great grandfather and a cousin also had haemophilia.<sup>4</sup> He was treated as a child at the local children's hospital and, from about the age of 13 or 14 years, at the regional hospital.<sup>5</sup>

---

<sup>1</sup> As detailed in the Appendix, in order to preserve their anonymity, each witness was given a pseudonym

<sup>2</sup> Day 75, pages 2–3 and page 56

<sup>3</sup> Ibid, page 3; Stephen's Witness Statement

<sup>4</sup> Day 75, pages 3–5

<sup>5</sup> Ibid, pages 5 and 10

**6.7** The first haemophilia treatment Stephen received was in 1968 when Russell's viper venom was applied to stop bleeding gums.<sup>6</sup> Stephen's next haemophilia treatment was in 1974 when he was treated with cryoprecipitate before and after dental extractions. Thereafter he continued to be treated with cryoprecipitate. The severity of his haemophilia meant that Stephen required treatment frequently: in 1974, on 13 separate occasions.<sup>7</sup>

**6.8** Stephen's mother recorded every treatment he received in a diary. On 2 February 1976 a diary entry records that Stephen received 'New stuff, not cryo ...'.<sup>8</sup> It seems likely that this is a record of Stephen's first treatment with Factor VIII concentrate. The diary then records that, on 24 April 1976, Stephen was admitted to hospital with 'jaundice, serum hepatitis ... discovered eyes yellow'.<sup>9</sup> He was treated with rest in isolation and remained in hospital for 32 days. This acute attack of hepatitis may have been acute Hepatitis B (screening of blood for HBV was still not completely reliable in early 1976) or conceivably an acute attack of Hepatitis C (NANB Hepatitis was barely recognised in 1976). Thereafter Stephen was treated variously with cryoprecipitate or Factor VIII until the early 1980s when his treatment became solely Factor VIII.<sup>10</sup>

**6.9** By early 1982, Stephen required treatment for his haemophilia approximately every third day. Each treatment involved a 64 mile round trip to the hospital. Stephen's mother usually took him for treatment as his father worked away from home a week at a time. Stephen missed school every time he attended for treatment but did not allow this to impact on his school work.<sup>11</sup> To his credit he left school having passed five higher and nine 'O' grade exams.<sup>12</sup> Contrary to the advice of his haemophilia consultant, he played golf, football and squash.<sup>13</sup> After leaving school, Stephen started working at a bank and, in his spare time, studied for a degree in management accounting. Having obtained his degree, he subsequently became a member of the Chartered Institute of Bankers and was awarded a Fellowship of the Institute.<sup>14</sup>

### *Stephen's diagnosis with HIV*

**6.10** In about February 1986, when Stephen was 18 years old, his then haemophilia consultant told him that he was HIV-positive.<sup>15</sup> In a letter to Stephen's GP dated 27 February 1986, the consultant confirmed that Stephen's HTLV-III antibody status was positive and wrote:

I discussed the situation and some of the implications of this positive test with him when I told him the result. The immediate implication is simply that he has met this virus at some point in the past and has made antibodies to it – the fact that this test is positive does not mean that he has got AIDS. We know that a small but uncertain proportion of people with this positive antibody do go on to develop AIDS in the future, but we cannot identify those who will.<sup>16</sup>

---

<sup>6</sup> Ibid, page 4

<sup>7</sup> Ibid, page 5

<sup>8</sup> Ibid, page 6

<sup>9</sup> Ibid

<sup>10</sup> Ibid, pages 7–8

<sup>11</sup> Ibid, pages 8–9

<sup>12</sup> Ibid, page 11

<sup>13</sup> Ibid, pages 16–17

<sup>14</sup> Ibid, page 12

<sup>15</sup> Ibid, page 11

<sup>16</sup> Ibid, page 13; Excerpts from the medical records recovered in respect of Stephen

**6.11** Stephen was unsure if the doctor told him all that is written in this letter but he remembers it being emphasised that although Stephen was HIV-positive, he did not have AIDS. The doctor warned Stephen of the risk of sexual transmission of the virus and of the care he needed to take discarding needles and if he were to cut himself.<sup>17</sup>

**6.12** Stephen knew what HIV was when he was told about his diagnosis. At that time there were 'hard hitting' advertisements on the television about AIDS featuring a falling tombstone.<sup>18</sup> Notwithstanding this, Stephen did not worry about his diagnosis. Stephen stated that he was not a person who worried: 'you don't worry about much in life when you are that age .... I have never let it worry me. I have got it and I have to deal with it. It's just as simple as that'.<sup>19</sup> Stephen immediately told his parents about his diagnosis but he cannot remember how they reacted to the news. He suspects that his parents may have hidden their reaction from him. He did not tell his sisters or anyone else at that time.<sup>20</sup>

### *Stephen's treatment for HIV*

**6.13** Stephen continued to attend the hospital for monitoring and blood tests every three months.<sup>21</sup> He commenced taking Zidovudine medication in August 1992.<sup>22</sup> He suffered no side-effects from it and it had no impact on his day to day life.<sup>23</sup> As Stephen's cousin's husband was the local pharmacist, arrangements were made for Stephen to obtain the medication from the pharmacy in a nearby town instead so that he could keep his diagnosis a secret.<sup>24</sup>

**6.14** Stephen's medical records show that triple therapy treatment for HIV was discussed with him in June 1998 but Stephen remained on AZT. Stephen accepted advice and recommendations of his doctors in relation to treatment.<sup>25</sup> In June 1998, Stephen was noted to have swollen parotid glands (salivary glands which lie in front of and just below each ear), a symptom of HIV.<sup>26</sup> In 2002 Stephen developed some degree of facial atrophy (wasting of fat from the face), a known side effect of AZT treatment.<sup>27</sup> Other than swollen glands, Stephen has had few symptoms of HIV and his viral load has remained undetectable.<sup>28</sup>

### *Specific impacts of Stephen's infection with HIV*

**6.15** Stephen's infection with HIV had an impact on relationships. In 1987 Stephen was in a relationship with a girl. Although he knew that he was not going to marry her, he felt 'forced to ... put her in front of the doctor to explain things ...'.<sup>29</sup> Stephen asked the doctor not to tell her that he was definitely HIV-positive. In June 1987 Stephen and his girlfriend met with the consultant and had 'a prolonged and wide-ranging discussion of the implications of HIV and haemophilia'.<sup>30</sup> In a letter following that meeting the consultant recorded:

---

<sup>17</sup> Day 75, pages 14 and 17

<sup>18</sup> Ibid, page 13

<sup>19</sup> Ibid, page 14

<sup>20</sup> Ibid, pages 15–16

<sup>21</sup> Ibid, pages 29 and 35

<sup>22</sup> Ibid, page 28; Excerpts from the medical records recovered in respect of Stephen; Zidovudine is a type of antiretroviral drug. It was the first drug approved for patients with HIV.

<sup>23</sup> Day 75, page 29

<sup>24</sup> Ibid, pages 29–30; Excerpts from the medical records recovered in respect of Stephen

<sup>25</sup> Day 75, page 40; Excerpts from the medical records recovered in respect of Stephen

<sup>26</sup> Day 75, page 42

<sup>27</sup> Ibid, page 44

<sup>28</sup> Ibid, page 17

<sup>29</sup> Ibid, pages 18–21

<sup>30</sup> Ibid, page 19; Excerpts from the medical records recovered in respect of Stephen

We discussed the following areas:

1. The fact that all severe haemophiliac patients in Scotland should be regarded as having met the HIV virus at some stage in the past regardless of any blood test ....
2. The result of 1, is that it is sensible to regard all severe haemophiliac patients as potentially infective and of course the commonest means of transmission of the virus is by sexual activity. The most effective means of preventing such transmission is the meticulous and invariable use of sheath.
3. As a result of 1 and 2, it is clearly sensible for the partners of haemophiliac men to plan not to conceive in the immediate future ....
4. When asked about [Stephen's] future I gave what had to be a guarded reply saying that we could not guarantee that he would not develop AIDS in the future although he appears in very good health at present. We would of course be keeping a close eye on his well-being.

The consultant further recorded that he thought that the information he had given was more than enough for them to digest. He asked them to go away and think about the situation and to return to see him any time they wished so that any misconceptions they would have could be clarified and any new questions answered.<sup>31</sup>

**6.16** A further impact of Stephen's diagnosis with HIV was in relation to travel. In 1992 Stephen married.<sup>32</sup> In order that he and his wife could travel to the USA for their honeymoon, they had to obtain the help of his then consultant. Unknown to Stephen at the time, she wrote to a local travel agent for advice about this. This travel agent was one of Stephen's clients and Stephen says that he was quite annoyed when he subsequently discovered the consultant had written to that company, although she had not specified Stephen's name. The letter was completely anonymous and could not have been understood to refer to Stephen. The travel agent, who had helped in dealing with the travel problems of other patients, in turn asked the US Embassy in London for advice. This advice in November 1991 was that aliens who were HIV-positive were ineligible for a visa under US law and therefore were ineligible to travel under the visa waiver pilot programme. This ineligibility could be waived in certain circumstances, including if the stay was 30 days or fewer and only for visits which involved public benefit outweighing public risk. Public benefit included family visits, medical treatment and business travel. A letter from a physician was required to support an application to waive the ineligibility, addressing the alien's current state of health, the risk to US public health and the risk of spread of infection.<sup>33</sup> The consultant wrote in support of Stephen's trip to the USA and Stephen was granted the necessary waiver. With regard to the requirement for travel insurance, Stephen and his wife eventually found a firm which specialised in haemophilia, HIV and Hepatitis C related illnesses, but obviously it was not easy for them. When trying to obtain insurance, Stephen was uncomfortable disclosing to the insurance agent that he was HIV-positive and later Hepatitis C-positive, 'But it was over the phone, so they wouldn't have known me supposing I walked past them today .....'<sup>34</sup>

---

<sup>31</sup> Excerpts from the medical records recovered in respect of Stephen

<sup>32</sup> Day 75, page 22

<sup>33</sup> Ibid, pages 24–25; Excerpts from the medical records recovered in respect of Stephen

<sup>34</sup> Day 75, page 28

**6.17** Since his honeymoon Stephen has travelled a number of times to the USA. Now he no longer needs to apply for a visa waiver but still he is questioned at immigration. After 9/11 Stephen had to attend in person at the American Embassy in Belfast to obtain the necessary visa, which involved the time and cost of travelling to Belfast. On a number of occasions, while on the aeroplane to the USA, Stephen has been required to fill out a different coloured immigration form to the majority of other passengers. At one time one of the questions on this form was, 'Are you a Nazi, a terrorist or HIV-positive?'<sup>35</sup> Stephen found these forms degrading. He considered they singled him out as different from other passengers.<sup>36</sup>

### *Stephen's diagnosis with Hepatitis C*

**6.18** It is unclear when Stephen first became aware of the fact that he had acquired Hepatitis C. There is an inconsistency between his recollection of finding out and what is stated in his medical records.

**6.19** Stephen can clearly remember being told he was HIV-positive, but he cannot remember ever having been told that he had acquired Hepatitis C: 'I don't remember the smack in the face that I remember with HIV'.<sup>37</sup> Stephen stated that having Hepatitis C was something that he became aware of.<sup>38</sup> He thinks that he first knew he had Hepatitis C in the late 1990s or the early 2000s. He stated that, had he known that he had Hepatitis C, he would have told his wife before they married in 1992 (he told her at this time he had HIV) or when she became pregnant in 1996.<sup>39</sup> Furthermore, when Stephen's wife became pregnant he and his wife asked that she be tested for HIV. He stated that had he known he had Hepatitis C they would have asked for her to be tested for this too.<sup>40</sup> In fact, on 26 September 1996 Stephen's wife was tested for both HIV and Hepatitis C, the results of both these tests being negative.<sup>41</sup> Stephen and his wife said they were unaware that she was tested for Hepatitis C until they saw the result of the test in his medical records in 2008.<sup>42</sup>

**6.20** In contrast to Stephen's recollection, the first mention in Stephen's medical records of the fact that he had acquired the Hepatitis C virus is a letter from the consultant to Stephen's GP dated 8 January 1992. This letter recorded that various viral investigations had shown that Stephen had antibodies to Hepatitis C.<sup>43</sup> Nothing in this letter suggests that Stephen was informed of this.

**6.21** The next mention of Hepatitis C in Stephen's medical records is a handwritten note on the bottom of a letter from the haemophilia consultant addressed 'To whom it may concern' dated 27 April 1995. This note appears to have been written at a subsequent clinic appointment on 8 June 1995 and states '[K]nows about Hep C. Wife had Hep A three years ago'.<sup>44</sup> A letter dated 9 June 1995 about this clinic appointment to Stephen's GP records, 'He is hepatitis C positive and does not want anything further done about this. He is, of course, HIV positive. His wife had hepatitis A 3 years ago but I have offered

---

<sup>35</sup> Ibid, page 27

<sup>36</sup> Ibid, Page 27

<sup>37</sup> Ibid, page 41

<sup>38</sup> Ibid, page 31

<sup>39</sup> Ibid, page 33; Stephen's Witness Statement

<sup>40</sup> Day 75, page 31

<sup>41</sup> Ibid, page 32

<sup>42</sup> Stephen's Witness Statement

<sup>43</sup> Day 75, page 32; Excerpts from the medical records recovered in respect of Stephen

<sup>44</sup> Day 75, page 33; Excerpts from the medical records recovered in respect of Stephen



that we check her out if he wants to'.<sup>45</sup> Stephen cannot remember this consultant ever speaking to him about Hepatitis C.<sup>46</sup> She ceased being Stephen's treating consultant in about March 1996 when a different consultant haematologist was appointed.

**6.22** A report from the Department of Medical Microbiology dated 28 July 1995 on a blood specimen obtained on 8 June 1995 recorded that Stephen was HCV PCR positive and that he had Genotype 3a of the virus.<sup>47</sup> On 29 August 1995 the consultant wrote to Stephen's GP advising him of these results and stating that Stephen would be suitable for Interferon.<sup>48</sup> At this time Stephen was undergoing liver function tests. Stephen stated that he used to have blood tests every three months which he thought were to check his CD4 ratio with regard to his HIV status. He accepted that 'liver function test' might have been mentioned to him but stated that he would not have associated that with Hepatitis C.<sup>49</sup> An ultrasound on 9 February 1996 revealed that Stephen's liver was enlarged, measuring over 17 centimetres in diameter, there were several gallstones within his gall bladder and his spleen was enlarged.<sup>50</sup> Stephen has no recollection of the ultrasound or of these results.<sup>51</sup>

**6.23** In a letter to Stephen's GP, dated 11 March 1996, his then consultant haematologist stated that at a clinic appointment the same day he discussed with Stephen 'the implications of HCV infection, our plans for its surveillance and the therapeutic options that are available for its treatment'. This letter records the doctor's impression that Stephen did not wish to have treatment with alpha Interferon 'in view of the side-effects and the very low rate of success for clearance of the virus and normalisation of ALT in HIV-infected haemophiliacs'.<sup>52</sup> Once again Stephen has no recollection of this. This letter also records that Stephen agreed to undergo an endoscopy and that the doctor planned to try to arrange this for May 1996. Stephen pointed out that he did not undergo an endoscopy until 2004 and this was borne out by his medical records.<sup>53</sup>

### *Stephen's discussions with doctors about treatment for Hepatitis C*

**6.24** Stephen remembers a discussion in the late 1990s/early 2000s with his consultant during which he was told that he should be more concerned about his infection with Hepatitis C than with HIV.<sup>54</sup> At that time, Stephen had no idea that Hepatitis C could cause him more harm than HIV.<sup>55</sup>

**6.25** The timing of this discussion coincides with the time when the consultant, like other clinicians, started to understand more about the likely consequences of patients' infection with Hepatitis C. Having initially considered it to be a fairly benign condition, clinicians came to realise that a large number of patients would develop major complications as a result of the virus, including cirrhosis and its complications.<sup>56</sup> This realisation impacted on clinicians' views about when to treat a patient, which also evolved over the years.<sup>57</sup> Prior to

<sup>45</sup> Day 75, page 33; Excerpts from the medical records recovered in respect of Stephen

<sup>46</sup> Day 75, page 34

<sup>47</sup> Ibid, page 34; Excerpts from the medical records recovered in respect of Stephen

<sup>48</sup> Day 75, page 34; Excerpts from the medical records recovered in respect of Stephen

<sup>49</sup> Day 75, page 35

<sup>50</sup> Ibid, page 36; Excerpts from the medical records recovered in respect of Stephen

<sup>51</sup> Day 75, pages 35–36

<sup>52</sup> Ibid, page 36; Excerpts from the medical records recovered in respect of Stephen

<sup>53</sup> Day 75, page 37

<sup>54</sup> Stephen's Witness Statement

<sup>55</sup> Day 75, page 44

<sup>56</sup> Professor Hayes – Day 78, page 80

<sup>57</sup> Report from Professor Hayes [PEN.018.0240] at 0245

2004, NICE<sup>58</sup> recommended that only those patients with severe disease should be treated and that the assessment of the severity of the disease should be based on a liver biopsy.<sup>59</sup> Due to the additional risks of a liver biopsy for those patients with haemophilia, they were exempted from this requirement.<sup>60</sup> In April 2004, at a Consensus Conference on Hepatitis C in Edinburgh, it was decided that a liver biopsy was no longer essential to the selection of patients for therapy. Then, in 2005, the Scottish Executive produced a 'Hepatitis C Action Plan for Scotland'.<sup>61</sup> This highlighted the importance of treating as many people as possible rather than tailoring treatment to those persons clinicians believed needed it most.<sup>62</sup>

**6.26** At a clinic appointment on 20 March 2000, Stephen and his consultant discussed treatment with Interferon and Ribavirin.<sup>63</sup> At this time the doctor was aware that being male and co-infected with HIV were major risk factors in the progression of Hepatitis C.<sup>64</sup> It was noted that Stephen's HIV infection was progressing extremely slowly with no significant morbidity and no significant fall in his CD4 count.<sup>65</sup> The doctor thought that there was no immediate urgency to start treatment. It was decided to await the outcome of further studies on the use of combination therapy for Hepatitis C in the context of HIV therapy, before deciding what treatment to pursue for Hepatitis C.

**6.27** In May 2002 Stephen had a further discussion with his consultant about treatment for Hepatitis C. The doctor told him that there was data available which showed that HIV-infected patients with high CD4 counts could safely be treated with alpha Interferon and Ribavirin, along with anti-HIV therapy, without significant problems. He also told him that success rates of around 40% for viral clearance using Pegylated Interferon and Ribavirin had been reported.<sup>66</sup> It was suggested to Stephen that one option which would inform the debate about treatment was to consider the possibility of a liver biopsy in order to ascertain the histological appearances of the liver. Stephen does not remember what he thought about a liver biopsy at this time.<sup>67</sup>

**6.28** Stephen tried to live life as normally as possible despite his diagnoses, but obviously they preyed on his mind to a certain extent. In November 2002, some fairly innocuous symptoms caused Stephen to become wrongly convinced that he had developed cancer.<sup>68</sup>

**6.29** At a clinic appointment on 17 February 2003 treatment for Hepatitis C, and the side-effects and expected outcomes of treatment were discussed once again with Stephen. Stephen did not wish to embark on the treatment over the summer holidays but indicated that he was happy to consider it in the autumn of that year.<sup>69</sup> In May 2003 Stephen developed high blood pressure. An ECG suggested that he might have developed left ventricular hypertrophy (thickening of the muscle of the left ventricle of the heart) but an echocardiogram did not confirm this.<sup>70</sup>

<sup>58</sup> National Institute for Health and Clinical Excellence

<sup>59</sup> Professor Hayes – Day 78, page 81 and Report [PEN.018.0240] at 0244; the severity of the disease is assessed by the pathologist who, having had regard to the amount of inflammation and scar tissue, grades the liver biopsy samples as mild, moderate or severe.

<sup>60</sup> Professor Hayes – Day 78, page 82; NICE Guidance on the use of Ribavirin and Interferon Alpha for Hepatitis C, October 2000

<sup>61</sup> <http://www.scotland.gov.uk/Publications/2006/09/15093626/0>

<sup>62</sup> Professor Hayes – Day 78, pages 84–85

<sup>63</sup> Day 75, Pages 42–44; Excerpts from the medical records recovered in respect of Stephen.

<sup>64</sup> Older age when the Hepatitis C virus is acquired and heavy alcohol consumption are also associated with more rapid disease progression. Obesity is associated with hepatic steatosis (fatty liver) which leads to more severe fibrosis. SIGN Guidelines [PEN.018.0298]

<sup>65</sup> Excerpts from the medical records recovered in respect of Stephen

<sup>66</sup> Day 75, page 45; Excerpts from the medical records recovered in respect of Stephen

<sup>67</sup> Liver biopsy is discussed in more detail in paragraphs 13.89–13.91 of Chapter 13, *Knowledge of Viral Hepatitis Now*.

<sup>68</sup> Day 75, pages 48–49; Excerpts from the medical records recovered in respect of Stephen

<sup>69</sup> Ibid, pages 49–50

<sup>70</sup> Ibid, pages 50–51

### *Stephen's treatment for Hepatitis C*

**6.30** Towards the end of 2003, Stephen decided that he wished to start treatment with Interferon and Ribavirin in an attempt to treat or at least slow down the progression of the virus.<sup>71</sup> In April 2004, Stephen attended an appointment with a Consultant Physician/Gastroenterologist and a Hepatology Clinical Nurse Specialist to discuss this. It was noted at this appointment that Stephen's liver enzyme levels had been deranged for some time and that he looked mildly jaundiced. He had a raised level of bilirubin (a sign of damage to the liver) and an alpha-fetoprotein of 14, the latter being noted as indicative of hepatocellular carcinoma but more likely to reflect cirrhosis against the background of Hepatitis C.<sup>72</sup>

**6.31** Stephen was told that there was increasing evidence that Hepatitis C co-infection should be treated in patients with HIV and that Hepatitis C was now the major cause of death among co-infected patients. He was also told that he had Genotype 3a of the virus and although this was one of the more favourable genotypes to treat, if he had cirrhosis as well as HIV infection then his chances of viral eradication would be much lower. He was advised that it was likely he would require 12 months of antiviral therapy with significant side-effects and around a 25% chance of being intolerant of the treatment.<sup>73</sup> The Consultant Physician told Stephen that if he did have cirrhosis then he would not tolerate the treatment and it may cause him to have hepatic decompensation. Stephen was provided with some literature on the treatment and given some web sources of information on it.<sup>74</sup> It was agreed that Stephen would undergo an ultrasound of his liver to exclude hepatocellular carcinoma (cancer of the liver) and an endoscopy check for oesophageal varices (varicose veins in the stomach and gullet). Stephen found the prospect of starting treatment 'a bit daunting but [he] knew it had to get done'.<sup>75</sup>

**6.32** In June 2004 Stephen underwent an endoscopy.<sup>76</sup> He did not know what an endoscopy was and so underwent it without an anaesthetic, something he will not repeat.<sup>77</sup> The endoscopy disclosed that Stephen had four varices.<sup>78</sup> The consultant would have prescribed Propranolol for Stephen to treat the varices but decided against it due to Stephen having suffered a life-threatening asthma attack in 1993.<sup>79</sup> An abdominal ultrasound scan in July 2004 revealed that Stephen had moderate hepatosplenomegaly (enlargement of the liver and the spleen). His spleen measured 20cm at its widest. His liver showed evidence of cirrhosis.<sup>80</sup>

**6.33** On 31 March 2005 Stephen started antiviral therapy for Hepatitis C.

**6.34** Treatment consisted of Pegylated Interferon Alpha 2b 150 mcg by subcutaneous injection once per week and Ribavirin capsules, 1200 mg daily divided into doses. It was planned that Stephen would receive 48 weeks of treatment with his Hepatitis C PCR response being checked at 24 weeks and a decision on whether to continue with

---

<sup>71</sup> Excerpts from the medical records recovered in respect of Stephen; Stephen's Witness Statement

<sup>72</sup> Excerpts from the medical records recovered in respect of Stephen. Cirrhosis means that there is scarring of the liver and regenerative nodules (lumps) – see Chapter 13, *Knowledge of Viral Hepatitis Now*, at paragraphs 13.8–13.9.

<sup>73</sup> Day 75, pages 51–52; Excerpts from the medical records recovered in respect of Stephen

<sup>74</sup> Day 75, page 53

<sup>75</sup> *Ibid*, pages 52–53

<sup>76</sup> *Ibid*, page 53

<sup>77</sup> *Ibid*, page 37

<sup>78</sup> *Ibid*, page 53

<sup>79</sup> Excerpts from the medical records recovered in respect of Stephen; Propranolol, a beta blocker, is not recommended for patients who have asthma.

<sup>80</sup> Day 75, page 54

the treatment for a further six months would be made at that time.<sup>81</sup> This was in line with 'stopping rules' which became more refined over the years and were eventually documented in the SIGN (Scottish Intercollegiate Guidelines Network) guidelines on the management of Hepatitis C, dated December 2006.<sup>82</sup> These rules defined when a person should stop treatment. For example, if a person with Genotype 1 of the virus failed to achieve an early viral response after 12 weeks of treatment then it was known that this person would be extremely unlikely to be cured and would simply suffer the complications and side-effects of the treatment.<sup>83</sup>

**6.35** The night he started his treatment, Stephen sat with his wife before giving himself the first injection of Interferon, wondering what effect it would have on him and how immediate such an effect would be.<sup>84</sup> In the event, initially Stephen did not suffer any severe side-effects and he found the treatment 'okay'.<sup>85</sup> In June 2005 the amount of Interferon Stephen was prescribed was reduced to 90 mcg due to a fall in his platelet count and neutrophils.<sup>86</sup> These are known side-effects of the treatment. A detailed summary of the known side-effects of Interferon and Ribavirin is given in Chapter 13, *Knowledge of Viral Hepatitis Now*, paragraph 13.107. When his PCR level was tested after six months of treatment, the result showed that Stephen had cleared the virus. Stephen thought that this was good and that it was worth carrying on with the treatment. He understood that it was hoped that the treatment would clear the Hepatitis C virus, but that he may still eventually need a liver transplant.<sup>87</sup> Unfortunately, Stephen's clearance of the virus proved to be temporary.

**6.36** In about mid-October 2005, Stephen began to feel generally unwell and his condition changed markedly. At this time Stephen was working full-time in a business development role at the bank, which involved him 'being out and about a lot'.<sup>88</sup> He usually worked 12 to 14 hours a day. Stephen felt tired and unable to work his usual working day. He was unable to do tasks which he normally took for granted. He would read things and not understand what he was reading. He found that he forgot what he had already read. His employers had been unaware of his diagnosis with Hepatitis C but Stephen felt that, due to these symptoms, the time had come to disclose this to them and ask them for their support. On hearing of his diagnosis, Stephen's employers were 'absolutely fantastic'.<sup>89</sup> He was subsequently absent from work for 22 months and his employers paid him his full salary for this period.

**6.37** Stephen experienced the following symptoms during the latter stages of his treatment which may have been due either to the side-effects of the treatment or to his liver disease: low levels of concentration, no energy, severe nose bleeds, loss of appetite, thinning of his hair, severe muscle cramps, including one occasion when he had cramp 'in just about every single joint in [his] body at the same time', insomnia, nausea and vomiting.<sup>90</sup>

---

<sup>81</sup> Ibid, pages 54–55; Excerpts from the medical records recovered in respect of Stephen

<sup>82</sup> Professor Hayes – Day 78, page 96; [PEN.018.0298] Management of hepatitis C – A national clinical guideline, December 2006

<sup>83</sup> Professor Hayes – Day 78, page 96; see also [PEN.018.0298] at page 19 which states that such a person has less than five per cent chance of achieving a sustained viral response.

<sup>84</sup> An overview of the side-effects of Interferon and Ribavirin is given in Chapter 13, *Knowledge of Viral Hepatitis Now*, paragraph 13.107.

<sup>85</sup> Day 75, page 55

<sup>86</sup> Ibid, page 55; Excerpts from the medical records recovered in respect of Stephen

<sup>87</sup> Day 75, page 57

<sup>88</sup> Day 75, page 59

<sup>89</sup> Ibid, pages 59–60

<sup>90</sup> Ibid, page 60

**6.38** On 3 October 2005 Stephen was prescribed medication, namely GCSF 105 mcg three times weekly by subcutaneous injection, in the hope of raising his neutrophil count so that his dose of Interferon could be increased.<sup>91</sup> His dose of Interferon was increased on 13 October 2005. At this time Stephen had a rash on his abdomen from the injection sites, had mild ascites (the accumulation of fluid in the abdomen) and was obviously jaundiced. He was prescribed Spironolactone 50 mg daily for fluid retention.<sup>92</sup>

#### *Deterioration in Stephen's condition and his admissions to hospital*

**6.39** On 17 December 2005 Stephen was admitted to hospital. On that morning he had passed a black stool and begun to vomit a large quantity of blood. On his admission to hospital his treatment with Interferon and Ribavirin was stopped. By this time Stephen had completed 37 weeks of this treatment. Stephen was noted as having been unwell for two weeks. He was lethargic, had a sore throat and dry mouth and his oral intake had reduced. Stephen was found to have bleeding from oesophageal varices and septicaemia. Stephen's condition deteriorated and he went into a coma. A couple of days after Stephen's admission to hospital, the treating doctor told Stephen's wife that Stephen had only a 40% chance of survival.<sup>93</sup> Stephen was treated with intravenous antibiotics for staphylococcus in his blood. He underwent injection sclerotherapy (a procedure to treat blood vessels by injecting a solution into them) of his oesophageal varices and underwent two banding sessions (endoscopic placement of bands over the varices).<sup>94</sup> He was found to have herpes simplex pharyngitis and this was treated with IV Acyclovir. He had hepatic decompensation with ascites and encephalopathy (damage to the brain characterised by confusion, cognitive impairment and lethargy) which required drainage, then control with diuretics. He had hypoalbuminaemia (abnormally low levels of albumin) and his INR, a measure of blood coagulation, rose to 2.7 at its worst. He developed a degree of renal impairment.<sup>95</sup> He did not regain consciousness until 26 December 2005.

**6.40** On 26 December 2005, a doctor in the GI Bleeding Unit advised Stephen's wife that the longer-term objective was to get Stephen assessed by the SLTU (Scottish Liver Transplantation Unit) in Edinburgh and that this depended on getting him through the current episode. She was told that the short-term objective was to treat the sepsis from which Stephen was suffering and to establish useful nutrition but that, at that time, they were not making progress. It was emphasised to her that the hospital would continue with active management but if Stephen's condition deteriorated, the hospital would have to review the treatment options and resuscitation preference.<sup>96</sup>

**6.41** Stephen made 'a remarkable recovery'.<sup>97</sup> His condition improved with treatment and he was discharged home on 17 February 2006. In his subsequent referral letter to the SLTU, his Consultant Physician/Gastroenterologist described this episode as 'a stormy time' and wrote that Stephen 'was very lucky to survive it'.<sup>98</sup>

**6.42** On his return home Stephen was 'very very weak' and was confined to a wheelchair.<sup>99</sup> He had no strength to walk. While he was in a coma Stephen's right knee, which had

---

<sup>91</sup> Ibid, page 60; Excerpts from the medical records recovered in respect of Stephen

<sup>92</sup> Day 75, page 60; Excerpts from the medical records recovered in respect of Stephen

<sup>93</sup> Day 75, page 62

<sup>94</sup> Professor Hayes – Day 78, page 89

<sup>95</sup> Day 75, pages 61–62; Excerpts from the medical records recovered in respect of Stephen

<sup>96</sup> Day 75, page 63; Excerpts from the medical records recovered in respect of Stephen

<sup>97</sup> Excerpts from the medical records recovered in respect of Stephen

<sup>98</sup> Ibid

<sup>99</sup> Day 75, page 64

previously been a target joint (a joint which has repeated bleeding episodes), became stuck in the foetal position. This required intensive physiotherapy and also limited Stephen's mobility. He was unable to do anything himself. Stephen's wife was given leave of absence from her work to care for him. A ramp was installed at their home for the wheelchair. Stephen also required nutritional support but was unable to tolerate a nasogastric tube. He was prescribed nutritional drinks and milk shakes instead. At this time thoughts of his daughter kept Stephen going. There were days when he thought, 'What's tomorrow going to bring?', but he never gave up hope, 'maybe because of the type of person I am' but also because of his family.<sup>100</sup>

**6.43** On 25 February 2006 Stephen was re-admitted to the local hospital with mild encephalopathy secondary to dehydration. He was very confused and did not recognise his family. He was also complaining of back pain. After treatment with lactulose (a laxative used to treat hepatitis encephalopathy) he was discharged home on 28 February.<sup>101</sup>

#### *Stephen's assessment for liver transplant*

**6.44** Stephen was admitted to the SLTU on 23 April 2006 for assessment for liver transplant. During this admission Stephen was found to have moderate to severe aortic incompetence (aortic valve not closing properly) and there was concern that this might represent recent infective endocarditis (infection on one or more valves of the heart) as a result of his recent sepsis. A cardiology opinion was sought and he had an echocardiogram performed. In addition to this, Stephen underwent further investigations for possible renal impairment and diabetes. His viral loads of both HIV and Hepatitis C were checked. Most of these investigations were carried out at the local hospital. During this time Stephen tried to remain positive. It came as a shock to him that he might be diabetic and have a heart murmur.<sup>102</sup>

**6.45** Following these further investigations Stephen was diagnosed with diabetes mellitus type 2.<sup>103</sup> Stephen believes his diabetes was caused by his liver disease and the pressure it put on his pancreas. The echocardiogram suggested mild, perhaps moderate, aortic regurgitation (the aortic blood leaks back into the heart after each contraction as the valve has failed to close completely). These complications were linked to his liver disease.<sup>104</sup> He was put on the liver transplant list in July 2006. His HIV viral loads were checked monthly after this and it was a condition of him remaining on the transplant list that his HIV viral load did not become positive.<sup>105</sup>

#### *Period between Stephen's assessment for liver transplant and undergoing the liver transplant*

**6.46** Between the beginning of March 2006 and the end of January 2007 Stephen was admitted to hospital on 19 separate occasions. Most of these admissions were due to episodes of encephalopathy which gradually worsened over time. He was also admitted on occasion due to ascites and for variceal banding (to reduce the risk of bleeding). During the episodes of encephalopathy, Stephen became drowsy, confused, nauseous, agitated and had spells of vomiting. These episodes must have been very frightening for Stephen's

---

<sup>100</sup> Ibid, page 66

<sup>101</sup> Excerpts from the medical records recovered in respect of Stephen

<sup>102</sup> Day 75, pages 67–68

<sup>103</sup> Ibid, page 68; Excerpts from the medical records recovered in respect of Stephen

<sup>104</sup> Stephen's Witness Statement

<sup>105</sup> Day 75, page 69

family, particularly his daughter. Stephen often went into a coma during these episodes for a period of 24 or 48 hours. Stephen used to know when such an episode was coming on and the severity of it depended on how quickly he was admitted to hospital. He was concerned about the long-term impact of such episodes on his brain but was reassured that there should be no impact.<sup>106</sup>

**6.47** He also attended regular review appointments at the SLTU. At an appointment in August 2006, Stephen was noted to be frail, jaundiced and very thin with no nutritional reserve:

I came from a guy who had huge upper body strength to being a guy who could do nothing for himself, in a wheelchair .... I did a lot of weight training, a lot of exercise, and to be struck down within a matter of months into a wheelchair, it's not the best.<sup>107</sup>

Latterly, his consultant told Stephen that he was becoming so weak that he might not survive many more episodes of encephalopathy. Stephen continued to suffer from ascites and eventually attended the hospital weekly to have the fluid drained.<sup>108</sup>

**6.48** Stephen was always told by the surgeons in Edinburgh that he needed 'a good liver'.<sup>109</sup> He was offered the option of a transplant from a living related donor or a close blood match. Such transplants were very uncommon at that time and this perhaps reflects the seriousness with which the surgeons viewed Stephen's condition and their wish to do the best for him. This procedure involves a significant abdominal operation for the donor which carried with it a risk of mortality of about 1%. Due to these risks Stephen never considered this as an option. He felt that he could never have forgiven himself if something happened to a relative like his sister, for the purpose of his survival. Unknown to him at the time, two people offered to be such donors for him, but one person who was subsequently tested was found not to be a match.<sup>110</sup>

### *Stephen's liver transplant*

**6.49** On 31 January 2007 Stephen was told that there was a liver available for transplant. By this time he was so ill he 'just wanted it done'.<sup>111</sup> When he received the telephone call telling him the news, everybody around him was crying and he thought, 'At last'.<sup>112</sup> He was keen to have the surgery carried out and then to try and rebuild his life as he best he could. He was admitted to the RIE that night and underwent various tests. There was concern that Stephen might have an infection as a result of his ascites but thankfully he did not.<sup>113</sup>

**6.50** On 1 February, Stephen underwent a liver transplant at the SLTU. During the surgery he was transfused with 17 units of white cell concentrate and a number of units of Factor VIII due to his haemophilia.<sup>114</sup> Following the surgery Stephen made good progress. Eight days after the procedure, an Infectious Disease Specialist prescribed Stephen triple combination antiviral therapy for HIV, namely Abacavir 300 mg, Lamivudine 150 mg

---

<sup>106</sup> Ibid, pages 69–72

<sup>107</sup> Ibid, page 72

<sup>108</sup> Ibid, page 77

<sup>109</sup> Ibid, page 76

<sup>110</sup> Ibid

<sup>111</sup> Ibid, page 77

<sup>112</sup> Ibid

<sup>113</sup> Ibid, pages 76–77

<sup>114</sup> Ibid, page 77; Excerpts from the medical records recovered in respect of Stephen

and two tablets of Kaletra, all twice a day.<sup>115</sup> Unfortunately, but not unexpectedly, this therapy led to drug interaction with tacrolimus, the immunosuppressant which Stephen was also prescribed following the surgery to prevent rejection of the transplanted liver. As a result of this Stephen developed tacrolimus toxicity. His dose of tacrolimus was withheld for a period and then restarted at a reduced level. In addition to the tacrolimus toxicity, Stephen's recovery from surgery was also complicated by development of renal impairment secondary to a combination of urinary sepsis and tacrolimus toxicity. After treatment this improved. Stephen remained extremely physically wasted. He continued to be fed through a jejunostomy tube (a tube surgically placed into the small intestine) in addition to whatever food he managed to take orally. For a while Stephen suffered from symptoms of diarrhoea and abdominal cramping as a result of the jejunostomy feeding. On 23 February he was transferred from the SLTU to the local hospital where he continued his recovery and received physiotherapy, dietetic input and monitoring.<sup>116</sup> He was discharged home from there on 6 April 2007. One outcome of the liver transplant was that the transplanted liver started producing Factor VIII and so Stephen no longer has haemophilia.<sup>117</sup>

**6.51** Stephen did not make the recovery he had hoped for from the liver transplant. He had a persistent high temperature. Various tests for the cause of this were inconclusive. On 13 April he was readmitted to the local hospital due to worsening peripheral oedema (swelling of the tissues in the lower limbs caused by the build-up of fluid) and marked shortness of breath. On 14 April an echocardiogram showed a grossly abnormal aortic valve and aortic regurgitation. There was also severe right and left systolic dysfunction (failure of the pump action of the heart). The cause of Stephen's aortic valve abnormality was infective endocarditis which had been caused by the septicaemia he had suffered in 2005.<sup>118</sup> Stephen's renal function began to deteriorate.<sup>119</sup> It was felt that Stephen needed urgent aortic valve replacement but the surgeons at the local hospital were extremely concerned about the risks to Stephen of this procedure and were not prepared to proceed with it.

**6.52** On 18 April doctors explained the poor prognosis to Stephen and his wife. They told them that Stephen had two to three days to live. Stephen and his wife were understandably very upset and shocked by this news. At the time of his admission, Stephen and his wife thought that asthma was causing his symptoms and had no idea that they were attributable to his heart. Although they understood why the surgeon would not operate on Stephen, they did not agree with his decision. Stephen slept very little that night as he was very scared.<sup>120</sup>

**6.53** The SLTU was informed of the deterioration in Stephen's condition and agreed to admit Stephen for assessment. On 19 April 2007 Stephen was transferred by 'blue light' ambulance to the RIE. Initially, the surgeons there were also reluctant to undertake the surgery due to the risks involved. However, a further opinion was sought from the Freeman Hospital, Newcastle, and this opinion was that they would proceed with aortic valve replacement. The SLTU asked the Freeman Hospital if Stephen could be transferred

---

<sup>115</sup> Excerpts from the medical records recovered in respect of Stephen; Abacavir and Lamivudine are both nucleoside reverse transcriptase inhibitors and Kaletra is a protease inhibitor. All are used to treat HIV infection.

<sup>116</sup> Day 75, page 78; Excerpts from the medical records recovered in respect of Stephen

<sup>117</sup> Excerpts from the medical records recovered in respect of Stephen

<sup>118</sup> Stephen's Witness Statement; Excerpts from the medical records recovered in respect of Stephen

<sup>119</sup> Day 75, page 80; Excerpts from the medical records recovered in respect of Stephen

<sup>120</sup> Day 75, pages 81–82



there but this was not possible due to a lack of beds in the Intensive Treatment Unit there. Given the disparity of these opinions, a further opinion was sought from Mr Campanella, a Cardiothoracic Surgeon at the RIE. He agreed to carry out the procedure.<sup>121</sup>

**6.54** Stephen believes that, had it not been for his wife, in consultation with Mr Hidalgo, the Consultant Surgeon who performed his liver transplant, he would not have undergone further surgery.<sup>122</sup> His wife insisted on the further opinions. She said she would rather tell her daughter 'that her Dad had died on the operation table than just ... left to waste away until he died at home'.<sup>123</sup> Were it not for his wife and Mr Campanella, he would not be here today.<sup>124</sup>

**6.55** Stephen underwent aortic valve replacement on 26 April 2007. At the time of the surgery, Stephen was six foot three inches in height but weighed less than six stone. Stephen produced photographs of himself at that time for the benefit of the Inquiry, and he was barely recognisable as the man in the witness box. Before the operation Stephen was told '...[w]e need a miracle'.<sup>125</sup> The odds of him surviving the surgery were less than 1% and as Stephen stated, 'You can't get worse odds than that'.<sup>126</sup>

**6.56** After the surgery, Stephen was managed in the Intensive Treatment Unit of the RIE. He required prolonged support there and was very slow to be weaned off ventilation.<sup>127</sup> After a few weeks he was transferred to the High Dependency Unit and latterly to the ward. In July 2007 Stephen was transferred back to the local hospital to continue his recuperation there. At that time the remaining issues in relation to his care were nutrition, monitoring of his diabetes, treatment of the cause of the infective endocarditis, his treatment for HIV and his mobility. He returned to work part-time at the end of July 2007.<sup>128</sup>

**6.57** In the 19-month period between December 2005 and July 2007, Stephen spent 309 days in hospital: 202 of these in his local hospital and 107 in the RIE. This period was 'an extremely traumatic time' for his family; in particular, for his wife and daughter.<sup>129</sup> Stephen's daughter was only about eight years old when he became unwell. Stephen's wife remained with him every day he was in hospital in Edinburgh and so their daughter was looked after by family and friends. She came to visit Stephen in hospital every second weekend but Stephen felt that he 'wasn't nice to look at' so the family protected her from this as best they could. At one point, Stephen and his wife told their daughter that Stephen was going to die. Stephen wanted to tell her as he did not wish this to be left to his wife to deal with. He will never forget her face during this conversation and, to this day, does not know what she was thinking at that time.<sup>130</sup>

**6.58** In her statement to the Inquiry, Stephen's wife said that during Stephen's period of illness, which began in December 2005, they had no family life. From December 2005 onwards, her life revolved around visiting him in hospital every day. She stopped working on 31 October 2006 for a period of 14 months. She stated that they had 'massive' family support throughout, without which she feels they would not have coped. She considered

---

<sup>121</sup> Ibid, page 82; Excerpts from the medical records recovered in respect of Stephen.

<sup>122</sup> Day 75, page 83

<sup>123</sup> Ibid, page 83

<sup>124</sup> Ibid

<sup>125</sup> Ibid

<sup>126</sup> Ibid

<sup>127</sup> Excerpts from the medical records recovered in respect of Stephen

<sup>128</sup> Day 75, pages 83–84

<sup>129</sup> Ibid, page 84

<sup>130</sup> Ibid, pages 84–85

that she was fortunate to have been able to stay in Edinburgh while their daughter stayed with her grandparents. During that time her daughter's grandparents effectively became her parents. She and Stephen missed a lot of their daughter's life during this time including school concerts and parents' evenings. Their daughter was unable to have friends to stay. She had to grow up very quickly.<sup>131</sup>

### *Stephen's condition now*

**6.59** Stephen has made a full recovery from his symptoms of liver disease and from his heart surgery. He required right knee surgery in June 2008 and a right knee replacement in 2009 to remedy the effects of the contracture of his knee during his coma in December 2005.<sup>132</sup> He continues to attend both the RIE and his local hospital for review and monitoring of his liver, HIV and heart. Initially he underwent blood tests every three months and tests of his heart once a year. Now he has these tests every six months and every two years respectively. His medications have now reduced from 49 tablets a day to 13 tablets – Amoxicillin, Diltiazem, Lansoprazole, Ramipril, Tacrolimus and Kaletra, and insulin injections twice a day for diabetes.<sup>133</sup>

**6.60** Stephen continues to be infected with both HIV and Hepatitis C, although presently he does not think that he has symptoms of either. He has never had any symptoms of HIV and is not aware of any symptoms at present of Hepatitis C.<sup>134</sup> With regard to HIV, his viral load remains persistently undetectable.<sup>135</sup> He is aware that Hepatitis C is more aggressive in a liver transplantee. He knows that at some time in the future he will have to undergo treatment again for Hepatitis C and this is not something he relishes. As he is in a better physical state now, he is hopeful that the side-effects of the treatment will be less severe than those he experienced before.<sup>136</sup> Nonetheless given what Stephen has been through in the past this must be a daunting prospect for him.

### *Specific impacts of Stephen's infection with HIV and Hepatitis C*

**6.61** Stephen came across as a very positive person and as such probably had a tendency to understate the effects of his infection on him.

**6.62** Before he became unwell, Stephen was very active. He was a good golfer with a single figure handicap. His inability to play for four years has affected his golf and he believes that he is not as good as he used to be. Due to the problems he developed with his right knee, Stephen has been unable to resume playing badminton and squash. He is unable to run the distances he ran previously. He is able to weight train but finds it harder to build up to the level he was before, age being a factor in this.<sup>137</sup>

**6.63** Stephen's friends are unaware that he has HIV. They are aware that he has Hepatitis C but this has had no effect at all on their relationship with Stephen.<sup>138</sup>

---

<sup>131</sup> Stephen's wife's Witness Statement

<sup>132</sup> Stephen's Witness Statement.

<sup>133</sup> Day 75, pages 85–86; Amoxicillin is prescribed as prophylaxis to prevent infections in his heart valve, Ramipril and Diltiazem are cardiac medications and Lansoprazole reduces acid in the stomach. As detailed above, tacrolimus is an immune suppressant to prevent rejection of the liver transplant and Kaletra is a protease inhibitor used to treat HIV.

<sup>134</sup> Day 75, page 86

<sup>135</sup> Excerpts from the medical records recovered in respect of Stephen

<sup>136</sup> Day 75, page 86

<sup>137</sup> Ibid, page 87; Stephen's Witness Statement

<sup>138</sup> Ibid, page 87

### *Financial impacts*

**6.64** Stephen believes that his ill-health has had a significant impact on his career and on his financial situation. Although Stephen did not suffer any loss of earnings as a result of his periods of ill-health, he believes that he incurred other losses. He normally received an annual bonus. He was paid this the first year he was absent from work but not the second. He believes that this bonus would have been at least £10,000. Stephen also believes that he missed out on promotion and the increased earnings this would have produced. Prior to his illness in December 2005, he was put forward for promotion. He was subsequently advised that, had he not then been absent from work, he would have been successful. This promotion would have resulted in a salary increase of at least £12,000 a year with associated increase of the salary related bonus. He has subsequently been promoted but due to the recession he did not receive the same salary increase as he would have done before.<sup>139</sup>

**6.65** Stephen's employment provides him with a number of benefits which he believes he would lose were he to find another job. He has a staff mortgage which includes life assurance in respect of the mortgage. He has no other life assurance. He believes that due to having HIV and Hepatitis C he would be unable to obtain any other life assurance. In about 1985 Stephen applied for life assurance from Scottish Amicable. His then consultant provided a report in respect of this application. The doctor was then asked by Scottish Amicable to carry out an HTLV-III test on Stephen. Rather than have Scottish Amicable refuse his application, as he thought it would do on receiving his test result, Stephen withdrew his application. Stephen is now anxious not to lose the life assurance he has as he does not wish his wife to be left with the debt of the mortgage, were he to die. He feels that she would have enough to cope with in such a situation without having to sell the house to clear the mortgage. His inability to obtain further life assurance precludes him and his family moving to a bigger house as they might like to do. His desire not to lose this life assurance has prevented Stephen from applying for other jobs which are better paid and have better benefits. He has also turned down a better job with a better salary and benefits.<sup>140</sup> As a result he believes that his ability to further his career has been severely limited by his infections with HIV and Hepatitis C.<sup>141</sup>

**6.66** Stephen's work pension has a death-in-service benefit of four times his salary. Once again Stephen does not wish to lose this benefit and is sure that he would not be able to obtain such a benefit at a new job due to having both HIV and Hepatitis C.<sup>142</sup>

**6.67** Stephen's wife lost earnings of about £7500 during her 14-month absence from work to care for him.<sup>143</sup>

**6.68** Stephen has received payments from both the Skipton Fund and the MacFarlane Trust.<sup>144</sup>

**6.69** Due to his medical conditions, Stephen has had to pay significantly more for travel insurance than his wife each time they have travelled. As an example of this, in October 2011 he had to pay £854 for travel insurance for himself for a three week holiday to

---

<sup>139</sup> *Ibid*, pages 88–89

<sup>140</sup> Additional information provided by Stephen

<sup>141</sup> Day 75, page 91

<sup>142</sup> *Ibid*, page 92; Stephen's Witness Statement

<sup>143</sup> Day 75, page 93

<sup>144</sup> *Ibid*, page 93

America. Some companies will not provide him with travel insurance. Due to his illness he has lost £700 in cancellation costs of a holiday.<sup>145</sup>

**6.70** He and his wife have incurred travel expenses attending hospital and medical appointments. They have also incurred car parking charges which Stephen estimates amount to over £1000. He regularly had to stay overnight in Edinburgh to attend appointments but was able to stay with family.<sup>146</sup>

**6.71** The financial impacts of Stephen's infection with HIV and Hepatitis C and, in particular, Stephen's inability to provide financially, as he would like, for his wife and child in the event of his death appear to be one of the most significant impacts on him of his infection with these viruses. His concerns for their future were he to die show that the uncertainty about his future weighs on his mind.<sup>147</sup>

### **Bridie**

**6.72** Bridie is a civil servant and lives in central Scotland. She has an older sister and a younger brother and gave evidence on behalf of them all about their mother's infection with Hepatitis C and its tragic consequences. Their mother acquired Hepatitis C from a blood transfusion in 1974 and died as a consequence of this on 10 April 2009, aged 62 years. Their father died in 2007.<sup>148</sup> For the purposes of this chapter, Bridie's mother will be referred to as 'Molly'.

### ***Molly's blood transfusion***

**6.73** On 18 October 1974 Molly was admitted to a maternity hospital in central Scotland<sup>149</sup> for the birth of her fourth child. The discharge note of this admission records:

Labour proceeded normally for about four hours when she suddenly took 'a fit' and became unconscious. She developed a marked tachycardia and, on examination was found to be almost fully dilated. At one point cardiac arrest occurred and the patient was resuscitated by external cardiac massage and given intravenous fluids.<sup>150</sup>

**6.74** Molly was then delivered by a low forceps application but sadly the baby girl died about 32 hours later. Molly bled profusely from the vagina and she was transfused in both arms under pressure, with the transfusions barely keeping up with the haemorrhage. Molly received almost three complete exchange transfusions. On examination a large cervical tear was found and a total hysterectomy was performed as this was thought to be the only way to save Molly's life. This surgery was complicated by hypofibrinogenaemia (acute bleeding caused by failure of the blood to clot) interfering with coagulation. During the surgery Molly deteriorated from time to time and for fairly long periods only a faint beat in the aorta could be detected. Initially the anaesthetist had 'great doubts about the recovery of her cerebral function as she remained deeply unconscious for some time'.<sup>151</sup> After the surgery Molly began to improve slowly and steadily. The senior obstetrician and gynaecologist who treated Molly thought that the cause of her collapse was possibly

---

<sup>145</sup> Ibid, Page 93

<sup>146</sup> Ibid, page 94

<sup>147</sup> Ibid, page 92

<sup>148</sup> Ibid, pages 2–3 and page 5

<sup>149</sup> Bridie wishes this hospital to remain anonymous

<sup>150</sup> Day 76, page 6; Excerpts from the medical records recovered in respect of Molly

<sup>151</sup> Excerpts from the medical records recovered in respect of Molly

an amniotic fluid embolism which caused the coagulation defect in the blood.<sup>152</sup> Molly spent some time in the Intensive Care Unit of the maternity hospital before transferring to another hospital where she recuperated. This was a severe, life-threatening episode and there is no doubt that the blood transfusions Molly received contributed to saving her life.

**6.75** Molly suffered long-term effects from this serious event. She became blind in her left eye, suffered weakness in her left hand side and had constant back and abdominal pains. She also became anxious and very worried about hospitals. When she attended an appointment at a hospital in 1988 she had an anxiety attack and felt hot, sweaty and faint at the thought of being in hospital again.<sup>153</sup> This must be borne in mind when considering what Molly subsequently endured as a result of her infection with Hepatitis C.

### *Molly during Bridie's early childhood*

**6.76** As a child Bridie remembers her mother always being at home and everything being tidy and ordered there. Her mother did not work and Bridie and her siblings now believe that this was because she was unwell. They heard that, before they were born, their mother used to be 'the life and soul of the party' but from about 1980 onwards it seemed to them that their mother was always ill and in her bed, except for the odd night out.<sup>154</sup> She complained of sore joints.<sup>155</sup> Their father worked initially in manual type work and then latterly in offices. He worked 14-hour shifts and so, as children, Bridie and her siblings saw him infrequently.

### *Molly's diagnosis with cirrhosis*

**6.77** In January 1992 Molly underwent an ultrasound of her kidneys which revealed coincidentally that she had gallstones.<sup>156</sup> She remained asymptomatic from these until about the middle of 1993 when she started to suffer from right upper quadrant abdominal pain radiating through to her back. On 4 July 1994 Molly was admitted to hospital for a laparoscopic cholecystectomy (removal of her gallbladder). During this procedure the surgeons noticed that she had what appeared to be cirrhosis of the liver. In order to help determine the cause of the cirrhosis the surgeons took a biopsy of her liver. Antibody studies were also carried out. The biopsy revealed changes of micronodular cirrhosis of indeterminate origin but there were some features suggestive of Hepatitis B infection.<sup>157</sup> The discharge note from Molly's admission to hospital records 'The lady herself denied any excess alcohol intake'.<sup>158</sup> It was common at the time for doctors to consider alcohol as a cause of cirrhosis. Molly and her family were shocked that she had cirrhosis and that it might have been caused by excess alcohol. Having had her drink spiked when she was younger, Molly only drank at Christmas time when she had a drink of Advocaat. Molly explained this to the doctors treating her but after she was diagnosed with cirrhosis she felt that she was treated differently by the staff as they presumed that she was an alcoholic. She heard people whispering about her.<sup>159</sup> Molly was mortified by this and very upset. She was told never to drink alcohol again.

---

<sup>152</sup> Ibid

<sup>153</sup> Ibid

<sup>154</sup> Day 76, page 4

<sup>155</sup> Bridie's brother's Witness Statement

<sup>156</sup> Day 76, page 9; Excerpts from the medical records recovered in respect of Molly

<sup>157</sup> Day 76, page 11; Excerpts from the medical records recovered in respect of Molly

<sup>158</sup> Day 76, page 10; Excerpts from the medical records recovered in respect of Molly

<sup>159</sup> Day 76, page 72

**6.78** Unfortunately as alcohol is such a common cause of abnormal liver function test results and liver disease, to this day medical staff and others make incorrect assumptions about patients found to have these. As Professor Hayes stated in his evidence:

[I]t still remains common that people who have abnormal liver tests are referred up to the clinic and they have had a good telling off from their GP about drinking too much alcohol when they insist that they are almost tee-total.<sup>160</sup>

This has been, and remains, a major issue for patients.

**6.79** Molly was told that she required follow-up from a Gastroenterologist and she asked that she be referred privately. She was referred to a Consultant Physician. She saw him in about August 1994. The Consultant Physician noted that Molly had palmar erythema (reddening of the palms) and was mildly jaundiced. Her liver was palpable just below the costal margin (lower edge of the chest). His initial suspicion was that the cirrhosis was caused by a Hepatitis B infection contracted after the blood transfusion she had received in 1974.<sup>161</sup> He also considered primary biliary cirrhosis or chronic auto-immune hepatitis as possible causes. He undertook further investigations of the cause of her cirrhosis including a liver blood test screen and a Hepatitis B surface antigen test but these were inconclusive.<sup>162</sup> The Consultant Physician saw Molly for the third time on 10 October 1994. He noted that she had no symptoms of chronic liver disease although the previous findings on examination persisted.<sup>163</sup> He noted that the latest liver function tests showed continual enzyme disturbance of a mild nature which was not significantly different from her previous visit. He noted also that there were antibodies to Hepatitis B surface antigen present in low titre, indicating a previous infection with an adequate immune response eventually. He concluded that she had developed Hepatitis B at the time of her blood transfusion. He suspected that she subsequently developed chronic hepatitis which damaged her liver although she eventually seroconverted and developed sufficient antibodies to stop the infection progressing. He told her to avoid alcohol and planned to see her at regular intervals. He saw her again in January 1995 when he noted that her liver function test results were not dissimilar to results from her previous visits. As her medical insurance had expired he planned to follow her up at a general hospital.<sup>164</sup> In the event this follow-up did not occur. Molly failed to attend an appointment with the doctor on 18 July 1995 and it seems she made no further appointment with him.<sup>165</sup>

### *Molly's diagnosis with Hepatitis C*

**6.80** In May 1996 Molly attended her GP to have her liver function monitored. As well as carrying out a liver function test, her GP also carried out a screening for Hepatitis C.<sup>166</sup> The result of this was positive. On 31 May 1996 Molly's GP wrote to her and stated:

The repeat liver tests showed no significant change from your previous results. However, I took a blood test to test for a new form of hepatitis recently discovered called hepatitis C. This was positive. It is therefore likely that it has been hepatitis C which is the problem causing your liver abnormalities rather than hepatitis B.<sup>167</sup>

---

<sup>160</sup> Day 78, page 104

<sup>161</sup> Day 76, page 12; Excerpts from the medical records recovered in respect of Molly

<sup>162</sup> Day 76, page 13; Excerpts from the medical records recovered in respect of Molly

<sup>163</sup> Ibid

<sup>164</sup> Day 76, pages 13–14; Excerpts from the medical records recovered in respect of Molly

<sup>165</sup> Ibid

<sup>166</sup> Day 76, page 14; Excerpts from the medical records recovered in respect of Molly

<sup>167</sup> Day 76, page 15; Excerpts from the medical records recovered in respect of Molly

**6.81** Bridie remembers very clearly when her mother found out she had Hepatitis C. Bridie was at home in her garden and her mother and father arrived. Molly said to Bridie, 'I have just been told I'm dying. I have got AIDS'.<sup>168</sup> Bridie stated that this was how her mother took the news that she had Hepatitis C as she did not know what it was and nor did her family. As far as Bridie is aware, Molly was not offered any counselling about the virus at this time.<sup>169</sup>

**6.82** Molly's GP referred her to Dr Datta, Consultant Physician. Molly's first appointment with him was on 26 June 1996. Bridie's father accompanied her to this and all her appointments as Molly was unable to travel to these on her own. Dr Datta found no abnormal clinical signs when he examined Molly. He carried out further blood tests and was of the view that she would need a repeat liver biopsy before a decision was made about treatment.<sup>170</sup>

### *Molly's symptoms of Hepatitis C*

**6.83** Bridie was asked if she thought that her mother was suffering from symptoms of Hepatitis C at the time she was diagnosed with it. In response to this she stated:

[W]e didn't know what the symptoms of Hepatitis C were, so that wasn't until later on, when we discovered what they were, that everything that we knew or we took as being my mum as a normal person was the Hepatitis C obviously ... she had various mood swings and she was constantly tired and she was – I hate to say, she was actually classed as a hypochondriac and she was the joke of the family. Everyone laughed at her and nobody obviously knew until later that it was obviously her illness. Nobody knew she was ill. We just took that to be, that's what she is like.<sup>171</sup>

She further stated:

She was always in her bed. She was always ill. She was always at the doctor's. She was always complaining of being sore, of being tired, of being sick .... I can't remember a time of her being anything other than in bed. She was in bed when I got married and I had my hen do. She was in bed upstairs while everyone was downstairs, and everybody took that to be she wanted to be the centre of attention, and everybody laughed at her. At that time we didn't know any better. We just thought that was what she was like.<sup>172</sup>

**6.84** In February 1997 Molly attended Dr Datta for further review. He carried out liver function tests and noted that Molly's AST (aspartate aminotransferase) and ALT (alanine aminotransferase) levels were marginally better than they were in July 1996.<sup>173</sup> He considered the question of liver biopsy but did not think it necessary at that stage. He also reconsidered Interferon therapy but, having reviewed Molly's liver function test results, decided against it. Dr Datta also considered that, in the near future, the results of the combination trial of Interferon and Ribavirin might give better results for treating Hepatitis C.<sup>174</sup>

---

<sup>168</sup> Day 76, page 15

<sup>169</sup> *Ibid*, page 18

<sup>170</sup> *Ibid*, page 14; Excerpts from the medical records recovered in respect of Molly

<sup>171</sup> Day 76, page 17

<sup>172</sup> *Ibid*, pages 17–18

<sup>173</sup> See Chapter 13, *Knowledge of Viral Hepatitis Now*, paragraph 13.7 for description of these tests

<sup>174</sup> Day 76, page 19; Excerpts from the medical records recovered in respect of Molly

**6.85** In March 1997 Molly was referred to Dr Zoma, Consultant Physician in Rheumatology, due to increasing joint pains affecting her shoulders, arms, hands and knees. In his letter of referral her GP noted that Molly ‘appears to be quite limited by her joint pains’.<sup>175</sup> Dr Zoma’s notes of Molly’s first attendance at his clinic on 2 June 1997 record that Molly complained of ‘Generalised aches and pains/cervical spondylosis for “many years”’. Now [complaining of] generalised pains involving neck, shoulders, elbows, hands, hips, knees, feet’.<sup>176</sup> Molly told Dr Zoma that she had difficulty dressing and bathing and that her walking was slow and uncomfortable. Bridie remembers that her mother was unable to walk very far at all and did not even manage to walk to the shop across the road from their house without help. She was always sore and when she did walk she would ‘end up in bed at the end of the day’.<sup>177</sup> Dr Zoma considered that the overall picture was suggestive of an evolving inflammatory arthropathy and wondered if it related to her established active hepatitis. Dr Zoma asked Dr Datta if it was possible for Molly to be prescribed any non-steroidal anti-inflammatory analgesics in view of her liver condition.<sup>178</sup> Although such drugs can affect the liver, Dr Datta agreed that they could be prescribed provided her liver function was monitored. In August 1997 Molly was prescribed Nabumetone 500 mg twice daily.<sup>179</sup> Bridie does not think the medication helped her mother as she remained sore, regardless of what medication she was on.<sup>180</sup>

**6.86** In November 1997, Molly was referred to Dr Morris, Consultant Gastroenterologist as Dr Datta was retiring. On 4 December 1997 Molly attended the nurse-led Liver Assessment Clinic where she was seen by Margaret Neilson, Clinical Nurse Specialist. In her notes about this appointment, Ms Neilson records that she discussed Hepatitis C with Molly ‘at length’ and that Molly was concerned about the possibility of a liver biopsy.<sup>181</sup> Ms Neilson advised her to wait to see if a liver biopsy was necessary. Ms Neilson also gave Molly information booklets about Hepatitis C, information about a support group and contact numbers.<sup>182</sup> Bridie did not know that her mother had been given all this information and was very surprised to learn of it as neither her mother nor her father mentioned it to her.<sup>183</sup>

### *Further investigations which Molly underwent*

**6.87** Molly attended Dr Morris’ clinic on 19 January 1998 where she was seen by a Specialist Registrar. Her liver function test results remained elevated. An ultrasound of her abdomen done in January 1998 showed that her liver was ‘of a patchy echogenicity, with irregular liver capsule suggesting underlying fibrosis’.<sup>184</sup> There was no splenomegaly, varices or ascites. The possibility of a liver biopsy was discussed with Molly but it was noted that ‘she is really not keen on this at the moment’.<sup>185</sup> The ultrasound also revealed that Molly had multiple gallstones in her gallbladder. As she had undergone a cholecystectomy, the presence of gallstones caused some confusion among those treating her. While this

<sup>175</sup> Day 76, pages 19–20; Excerpts from the medical records recovered in respect of Molly

<sup>176</sup> Day 76, page 20; Excerpts from the medical records recovered in respect of Molly

<sup>177</sup> Day 76, page 20

<sup>178</sup> Excerpts from the medical records recovered in respect of Molly

<sup>179</sup> Ibid; Nabumetone is a non-steroidal anti-inflammatory drug

<sup>180</sup> Day 76, page 30

<sup>181</sup> Ibid, page 23; Excerpts from the medical records recovered in respect of Molly

<sup>182</sup> Day 76, page 24; Excerpts from the medical records recovered in respect of Molly

<sup>183</sup> Day 76, pages 24–25

<sup>184</sup> Excerpts from the medical records recovered in respect of Molly

<sup>185</sup> Day 76, page 26; Excerpts from the medical records recovered in respect of Molly. It is not noted that she had had a biopsy at the time of her cholecystectomy in July 1994 which showed cirrhosis



was investigated it also caused Molly some distress.<sup>186</sup> Subsequently, an MRI scan revealed that unusually Molly probably had a second gallbladder which was not removed during the cholecystectomy.<sup>187</sup>

**6.88** On 1 June 1998 Molly attended a clinic appointment with another Specialist Registrar. At this time it was noted that Molly had been reluctant to undergo a liver biopsy as she was unsure of the risks involved.<sup>188</sup> Molly was told that there was a risk of bleeding or even death but that this risk was reasonably low in a patient who is well. She was also told that the test could be done under ultrasound guidance if she wished it as she had multiple adhesions (fibrous bands which form between tissue and organs). Molly agreed to a liver biopsy on this basis. On 8 June 1998 the liver biopsy was carried out. Molly was admitted to the ward at 10 am for the biopsy to be carried out in the afternoon. She was told not to eat or drink anything after 8 am that morning. After the biopsy she was kept in the ward overnight.<sup>189</sup> Given Molly's fear of hospitals this must have been a difficult experience for her. Bridie thought that that her mother found the biopsy painful.<sup>190</sup> The histology report of the liver biopsy noted that there appeared to be 'a moderate increase in fibrous tissue and a suggestion of nodularity ...'.<sup>191</sup> It concluded that 'The overall appearances are entirely consistent with a hepatitis C related chronic active hepatitis'.

**6.89** In November 1998 Molly was prescribed oral Prednisolone for her rheumatoid symptoms.<sup>192</sup> It is unlikely that her bad joint symptoms were related to Hepatitis C. Her general malaise at the time may have been associated with Hepatitis C, or a combination of that and arthritis.

### *Molly's treatment with Interferon and Ribavirin as part of a clinical trial*

**6.90** In March 1999 Molly started treatment with Interferon and Ribavirin. She received this treatment as part of a clinical study entitled 'Viraferon plus ribavirin for the treatment of chronic hepatitis C'.<sup>193</sup> Prior to starting this treatment, Molly signed a Patient Consent Form confirming that she had been given a copy information sheet and the nature, purpose, duration and foreseeable effects of the study had been discussed with her.<sup>194</sup> Being included in a controlled clinical trial did not necessarily mean that the patient received the new treatment, as half of those participating in a trial received the standard treatment and half the new treatment.<sup>195</sup> However, on 9 March 1999 Molly was prescribed 6 million units of Interferon three times per week by subcutaneous injection and Ribavirin 1000 mg daily taken orally.<sup>196</sup> Molly was taught to self-inject. Bridie remembers that her mother 'was never keen on needles' and so this must have been difficult for her.<sup>197</sup> In the event her joint pain made it difficult for her to self-inject and so Bridie's father administered most of the injections of Interferon.<sup>198</sup>

<sup>186</sup> Day 76, pages 26–27; Excerpts from the medical records recovered in respect of Molly

<sup>187</sup> Day 76, page 26; Excerpts from the medical records recovered in respect of Molly

<sup>188</sup> Ibid

<sup>189</sup> Ibid

<sup>190</sup> Day 76, page 41

<sup>191</sup> Excerpts from the medical records recovered in respect of Molly

<sup>192</sup> Ibid. Prednisolone is a corticosteroid drug used to treat a number of conditions, including rheumatoid arthritis.

<sup>193</sup> Day 76, page 31; Excerpts from the medical records recovered in respect of Molly. Clinical trials are discussed in more detail in Chapter 13, *Knowledge of Viral Hepatitis Now*, paragraphs 13.95–13.96

<sup>194</sup> Excerpts from the medical records recovered in respect of Molly

<sup>195</sup> Professor Hayes – Day 78, pages 54–55

<sup>196</sup> Day 76, page 32; Excerpts from the medical records recovered in respect of Molly

<sup>197</sup> Day 76, page 31

<sup>198</sup> Ibid, page 32

### *The side-effects of treatment which Molly experienced*

**6.91** Molly looked forward to starting the treatment and dreaded it at the same time. She was keen to get rid of the virus.<sup>199</sup> On 15 March 1999, a week after she had started treatment, Molly attended the nurse-led clinic for review. In the notes of this appointment it is recorded that, during the first week of treatment, Molly suffered from general fatigue and sore bones.<sup>200</sup> Her mobility was affected and she had a dull headache which was relieved with paracetamol. She was irritable and emotional. Molly continued to attend this clinic weekly. On 22 March 1999 it was noted that she continued to suffer from the same symptoms as before. On 29 March 1999, three weeks after starting treatment, Molly was noted to be suffering from general fatigue, loss of appetite, weight loss (she had lost four pounds), nausea and a skin rash on her arms and trunk.<sup>201</sup> She was tearful and irritable. Arthritis and general fatigue caused her reduced mobility and her haemoglobin had reduced by 4 gm/dL in two weeks.<sup>202</sup> At this time her dose of Ribavirin was reduced from 1000 mg daily to 600 mg daily and the Interferon from 6 million units to 3 million units three times a week.

**6.92** The notes of the next appointment on 8 April 1999 record that initially Molly felt better on the reduced doses but unfortunately this improvement did not last. She then stopped taking the Ribavirin for a few days and felt better. She described general fatigue, nausea and sleeplessness. It was noted that she was struggling to cope with the treatment. One of the doctors was consulted and he recommended that she stop taking the Ribavirin for a week and increase the dose of Interferon back to its original dose of 6 million units three times a week.<sup>203</sup> A week later Molly reported a marked reduction in side-effects. Her appetite had returned and she was suffering from fewer headaches. So she continued on Interferon monotherapy. Four weeks later, in May 1999, it was noted that Molly was suffering from general tiredness – she was sleeping a lot, and had poor appetite and general aches and pains with arthritis. On 3 June, having completed 12 weeks of Interferon treatment, Molly continued to suffer from fatigue and to sleep a lot. Her platelet count was reduced. Her dose of Interferon was again halved to three million units, three times a week.<sup>204</sup>

**6.93** A virology result dated 18 June, 12 weeks after Molly started treatment, was HCV PCR negative showing that the virus had been cleared. It is unclear if this information was conveyed to Molly. Bridie was unaware of this test result.<sup>205</sup> As a result of the negative PCR test it was planned that Molly continue with treatment with Interferon monotherapy with a view to completing a year's course of it.<sup>206</sup> Molly continued to suffer from general fatigue and to sleep a lot. Bridie recalls that her mother's 'days and her nights were turned round about and ... she was always sore'.<sup>207</sup> Candidly she admitted, 'you tended to listen to my mum and it went in one ear and out the other, because you got to a stage where you got fed up hearing it'.<sup>208</sup> In August 1999 Molly was prescribed sleeping tablets by her GP and

<sup>199</sup> Ibid, pages 31–32

<sup>200</sup> Ibid, pages 33–34; Excerpts from the medical records recovered in respect of Molly

<sup>201</sup> Day 76, page 34; Excerpts from the medical records recovered in respect of Molly

<sup>202</sup> The normal level in adult females 12–16 gm/dL

<sup>203</sup> Excerpts from the medical records recovered in respect of Molly

<sup>204</sup> Ibid

<sup>205</sup> Day 76, page 35

<sup>206</sup> Excerpts from the medical records recovered in respect of Molly

<sup>207</sup> Day 76, page 36

<sup>208</sup> Ibid

she found these helpful.<sup>209</sup> She completed the prescribed Interferon course of 48 weeks of treatment on 14 February 2000. At that time it was noted that the nails on both her hands and her feet were splitting and she was trying to stop taking the sleeping tablets.<sup>210</sup> A month after the treatment had stopped it was noted that Molly remained tired but that her appetite had improved. A further blood test dated 1 March 2000 confirmed that Molly remained HCV PCR negative at the end of her treatment.<sup>211</sup> Once again it is unclear if this result was conveyed to Molly and Bridie was unaware of it.

**6.94** As was standard procedure, a further HCV PCR test was carried out six months after Molly's treatment finished. Unfortunately the result of this test was positive. Molly was told this result at a clinic appointment on 11 September 2000. She attended this appointment with her husband and was seen by a Research Fellow and Sister Neilson. In a letter to Molly's GP about this appointment, the Research Fellow wrote that Molly had 'a tearful reaction to the news' but that they stressed to her the importance of remaining positive.<sup>212</sup>

### *Molly's condition after treatment and her deterioration*

**6.95** Molly continued to attend Dr Morris's clinic for monitoring of her rheumatoid arthritis. The discomfort she suffered from her arthritis and her difficulty sleeping persisted.<sup>213</sup> Doctors from both these clinics liaised about appropriate treatment for her rheumatoid arthritis. Dr Zoma had no doubt that her joint symptoms were linked to her chronic Hepatitis C infection.<sup>214</sup> Around this time she was prescribed low dose Prednisolone, Tramadol (pain relief medication) and Lansoprazole.<sup>215</sup>

**6.96** On 9 September 2002, at Dr Morris's clinic, Molly discussed treatment for Hepatitis C with the Specialist Registrar she saw.<sup>216</sup> The issue of retrying combination therapy was raised. Molly told the doctor that she felt she had not tolerated the treatment before as her sister had recently passed away and she was feeling quite depressed. This suggests that perhaps Molly thought she might tolerate the treatment better under different circumstances and she was obviously keen to try it again. The Specialist Registrar arranged for Molly to be reviewed by the Liver Specialist Nurse so that she could discuss this further. On 28 July 2003, Molly attended an appointment with Dr Morris. He wrote to her GP that he had had a detailed conversation with her about the information she had received at her previous appointment about re-treatment. It was his opinion and that of Sister Neilson that Molly should not be reconsidered for treatment of combination Interferon and Ribavirin because of the marked side-effects that she experienced when this was tried initially. He further wrote, 'I am unclear why her expectations were raised in this manner but have offered my apologies for any undue anxiety caused'.<sup>217</sup> It must have been very disappointing for Molly to believe, for 10 months, that she might receive further treatment when in fact this was not the case.

---

<sup>209</sup> Excerpts from the medical records recovered in respect of Molly

<sup>210</sup> Ibid

<sup>211</sup> Ibid

<sup>212</sup> Day 76, pages 37–38; Excerpts from the medical records recovered in respect of Molly

<sup>213</sup> Day 76, page 38

<sup>214</sup> Excerpts from the medical records recovered in respect of Molly

<sup>215</sup> Prednisolone is a corticosteroid drug used to treat a variety of inflammatory conditions including rheumatoid arthritis; Tramadol is a painkiller used to treat moderate to severe pain; Lansoprazole is a proton pump inhibitor which reduces the amount of acid produced in the stomach.

<sup>216</sup> Excerpts from the medical records recovered in respect of Molly

<sup>217</sup> Day 76, page 39; Excerpts from the medical records recovered in respect of Molly

**6.97** At a review appointment on 12 July 2004, it was noted by a Senior House Officer, that Molly remained asymptomatic from her Hepatitis C.<sup>218</sup> An ultrasound of Molly's abdomen performed in May 2004 was normal and liver function test results showed slight overall improvement. Once again, Molly raised the question of treatment and she asked about Pegylated Interferon therapy. This doctor reiterated that this treatment was not in her best interests as her previous treatment had been unsuccessful and she had also experienced significant side-effects.<sup>219</sup>

**6.98** Around this time Molly started suffering from recurrent urinary tract infections. In 2004 she attended the renal department of the Glasgow Royal Infirmary (GRI) for investigation of this. An abdominal ultrasound in May 2004 demonstrated normal kidneys.<sup>220</sup> She was also found to have high blood pressure and started receiving treatment for this.<sup>221</sup>

**6.99** Molly continued to attend the hospital for monitoring. In 2006 Dr Stanley, Consultant Gastroenterologist, became the consultant in charge of her care. A liver ultrasound in May 2006 showed liver cirrhosis and this was in keeping with her blood tests at the time.<sup>222</sup> The doctor who saw Molly at her clinic appointment on 31 July 2006 discussed the possibility of a liver biopsy to clarify whether or not she was cirrhotic. Molly was not keen on this and said that she would only consider a further liver biopsy if it could be carried out under general anaesthetic. This was not an option and so the doctor proceeded on the assumption that Molly was cirrhotic and, on the basis of this assumption, commenced screening her for varices and hepatocellular carcinoma.

**6.100** Molly underwent an endoscopy on 28 September 2006. The report of this noted that Molly was 'very anxious' and that the endoscopy was 'very poorly tolerated'.<sup>223</sup> The endoscopy revealed four Grade 2 varices.<sup>224</sup> There was no evidence of bleeding. Molly was subsequently prescribed Propanolol as primary prophylaxis in respect of the varices.

**6.101** In 2007 Bridie's father died very suddenly as a result of a heart attack. Until his death he had been Molly's main carer. His death had a significant effect on the whole family. Following his death Bridie took over caring for her mother while also trying to continue with her full-time job. She described this as difficult and when asked to explain what caring for her mother entailed she stated:

It probably would have been easier moving in with her. [O]bviously I had to take her to and from hospitals and doctor appointments. She couldn't do her shopping on her own, so I had to collect her, do her shopping with her. And she couldn't carry anything on her own. She couldn't actually get into the bath and out of the bath. So I had to arrange my time when she needed a bath to actually be in the house to make sure she could get herself organised that way. And I was on 24-hour call almost, just simple things. I think about the

---

<sup>218</sup> Day 76, pages 39–40; Excerpts from the medical records recovered in respect of Molly. Presumably the doctor excluded Molly's symptoms of arthritis when she recorded that Molly was asymptomatic. The section of the letter headed 'Diagnoses' includes 'Generalised Polyarthralgia'.

<sup>219</sup> Day 76, pages 39–40; Excerpts from the medical records recovered in respect of Molly

<sup>220</sup> Ibid

<sup>221</sup> Day 76, page 40

<sup>222</sup> Ibid, page 42; Excerpts from the medical records recovered in respect of Molly

<sup>223</sup> Day 76, page 43; Excerpts from the medical records recovered in respect of Molly

<sup>224</sup> The UK Guidelines on the Management of Variceal Haemorrhage in Cirrhotic Patients (2000) [gut.bmj.com/content/46/suppl\\_1/iii1](http://gut.bmj.com/content/46/suppl_1/iii1). full describes 3 grades of varices – Grade 1 – varices that collapse to inflation of oesophagus with air; Grade 2 – varices between Grade 1 and Grade 3; Grade 3 – varices which are large enough to occlude the lumen (the space in the vein).

only thing she could do was get herself almost dressed and cook herself a bit of dinner. Everything else was me.<sup>225</sup>

**6.102** Molly tended to be wakeful during the night and then mid-afternoon would lie on the couch with a blanket. Bridie and her sister received numerous phone calls from their mother during the night. In retrospect, the reversal of her normal sleep rhythm was a sign of early encephalopathy.<sup>226</sup>

**6.103** Having taken over the care of her mother, Bridie and her siblings realised what their father had endured during the last ten years of his life. Bridie's parents had been together since her mother was 15 years old. Bridie described them as 'lifetime soulmates'.<sup>227</sup> Previously Bridie's father was an active union man with a deep love of politics. He lived life to the full and had an interest in junior football and local pool leagues. He was pool champion and won numerous awards and trophies. He was the focal point of his immediate and extended family. As the burden of caring for Molly began to take its toll on him, his life changed. In March 1998, at the age of 55 years, Bridie's father, who had been unemployed for about a year and looking for work, decided that he needed to stop work and care for his wife due to her deteriorating health.<sup>228</sup> He lost contact with his work mates, stopped socialising with his friends and stopped playing and watching sports. He eventually became 'a virtual recluse'.<sup>229</sup> On one occasion Bridie's father broke down in tears when Bridie's sister was visiting as he was so worried about his wife. Molly confided in Bridie that she had been advised after her diagnosis with Hepatitis C to cease sexual relations and so Bridie's parents close physical relationship ended at that time. Bridie thinks that this affected them profoundly and on a level she will never be able to understand.<sup>230</sup>

### *Molly's diagnosis with hepatocellular carcinoma*

**6.104** In February 2008 Molly's alpha-fetoprotein was found to have risen to 26.<sup>231</sup> As a result of this she attended an urgent clinic appointment with a Specialist Registrar, on 3 March 2008. At this appointment she was noted to have lost a lot of weight. Bridie stated that Molly 'wasn't eating at that point' due to the death of her husband.<sup>232</sup> She underwent an ultrasound scan which showed that the extra-hepatic biliary tree was 'essentially normal'.<sup>233</sup> It was decided at this clinic appointment that Molly should undergo a triple phase CT scan to test for hepatocellular carcinoma. On 28 March 2008 Molly attended for the CT scan. Unfortunately, she was so scared that she ran out of the room without undergoing the scan.<sup>234</sup>

**6.105** On 1 September 2008 Molly attended for a further review with a Specialist Registrar. Bridie accompanied her mother to this appointment. At this time Molly was reported to be 'keeping well'.<sup>235</sup> She had no symptoms or signs of hepatic decompensation and the doctor considered the overall clinical picture to be 'reassuring'. He discussed with Molly her fears about undergoing a CT scan and, in particular, her fear that she would be

---

<sup>225</sup> Day 76, page 44

<sup>226</sup> Ibid, page 45; Bridie's brother's Witness Statement

<sup>227</sup> Day 76, page 48

<sup>228</sup> Ibid, pages 66–67

<sup>229</sup> Ibid, pages 46–47

<sup>230</sup> Ibid, page 48

<sup>231</sup> An increase in a person's alpha-fetoprotein level is suggestive of hepatocellular carcinoma

<sup>232</sup> Day 76, page 49; Excerpts from the medical records recovered in respect of Molly

<sup>233</sup> Day 76, pages 49–50; Excerpts from the medical records recovered in respect of Molly

<sup>234</sup> Day 76, page 49; Excerpts from the medical records recovered in respect of Molly

<sup>235</sup> Ibid

enclosed during the CT scan. Molly had previous experience of an old-style scanner which she had found extremely claustrophobic. At Bridie's suggestion Molly was able to view the scanner to try to alleviate her concerns about it. She subsequently underwent a second ultrasound scan and had repeat alpha-fetoprotein measured. The ultrasound suggested a 3.8cm left liver lobe lesion. Her alpha-fetoprotein had risen from normal in 2007 to 26 in February 2008, and to 42 in September 2008. Dr Stanley was suspicious that there was liver cancer.

**6.106** She and Bridie then attended a further appointment with Dr Stanley on 23 September 2008. In his letter to Molly's GP about this appointment, Dr Stanley stated that he spoke with Bridie and her mother and explained the suspicion of a primary liver cancer.<sup>236</sup> Bridie was adamant that no one mentioned the suspicion of cancer or used the word 'cancer' to either her or her mother at that time. She stated that she would have remembered had he or someone else done so and she would not have kept it from the rest of her family. In the letter dated 6 October 2008 referred to below, Dr Stanley referred to 'the liver nodule' (another way of describing cancer), and it may be that he used this expression during his discussions with Bridie and her mother as opposed to using the word 'cancer'. At the time of giving evidence, Bridie did not understand what 'liver nodule' meant and accepted it was possible that Dr Stanley had used this expression instead of the word 'cancer' when he spoke to them.<sup>237</sup> During this appointment Bridie was aware that the doctors wished her mother to undergo an urgent CT scan 'because they saw something'.<sup>238</sup>

**6.107** Following this appointment, on 26 September 2008, Molly attended for and underwent a three-phase CT scan. The report of this concluded that there was hepatocellular carcinoma with high suspicion of tumour invasion of the left anterior portal vein.<sup>239</sup> Dr Stanley then wrote to Molly by letter dated 6 October 2008:

We have now reviewed your CT scan in the context of the discussion we had at clinic regarding the liver nodule. The scan remains indeterminate and the unanimous view of those present at the meeting is that you now require an MRI scan of the liver to optimise the information we have prior to discussing treatment options.

I appreciate the difficulties you have tolerating these imaging procedures, but I emphasise that it is extremely important that you attend and undergo the test so that we have all the information required to manage this problem. You should be hearing from the radiologists regarding the date and time to attend for the test, which may be undertaken at Gartnavel due to their speciality interest. Please let me know if there are problems regarding this.<sup>240</sup>

**6.108** On 13 October 2008 Bridie's brother took their mother to the Gartnavel Hospital for the MRI scan. Once again, she was very nervous about the scan because of feelings of claustrophobia. Bridie's brother wore a lead vest and stood by her side throughout. He described the experience as 'very traumatic' for them both.<sup>241</sup> The report of the MRI scan described that Molly 'did not tolerate the procedure very well and the liver specific scans

---

<sup>236</sup> Day 76, page 51; Excerpts from the medical records recovered in respect of Molly

<sup>237</sup> Day 76, pages 54–55

<sup>238</sup> Ibid, page 52

<sup>239</sup> Ibid, pages 52–53; Excerpts from the medical records recovered in respect of Molly

<sup>240</sup> Day 76, pages 53–54; Excerpts from the medical records recovered in respect of Molly

<sup>241</sup> Day 76, page 54

could not be performed'.<sup>242</sup> The impression given by the MRI scan taken together with the recent CT image was thought to be consistent with a diffuse type hepatocellular carcinoma within segment 3 of the left lobe, extending into the portal vein branch. Molly and Bridie attended an appointment with Dr Stanley on 18 November 2008. Bridie remembers that Dr Stanley told them that they had found a 3cm growth on Molly's liver and that he would refer her to the RIE as that was where the relevant specialist was. He advised them that, due to Molly's age, she would not be a candidate for a liver transplant but they would discuss whether they could cut or burn the growth off. Again, Bridie does not remember the word 'cancer' being used and so she and her mother remained ignorant that her mother had cancer. In his letter to Molly's GP about this appointment, Dr Stanley stated that the recent MRI confirmed the CT findings of 'a likely 8cm diffuse hepatoma in the left liver lobe'.<sup>243</sup> He stated in the letter that he had explained the findings to Bridie and her mother but it appears that the fact that Molly had a liver cancer was not understood by them.

**6.109** On 23 December 2008 Molly, Bridie and her brother attended an appointment with a Consultant Surgeon at the RIE. At this time Bridie and her brother reported to the surgeon that their mother was experiencing episodes of confusion and dizzy spells.<sup>244</sup> The surgeon told them that Molly had hepatocellular carcinoma. This was the first time anybody had mentioned the words 'hepatocellular cancer'.<sup>245</sup> They were all extremely shocked as they had not realised how seriously unwell she was. Molly cried and was inconsolable. Bridie said, 'I think [the Consultant Surgeon] was quite shocked because we were shocked'.<sup>246</sup> The surgeon told Bridie's brother on a one-to-one basis that the prognosis was not good.<sup>247</sup> It was decided that Molly should be referred for chemoembolisation treatment as there were no other available treatment options due to the size of the tumour and vascular involvement.<sup>248</sup> Bridie's brother was told that the success rate of this chemoembolisation treatment was poor, and that Molly probably had about four to six months to live. Molly told Bridie and her brother that she did not know how long she had to live, and had no wish to know so Bridie and her brother decided not to tell her.

### *Molly's treatment for hepatocellular carcinoma*

**6.110** On 18 January 2009 Molly was admitted to the RIE. The chemoembolisation treatment was carried out the following day. Following this procedure Molly was sleepy and sore. On 21 January, Bridie telephoned the hospital and spoke to her mother who seemed to be confused and 'wasn't herself'. On 22 January Bridie's brother visited his mother and was extremely shocked at what he saw: 'she was an old woman who didn't recognise me and couldn't get up from bed'.<sup>249</sup> Bridie's sister visited her mother from England on 23 January and she, too, was shocked and extremely upset to see her mother in such a state. On 27 January Molly was discharged from hospital. On her return home Molly was very difficult to live with. She was confused and aggressive towards Bridie and her siblings.<sup>250</sup> She suffered from mood swings and was unable to carry out simple tasks.<sup>251</sup>

<sup>242</sup> Ibid, page 55; Excerpts from the medical records recovered in respect of Molly

<sup>243</sup> Day 76, page 56; Excerpts from the medical records recovered in respect of Molly

<sup>244</sup> Ibid

<sup>245</sup> Day 76, page 57; Bridie's brother's Witness Statement

<sup>246</sup> Day 76, page 57

<sup>247</sup> Ibid, page 58

<sup>248</sup> Chemoembolisation treatment involves giving chemotherapy directly into the affected part of the liver and cutting off the blood supply to the tumour. Hepatocellular carcinoma and treatment of it is discussed in Chapter 13, *Knowledge of Viral Hepatitis Now*, paragraphs 13.111–13.114.

<sup>249</sup> Day 76, page 59

<sup>250</sup> Excerpts from the medical records recovered in respect of Molly

<sup>251</sup> Day 76, pages 60–61

**6.111** Three days after her discharge from hospital, on 30 January 2008, Molly became very confused. She was unable to dress herself so Bridie and her siblings called an ambulance. Molly threw the paramedics out of her house, but eventually her GP persuaded her to go to the hospital. The GP's letter of referral stated that, as well as becoming more confused and aggressive, she had developed worsening abdominal swelling and leg oedema.<sup>252</sup> An abdominal ultrasound carried out on admission revealed a small amount of ascitic fluid.<sup>253</sup> Molly's encephalopathy was treated with oral Lactulose and she was discharged home on 4 February 2009.

**6.112** At the beginning of February 2009 Bridie's GP signed Bridie off work and she began to care for her mother full-time. Due to the amount of time she spent caring for her mother Bridie saw less of her own son so her partner began to work part-time so that he could help look after him. About this time, Molly started to receive home help twice a day and this help assisted Molly with dressing and meal times. This was funded by the Social Services Department. Initially Molly hated having home help, but then she became dependent on it.<sup>254</sup>

**6.113** Molly had a further admission to hospital between 6 and 11 February 2009 due to symptoms of encephalopathy. At this time she was dark yellow in colour. She was constantly dozing, and her day and night were interchangeable. Her short term memory was affected.<sup>255</sup> A few times her behaviour bordered on violent and, as Bridie stated, 'She wasn't my mum really'.<sup>256</sup> Caring for their mother became a 24-hour occupation for Bridie and her siblings. Molly's GP was a great help to them. Bridie's brother researched other treatment options which might be open to their mother and, as a result of this, Molly went to see a professor at the Beatson Oncology Centre in the hope of being prescribed a drug called Sorafenib.<sup>257</sup> In order to assess if this drug was likely to be of benefit to Molly, he repeated her blood profile to calculate her Child Pugh score.<sup>258</sup> The result of this was 9 and this meant that there was no evidence that Sorafenib would provide any benefit to her.<sup>259</sup> This must have been extremely disappointing news for both Molly and the family to hear.

**6.114** Molly was again admitted to hospital between 16 and 25 March 2009 due to increased confusion, nausea and vomiting.<sup>260</sup> Her family was told that she had only weeks to live. They felt that she had no quality of life in the hospital and so they asked that she be discharged home on 25 March. They took her home in a wheelchair. Molly received palliative care from MacMillan nurses, and various alterations were carried out to the house. These included the provision of a hospital bed, a frame to enable her to use the toilet, a bath lift and chair.<sup>261</sup>

**6.115** As late as March 2009 Bridie's family were unaware of the risk of transmission of the Hepatitis C virus. By this time Molly had semi-constant faecal soiling and her family used to assist her in the hospital, and at home. They were not advised to wear gloves

---

<sup>252</sup> Excerpts from the medical records recovered in respect of Molly

<sup>253</sup> Ibid

<sup>254</sup> Day 76, pages 61–62

<sup>255</sup> Excerpts from the medical records recovered in respect of Molly

<sup>256</sup> Day 76, page 62–63

<sup>257</sup> Day 76, pages 63–64; Excerpts from the medical records recovered in respect of Molly; Sorafenib is a drug approved for the treatment of primary kidney cancer.

<sup>258</sup> Child Pugh score assesses the clinical severity and hence the prognosis of chronic liver disease.

<sup>259</sup> Excerpts from the medical records recovered in respect of Molly

<sup>260</sup> Ibid

<sup>261</sup> Day 76, page 64



or aprons and they did not do so when they helped her.<sup>262</sup> As stated above, Molly was provided with information about the Hepatitis C virus and, as Bridie stated, she and her siblings were dependent on their mother to pass on such information.<sup>263</sup>

**6.116** Molly continued to deteriorate. On the evening of 5 April 2009 she became very upset, confused and agitated. She was convinced that someone was going to take her away. She was very frightened and made the comment 'I am not ready for this'.<sup>264</sup> It took Bridie, her sister and the MacMillan nurse to settle her. She required subcutaneous sedation via a syringe driver and then further sedation during the night. The following morning Molly did not wake up as expected and she fell into a coma. She remained in a coma until her death a week later. During this period Bridie stayed at her mother's home, only returning home for an hour each day to see her son. Bridie and her siblings felt unprepared for their mother's death as they had expected her to wake up after being sedated.<sup>265</sup>

**6.117** Bridie and her siblings did not have a good relationship during the 1980s and 1990s. They all felt that they were driven out of the house because everyone's attention was focused on their mother, and they rarely spoke. Their mother's deterioration brought them 'back together' and Bridie stated that they have never been closer.<sup>266</sup>

### *Financial impact of Molly's infection with Hepatitis C*

**6.118** Other than one unsuccessful part-time job in the 1980s, Molly did not work.<sup>267</sup> Bridie believes that her mother would have worked had she not suffered from symptoms of Hepatitis C. This meant that only Bridie's father's salary supported their household and money was tight. When they were younger Bridie and her siblings used to wear second-hand clothes as their parents could not afford new ones. Bridie and her siblings were unable to go on school trips due to the cost of these. Other than visiting relatives in England on a couple of occasions, they had no family holidays. When they left school Bridie and her siblings obtained work so that they could bring money into the family home instead of attending further education. Had she been able to, Bridie would have liked to attend Art school. Her sister would have liked to study catering. Due to his Molly's symptoms of Hepatitis C and his father's main focus being to care for his wife, Bridie's brother's attendance at school was poor. He believed that his parents did not care whether he went to school or not. He left school with few qualifications. He has since obtained various qualifications through his work.

**6.119** Molly never claimed unemployment benefit. When Bridie's father stopped working, Molly applied for Disability Living Allowance and was awarded the lower rate of this allowance. On numerous occasions Bridie's parents had to borrow money from family members to pay the mortgage and to buy food. After her father made the decision not to work again, in 1998, Bridie's uncle paid off the mortgage on Bridie's parents' house so they no longer worried about losing their home. He also gave them money to buy a car so that Bridie's father could drive his wife to her hospital appointments. Bridie and her siblings used to give their parents money for food, bills, car repairs and petrol. When Bridie's parents cared for Bridie's son, Bridie used to bring food and anything else he might need so her parents did not need to buy it.

---

<sup>262</sup> Ibid, pages 70–71; Bridie's brother's Witness Statement

<sup>263</sup> See paragraph 6.86

<sup>264</sup> Bridie's brother's Witness Statement

<sup>265</sup> Day 76, page 65; Bridie's brother's Witness Statement

<sup>266</sup> Day 76, pages 65–66

<sup>267</sup> Submission by Thompsons received with letter dated 26 May 2011

**6.120** Bridie's parents had no pension and no life assurance as they could not afford either. On the few occasions that her parents went on holiday, her mother travelled without travel insurance. Her parents incurred the expenses of her mother's prescriptions until she was 60 years old, petrol for travelling to and from medical appointments and extra heating costs. Molly felt the cold and so their house used to be kept very warm. During the last 18 months of their mother's life, Bridie and her siblings incurred significant expenses, namely the cost of petrol both driving Molly to and from medical appointments, visiting her in hospitals – including the RIE, hospital car parking charges and the cost of buying food for their mother, as she would not eat hospital food. Each of the children, at some point, took time off work to care for their mother. Bridie used annual leave for two weeks before being signed off work sick to care for her mother. She estimated that she lost about £150 a month, for at least two months, in flexi-time payments. She used up her sick pay entitlement during the period she cared for her mother. This affected her rate of sick pay afterwards and meant that, for a while, she felt unable to take any time off work sick. Bridie's sister incurred travel costs from her home in England to visit and to care for her mother. She too took sick leave from work to care for Molly. The time she spent caring for her mother used up her entitlement to sick leave and so when she was absent from work subsequently, she was only entitled to Statutory Sick Pay.

**6.121** Molly received two payments from the Skipton Fund.

### Colin

**6.122** Colin was 57 years old when he gave evidence to the Inquiry. He is married and he and his wife have three grown-up children. He lives in Scotland.<sup>268</sup>

**6.123** Colin is the third of four brothers. He had Haemophilia B, as did two of his three brothers. All three brothers with Haemophilia B contracted Hepatitis C from their treatment with blood products. Both of Colin's brothers have received treatment for the virus, and one has received a liver transplant.<sup>269</sup>

### *Colin's diagnosis with and treatment for Haemophilia B*

**6.124** Colin was diagnosed with Haemophilia B when he was about three years old.<sup>270</sup> As a child, he was treated at Maryfield Hospital, Dundee until 1973 when his care was transferred to Ninewells Hospital, Dundee.<sup>271</sup> He was told that he had severe haemophilia with a clotting factor of less than 1%. He used to carry a green card in case of an accident and this stated that he had severe haemophilia. A letter in his medical records dated 13 November 1973 recorded Colin's Factor IX assay as 8%.<sup>272</sup> It is likely that, as Colin himself stated, his Factor IX assay varied over the years.

**6.125** Colin was first treated for a bleed (in his right ankle) when he was about seven years old, in 1961. He was admitted to Maryfield Hospital. He was treated with rest, a compression bandage with a wire splint and then an Elastoplast stirrup strapping. He remained in hospital for about two weeks.<sup>273</sup> He had a further bleed in the same ankle the following year. He was treated with bed rest and a compression bandage. His foot was then splinted with Kramer wire.<sup>274</sup>

<sup>268</sup> Day 77, pages 2–3

<sup>269</sup> Ibid, pages 3–4

<sup>270</sup> Ibid, page 7; Excerpts from the medical records recovered in respect of Colin

<sup>271</sup> Colin's Witness Statement

<sup>272</sup> Excerpts from the medical records recovered in respect of Colin.

<sup>273</sup> Day 77, page 7; Excerpts from the medical records recovered in respect of Colin

<sup>274</sup> Ibid

**6.126** Having haemophilia did not affect Colin greatly as a child:

I led quite a normal life. At times I didn't even bother about it. I used to play football, which I was told I shouldn't do. Even late on in my teens, I was a good skier. I used to water ski, snow ski, things that you should never do.<sup>275</sup>

**6.127** Colin recalls being admitted to hospital in 1972 when he was 18 years old, due to a bruised and swollen hand. He then received treatment with fresh frozen plasma. Unfortunately, he suffered an allergic reaction to it known as 'Stevens-Johnson syndrome'. This reaction was successfully treated. The discharge letter from this admission states that Colin 'once again' developed an allergic reaction to fresh frozen plasma, suggesting that this may have not have been his first treatment with this product.<sup>276</sup> There is, however, no record in Colin's medical records of an earlier treatment with fresh frozen plasma or any other blood product.<sup>277</sup> As with all haemophilia patients, over the years Colin's treatment became Factor IX instead of fresh frozen plasma. The first note in his medical records of Factor IX being administered is when he had a tooth extracted in 1981.<sup>278</sup>

**6.128** Colin was reluctant to receive treatment for bleeds as in his mind it weakened his immune system. He only went to the hospital for treatment if he had a severe bleed. He thought that if he had a bleed and received Factor IX treatment, the effects of a further 'bump' were more severe than if he had not just had Factor IX.<sup>279</sup> Colin estimates that, prior to 1994 he received treatment for bleeds a maximum of half a dozen times and each time in hospital. Some of these treatments were to cover dental treatment. His longest stay in hospital was three or four days, and there was a period of many years when he was 'never near a hospital'.<sup>280</sup>

**6.129** Colin left school when he was 15 years old. He started working in the men's sales department of a national clothing retailer and in his first year of employment, won the sales person of the year award for the retailer's 52 stores. After 18 months the retailer closed the store where he worked and Colin started his own small clothing company. It was apparent that Colin has a strong and impressive work ethic. He did not let his haemophilia interfere with this: 'when I was working, rather than go and get treatment, I used to go to work with black and blue legs and arms ...'.<sup>281</sup> Colin ran his clothing store for about seven years. Sourcing products involved a fair amount of travelling. Due to the limitations on the income from this clothing shop, Colin also began doing door-to-door deliveries of morning rolls for extra money. He and his brother began producing their own rolls and then they opened a baker's shop.<sup>282</sup> A company in Glasgow later took over the business and Colin became the general manager.<sup>283</sup>

**6.130** In 1994 Colin became very unwell with a high temperature and rigors. He was admitted to King's Cross Hospital, Dundee with a two-week history of malaise and lethargy, and a four-day history of dysuria (painful urination), right loin pain and rigors. He underwent blood tests and urinalysis revealed protein and blood. He was given morphine

---

<sup>275</sup> Day 77, page 11

<sup>276</sup> Excerpts from the medical records recovered in respect of Colin

<sup>277</sup> Day 77, pages 8–9; Excerpts from the medical records recovered in respect of Colin

<sup>278</sup> *Ibid*

<sup>279</sup> Day 77, page 10

<sup>280</sup> *Ibid*, pages 9–11

<sup>281</sup> *Ibid*, page 11

<sup>282</sup> *Ibid*, pages 11–14

<sup>283</sup> *Ibid*, page 28

for the pain. Colin felt very unwell and stated that he looked so ill that his friends who came to visit him 'didn't think that I was going to be coming out'.<sup>284</sup> He was diagnosed with right pyelonephritis, (a kidney infection) and discharged home after treatment with IV antibiotics on 10 April 1994.<sup>285</sup> With regard to his recovery, Colin stated, 'It actually took me longer to recover from that than it did from my liver transplant. That took so much out of my system that ... my whole body was wasted. It was very difficult'.<sup>286</sup> It took him a long while to build up his strength after this episode.<sup>287</sup>

### *Colin's diagnosis with Hepatitis C*

**6.131** In 1995 Colin and his two brothers were asked to attend Ninewells Hospital, Dundee. When they attended there, they were told that they should be tested for Hepatitis C. A letter dated 29 August 1995 from Professor Cachia, Consultant Haematologist, to Colin's GP, records that Colin attended the hospital on 11 August 1995.<sup>288</sup> It was noted in this letter that Colin had never attended the hospital for regular review as he had few bleeding problems and had enjoyed an active lifestyle without developing any chronic joint problems. It was further noted that Colin had been tested, and found to be negative, for antibodies against Hepatitis B and HIV. A blood sample was taken from Colin at this appointment. The report of the sample dated 15 August 1995 confirms that Colin was found to be positive for Hepatitis C.<sup>289</sup>

**6.132** Colin's two brothers were informed in January 1996 of the results of their blood tests for Hepatitis C. They were both positive. As Colin still had not received the result of his blood test he telephoned the hospital to ask for it. He cannot remember who he spoke to. He told this person that his two brothers had received their results, but he had not received his. Colin was told that if his two brothers were positive for Hepatitis C then 'of course you have got it'.<sup>290</sup> Colin commented, 'It was actually a very short conversation'.<sup>291</sup>

**6.133** Colin and his wife then attended an appointment with Professor Cachia on 19 January 1996. The note of this appointment records that Hepatitis C was discussed fully with Colin, including the risks of developing cirrhosis and hepatocellular carcinoma, monitoring, treatment and the risk of sexual transmission. Colin's abnormal liver function test results were discussed, his ALT at this time being 213. The note also recorded that Colin 'Drinks regularly. Current intake 26 units per week'.<sup>292</sup> Colin disputes that he told Professor Cachia that his intake was 26 units a week. He stated that there were long periods when he did not drink at all and he would never drink that number of units in a week, except 'maybe if I had been away somewhere with the guys for a week' and added: 'with the amount I used to try and work and was working, alcohol was very low in my priority list as far as that's concerned'.<sup>293</sup> Colin was advised of the potential interaction between Hepatitis C and alcohol and advised to stay within the government's current recommendations for alcohol intake.

---

<sup>284</sup> Ibid, pages 16–17

<sup>285</sup> Excerpts from the medical records recovered in respect of Colin

<sup>286</sup> Day 77, page 18

<sup>287</sup> Ibid, page 18

<sup>288</sup> Excerpts from the medical records recovered in respect of Colin

<sup>289</sup> Ibid; Colin – Day 77, pages 20–21; See Chapter 34, *An Investigation into the Systems in Place for Informing the Patients about the Risks – Hepatitis C*, paragraphs 34.129–34.159 in respect of testing for Hepatitis C at Ninewells Hospital.

<sup>290</sup> Day 77, page 21

<sup>291</sup> Ibid, page 21

<sup>292</sup> Excerpts from the medical records recovered in respect of Colin; Day 77, pages 22–23.

<sup>293</sup> Ibid, page 23

**6.134** Colin's wife was subsequently tested for the virus and found to be negative. Colin's Hepatitis C PCR test dated 6 April 1996 revealed that he had Genotype 1a of the virus. Colin was told that this genotype was the easiest to get rid of when in fact it is the hardest genotype to treat.<sup>294</sup> Colin considers that the advice he received about the virus was 'very low key':<sup>295</sup>

We were all told, 'There is bad news and good news. The bad news is you have got Hepatitis C but the good news is you have got a strain of the virus that is a low strain and it will probably never affect you. So go on and lead a normal life'.<sup>296</sup>

Colin stated that it was now 'common knowledge' that in 1992 there was screening of haemophilia patients for Hepatitis C in the Dundee area and that these patients did not know what they were being tested for.<sup>297</sup> He and his brothers were not included in this.

### *Colin's symptoms of Hepatitis C*

**6.135** Colin started to attend the Haematology Clinic, Ninewells Hospital, regularly for monitoring. He reduced his alcohol intake. Colin's health then began to deteriorate.<sup>298</sup>

It was funny how it started to happen. I was losing strength, losing concentration, and I just put it down to maybe having a bug. In my whole life I have never had the flu. I don't know what the flu is. I very rarely take colds. So for being haemophiliac, general illnesses I was never bothered with. But I started getting aching pains, aching joints and it wasn't right. I thought I had a bug for a while.<sup>299</sup>

**6.136** Initially Colin started to have a few bad days once a month. On these bad days Colin felt tired and sometimes had aches and pains too. Then the bad days gradually increased so that he had more bad days in a month than good ones.<sup>300</sup> Colin's liver function tests deteriorated too and the hospital told him that the virus was causing his symptoms. During one 18-month period he suffered from several bouts of cellulitis (a common skin and soft tissue infection caused by bacteria), each requiring antibiotic treatment. By this time Colin had stopped working due to his symptoms.<sup>301</sup> He received incapacity benefit and found living on benefits 'just a nightmare'.<sup>302</sup>

**6.137** In 1998 Colin was referred to a liver specialist, Dr Dillon, Consultant Physician. Colin attended a clinic appointment with him in July 1998. At this time Colin continued to be troubled with lethargy and muscular aches and pains. He also suffered from periods of breathlessness and episodes of severe sweating. Both of these symptoms were investigated but no cause was found. Over time the periods of breathlessness had stopped. At this appointment the option of a liver biopsy was discussed with Colin. He was aware that there was an increased risk to him from such a procedure due to his haemophilia. This risk concerned Colin so he decided that he wanted a biopsy only if his liver function tests were severely abnormal. The option of combined antiviral therapy with Interferon and Ribavirin

---

<sup>294</sup> See Chapter 13, *Viral Hepatitis Now*, at paragraph 13.14

<sup>295</sup> Day 77, page 25

<sup>296</sup> *Ibid*, pages 24–25

<sup>297</sup> Colin's Witness Statement; this is discussed in more detail in Chapter 34, *An Investigation into the Systems in Place for Informing the Patients about the Risks – Hepatitis C*, Paragraphs 34.142–34.145

<sup>298</sup> Day 77, page 26

<sup>299</sup> *Ibid*, page 27

<sup>300</sup> *Ibid*, page 28

<sup>301</sup> *Ibid*, page 28

<sup>302</sup> *Ibid*, page 57

as part of a clinical trial was also discussed with Colin. Colin pushed to start treatment as he wished to try anything to stop the decline of his health. As he stated 'being a generally active person, I wanted to try and get the problem resolved, if it could be resolved'.<sup>303</sup>

**6.138** Around this time Colin started taking milk thistle. He did this at his own instigation having read up on hepatitis and the liver. He discovered that this was something which people took to cleanse their liver and to help their liver function. He believes that it helped him.<sup>304</sup>

### *Colin's first course of treatment with Interferon and Ribavirin*

**6.139** In October 1998 Colin started treatment with Interferon and Ribavirin. Colin was told that he was the first haemophilia patient in Ninewells Hospital to receive this treatment. Before starting it he was warned that he would suffer flu-like symptoms. He was also told that it had different effects on different people depending on their basic wellbeing. Initially the treatment did not cause him any problems but after a week he began to suffer side-effects of it. He felt unwell with a feeling of exhaustion and joint aches which were more severe than those he had experienced before. Despite this he was keen, at this stage, to continue with the treatment. By 10 December 1998 Colin was suffering from severe side-effects namely joint pains and aches, muscle weakness and feeling 'completely washed out, weak and exhausted'.<sup>305</sup> The effects were severe enough to make him want to stay in bed sometimes all day, several times a week. At these times he had to crawl to the toilet on his hands and knees.<sup>306</sup> Colin's neutrophil (a type of white blood cell which protects against infection) count also dropped. As a result of this his prescribed dose of Interferon was halved. His white cell count then returned towards the normal level. His liver function test results also returned nearer to normal with his ALT dropping from 283 in June 1998 to 119 at the beginning of November 1998, although these measurements did fluctuate.<sup>307</sup> During this period Colin was assessed as being entitled to Disability Living Allowance.<sup>308</sup>

**6.140** On 6 January 1999 Colin received the result of a PCR test which had been taken the previous December. The result of the test was that the Hepatitis C PCR remained positive which the doctors took as an indication that the treatment was not working satisfactorily.<sup>309</sup> At this point, approximately 12 weeks after starting the treatment, Colin was advised to stop it. He understood that the reason for this was that his immune system 'was so low'<sup>310</sup> but it seems likely that this PCR test result was an important factor in this decision.

**6.141** Colin felt 'devastated' at having to stop the treatment, particularly having seen some positive benefit of the treatment with regard to his liver function test results. However, he knew that he was unable to continue with the treatment as the side-effects were so severe.<sup>311</sup> It took 'quite a while' for the side-effects of the treatment to wear off and some wore off more quickly than others. Following this Colin then had 'a reasonable period of stabilised health ... where I was only suffering from the aches and pains but my wellbeing was good. It seemed to have done some good to the liver function'.<sup>312</sup>

---

<sup>303</sup> Ibid, pages 31–33; Excerpts from the medical records recovered in respect of Colin

<sup>304</sup> Day 77, page 33

<sup>305</sup> Ibid, page 36; Excerpts from the medical records recovered in respect of Colin

<sup>306</sup> Day 77, page 58

<sup>307</sup> Excerpts from the medical records recovered in respect of Colin

<sup>308</sup> Day 77, page 58

<sup>309</sup> Excerpts from the medical records recovered in respect of Colin; Day 77, pages 37–38

<sup>310</sup> Ibid, page 37

<sup>311</sup> Ibid, page 39

<sup>312</sup> Ibid, page 39

### *Colin's condition after treatment with Interferon and Ribavirin*

**6.142** Colin continued to attend the hospital on a regular basis for monitoring. Around this time Colin felt well enough to resume working. He felt unable to work for someone else due to the days when he was unwell and so he decided to work for himself. He bought a franchise for sweet sales. The sweets had a long shelf life and were pre-packed. He planned to sell the sweets when he felt well enough to do so. He built the business up to be 'quite a reasonably good going business over the months'.<sup>313</sup> After time he employed someone to work alongside him. This person worked the days Colin did not and the business then operated five days a week.

**6.143** In March 1999 Colin underwent an endoscopy to check for varices. This revealed none.<sup>314</sup> As time went on his condition worsened and it was decided that Colin should undergo a liver biopsy to determine the state of his liver. Colin read a Patient Information Sheet about Laparoscopic Liver Biopsy for those with haemophilia which explained the procedure. He understood that it was 'pretty straightforward'; although since he had haemophilia he would be required to remain in hospital for about four or five days after the procedure.<sup>315</sup> Colin underwent the liver biopsy on 19 October 1999. This required him to have two PICC lines (peripherally inserted central catheters) inserted for intravenous access, one for the factor treatment and one for taking blood samples. Unfortunately following the procedure he developed a left axillary (armpit) vein thrombosis, an unusual complication for a person with haemophilia. He was subsequently told that he was the only person on record as having severe haemophilia and developing a thrombosis.

**6.144** Following the biopsy procedure, Colin's face began to swell: 'my face was out about four or five inches'.<sup>316</sup> His mouth was so swollen that he was unable to swallow and he was dribbling. He developed pains in his body. His whole body started to bruise: 'My whole chest was black and blue and down my arm was black and blue ...'.<sup>317</sup> In order to ascertain what was causing these symptoms Colin underwent a number of x-rays but each of them came back normal. After a number of days a venogram (an x-ray of the veins) revealed that Colin had developed a thrombosis. It was difficult for the doctors to treat. He was prescribed tablets to thin his blood and Factor IX to prevent any internal bleeding. Colin was told that if his blood was thinned too quickly then there was a risk of a clot coming away and that this could be fatal. It was a slow process and there were times when Colin was concerned that he would not live. In the event, the treatment was successful and Colin was discharged home on 1 November 1999.<sup>318</sup> He had to be re-admitted to hospital a week later due to a viral infection. He remained in hospital for four days.<sup>319</sup>

**6.145** Colin's liver biopsy revealed appearances consistent with chronic Hepatitis C. The intensity of inflammation corresponded to Grade 2 and the degree of fibrosis to Stage 2.<sup>320</sup> The appearances fell short of cirrhosis.<sup>321</sup>

---

<sup>313</sup> Ibid, page 59

<sup>314</sup> Ibid, page 52

<sup>315</sup> Ibid, page 40

<sup>316</sup> Ibid, page 41

<sup>317</sup> Ibid, page 41

<sup>318</sup> Ibid, pages 41–42; Colin's Witness Statement

<sup>319</sup> Day 77, pages 42–43

<sup>320</sup> There are several different scoring and grading systems for liver biopsies and the same numbers are not comparable with another system. The systems used in the UK are the Ishak HAI and the Knodell systems and the Child Pugh grading for cirrhosis. The Hepatitis C Trust [www.hepctrust.org.uk](http://www.hepctrust.org.uk)

<sup>321</sup> Day 77, page 43; Excerpts from the medical records recovered in respect of Colin

**6.146** Colin continued to experience symptoms of the virus:

You never knew from day to day what it was going to be, to be honest, and as I say, you could have three or four days where you thought, 'Oh, there is nothing wrong with me, apart from a few aches and pains,' and you could get up the next morning and you would be just sore all over and sweating and not right, like the flu symptoms again. That's just the way it went.<sup>322</sup>

**6.147** He continued to take a close interest in available treatments for his condition. He gleaned information about this from discussions with Dr Dillon, internet searches and meeting with other people with haemophilia. At the meetings, it appeared to Colin that patients from Glasgow and Edinburgh were better informed than those in his own area. In his oral evidence to the Inquiry, Colin stated that he had heard from Dr Dillon that Pegylated Interferon was likely to become an option to treat Hepatitis C. Dr Dillon told him that it was slow release and the side-effects would be less severe than Interferon. Colin believed that this would be a better treatment option for him as his liver function test results had improved for a while during his previous treatment with Interferon and he believed the severity of the side-effects he had suffered previously had been a factor in stopping the treatment. Colin stated that he 'fought' to be treated with Pegylated Interferon but, initially, the hospital would not give him this treatment due to its expense.<sup>323</sup> Colin sought help from his local MSP and offered to pay for part of the treatment himself. Colin's medical records show that, in fact, the treatment Colin wished to start was Ribavirin monotherapy.<sup>324</sup> Whichever regime it was, this shows that Colin was keen to receive further treatment for Hepatitis C and was very proactive in trying to obtain it.

**6.148** Colin's efforts to obtain further treatment added to the stress which he was already under due to his symptoms of Hepatitis C. In April 2000 Professor Cachia referred Colin to a psychiatrist to give Colin 'the opportunity to discuss his feelings and concerns about his health now and in the future'.<sup>325</sup> In his referral letter Professor Cachia noted that '[Colin's] symptoms have become more and more disabling over the last few months .... [Colin] is very angry about the Hepatitis C infection and the lack of options that we can offer to improve his health at present'. The psychiatrist concluded that although Colin described various depressive features which generally 'wax and wane' with his general health, he did not consider that there was evidence to warrant a diagnosis of co-morbid depressive disorder. He noted that much of Colin's concern centred around uncertainties about his prognosis and possible treatment strategies: 'Consequently, he has not yet made the psychological shifts necessary for him to come to terms with his deteriorating physical health, although I got the impression that this was perhaps now beginning to happen'.<sup>326</sup> Colin stated:

In my mind it wasn't depression, that's obviously why they sent me there. My attitude has always been if there is something wrong then you sort it, but unfortunately I couldn't sort this. It was something that was just getting worse.<sup>327</sup>

---

<sup>322</sup> Day 77, pages 43–44

<sup>323</sup> Ibid, pages 44–47; Colin's Witness Statement

<sup>324</sup> Excerpts from the medical records recovered in respect of Colin

<sup>325</sup> Ibid

<sup>326</sup> Day 77, pages 47–48; Excerpts from the medical records recovered in respect of Colin

<sup>327</sup> Day 77, page 48



This highlights one of the difficult features of Hepatitis C and its treatment – the inability at times of a patient to take treatment and effectively to tackle the virus head on, no doubt resulting in feelings of helplessness and frustration. This would have been particularly so at a time when new, possibly improved, treatments were recognised but were not yet available.

**6.149** In October 2000 Colin was referred to the Pain Clinic at Ninewells Hospital in relation to the muscular pains he suffered. He was provided with a TENS machine. This seemed to exacerbate Colin’s muscle spasms and so he stopped using it. He was also prescribed Dihydrocodeine. He declined morphine.<sup>328</sup> About this time Colin started to experience what he called ‘shutdown’:

[I]t was like your whole body shut down. Even when I was driving, I could feel that – you were losing the feel of even the steering wheel, and it was just your whole body was on – it was like somebody had flicked a switch and your system wasn’t working. You couldn’t concentrate, you couldn’t think. It was debilitating totally, and that was just the way it was, that – and I could have that two or three times in a week and not have it for a fortnight. It was one of these things that would come and go, and when it came – you could feel it coming on and it was like being partly paralysed but you weren’t ....<sup>329</sup>

#### *Colin’s treatment with Pegylated Interferon and Ribavirin*

**6.150** On 4 May 2001 Colin started treatment with Pegylated Interferon and Ribavirin as part of a trial. Once again he was warned about the side-effects of the treatment. He was also told that, as the first treatment had failed, there was only a slightly higher chance of this treatment being successful. Five days after starting treatment Colin attended the hospital for review. It was noted that, within four to six hours of receiving his first dose of Pegylated Interferon, Colin had shaking, nausea, sweatiness and a feeling of being unwell which waned as the day progressed. He continued to suffer from nausea in the mornings. At this appointment Colin also mentioned that about a week to 10 days before that appointment he had suffered an episode of melaena.<sup>330</sup> Colin then underwent an endoscopy to discount varices as a cause of the melaena, and no varices were found.<sup>331</sup>

**6.151** At his next review on 21 May 2001, it was noted that since the first review Colin had been suffering from increasing side-effects such as chest tightness, palpitations and widespread aches and pains.<sup>332</sup> He was also suffering from lower back pain spreading to his legs, earache, reduced haemoglobin and reduced neutrophils. Analgesia was having little effect. At this time Colin wanted to stop the treatment. He was seen by Professor Cachia and it was decided that Colin should continue taking Ribavirin but skip his dose of Pegylated Interferon that week. It was planned to admit Colin to hospital if these symptoms worsened.

**6.152** One week later Colin was feeling ‘much improved’.<sup>333</sup> He had experienced slight chest tightening and palpitations two to three hours after a dose of Ribavirin. It was

---

<sup>328</sup> Ibid, page 49

<sup>329</sup> Ibid, page 50; In retrospect, this ‘shutdown’ may have been caused by the effect of the Hepatitis C virus on Colin’s brain – see Chapter 13, *Knowledge of Viral Hepatitis Now*, Paragraph 13.18, re ‘brain symptoms’ and brain fog. At that time the ‘brain complications’ of Hepatitis C were only just being recognised.

<sup>330</sup> Melaena is indicated by dark stools with part digested blood, suggesting bleeding from the stomach.

<sup>331</sup> Day 77, pages 51–52; Excerpts from the medical records recovered in respect of Colin

<sup>332</sup> Ibid, pages 52–53

<sup>333</sup> Ibid, page 53

agreed that Colin would continue taking Ribavirin and recommence Pegylated Interferon at a reduced dose. Colin was keen to continue with the treatment.

**6.153** At the review the following week, on 4 June 2001, Colin complained of suffering from chest pain and palpitations after most Ribavirin doses.<sup>334</sup> He had missed a dose of Ribavirin due to these symptoms. He also complained of pain over his abdomen/kidneys and continued to suffer from general aches and pains, joint and muscle pain and sweats which were attributed to Hepatitis C. At this appointment Colin's neutrophils were noted to be reduced. Following discussion with Professor Cachia, it was agreed that due to these side-effects Colin should miss his dose of Interferon and stop Ribavirin. It was planned that Professor Cachia would discuss Colin's treatment with Dr Dillon, Consultant Physician, and the pharmacist. Colin was keen to continue with the treatment and asked especially if he could continue taking Ribavirin only. It was noted at the next review appointment that if Colin's palpitations persisted then consideration should be given to Colin undergoing a 24-hour ECG.

**6.154** At the next review appointment a week later, Colin reported continuing to feel very unwell with kidney pain, palpitations and chest tightness. He had once again stopped taking Ribavirin himself the previous week. Colin stated that due to the side-effects of the treatment and the detrimental effect on his quality of life he wished to stop taking the treatment. He stated 'I knew myself I couldn't continue on it but also once again my immune system got so low that they advised me that even if I wanted to continue it would be unwise'.<sup>335</sup> About five weeks after starting the treatment Colin stopped taking it. It was a difficult decision for Colin to take as, 'I knew that there was nothing else out there. I knew after that there was nothing else going to be able to help me'.<sup>336</sup>

**6.155** After Colin's treatment stopped he felt better for a while. He felt that the treatment had 'done some good'.<sup>337</sup> He continued to experience 'shutdown' episodes. On good days Colin had a tendency to do too much, and this would make him worse:

[I]t's very difficult when you have worked all your life, a lot of time, and worked for yourself, you put a lot of hours in, and to sit and do nothing wasn't in my nature. So if there was anything I could do when I was feeling good, I did it. And of course, I then paid the consequences for it, but as the months past I realised I just had to do nothing and accept it.<sup>338</sup>

### *The deterioration in Colin's health*

**6.156** Once again Colin's health deteriorated. During 2001 Colin was often bed-ridden. He found that he was operating his business from his house, and often from his bedroom. His employee effectively became the full-time worker. In 2002 he reached the difficult decision to sell his sweet sales business. By this time there was little profit left after paying his employee's wages and expenses, '[s]o the headaches and the cashflow outweighed the benefits of the business'.<sup>339</sup> Colin started claiming Incapacity Benefit again and was awarded the higher rate.<sup>340</sup>

---

<sup>334</sup> Day 77, pages 53–54; Excerpts from the medical records recovered in respect of Colin

<sup>335</sup> Day 77, page 55

<sup>336</sup> Ibid, page 55

<sup>337</sup> Ibid, page 56

<sup>338</sup> Ibid, page 57

<sup>339</sup> Ibid, pages 59–60

<sup>340</sup> Ibid, pages 60–61

**6.157** Colin's wife started to spend more and more time caring for him and his illness took its toll on her. She had worked as a classroom assistant for 13 years without a day's illness. She became unwell with the stress of Colin's illness, and by 2004 she had given up working.<sup>341</sup> Although this meant that money became 'exceptionally tight', Colin thinks that his wife having stopped working helped her. For a while, after she had finished her college course, Colin's daughter came to the house every day to give Colin his lunch. Colin's wife attended her GP and he prescribed medication for a period in respect of her stress and anxiety.<sup>342</sup>

**6.158** In March 2004 Colin's symptoms were exhaustion, blotchy skin and generalised arthralgia (joint pain) and myalgia (muscle pain) with associated sweats. His ALT level was 115. An ultrasound scan then revealed evidence of portal hypertension and significant splenomegaly, the spleen measuring 15cm in length. A subsequent endoscopy revealed four barely visible varices and Colin started treatment with Propranolol for these.<sup>343</sup>

**6.159** By July 2005 it was clear that Colin had developed cirrhosis. An ultrasound scan and gastroscopy revealed splenomegaly and gastric varices. Colin wished to meet a hepatologist to discuss the possibility of liver transplantation.<sup>344</sup> On 27 July 2005 Colin attended an appointment with the Specialist Registrar to Dr Dillon.<sup>345</sup> Colin took some clippings from the *Daily Mail* about stem cell transplantation. Dr Cotton explained to Colin that this was at the very early stages of experimentation and was not a routine treatment. Dr Cotton told Colin that he was not yet at a stage where they would consider liver transplantation. It was agreed that Colin would continue to attend the Haematology Department in respect of his Hepatitis C and that he would be seen at the Hepatitis C Clinic as and when required.

**6.160** Colin's condition continued to deteriorate. His wife and family started to notice that when he was talking to them there were gaps in his conversations. He often appeared as if he was drunk when, in fact, Colin had not taken alcohol since 1994: '[o]nce I found out I had a liver problem, I didn't touch alcohol, not even at New Year'.<sup>346</sup> Colin had stopped drinking to make sure that his liver was not being damaged by anything else. At one of his appointments in March 2006, Colin's wife asked about the cause of these episodes. She was told that it was caused by the effect of Hepatitis C on Colin's liver and the build up of toxins in his body.

**6.161** In November 2006 Colin sold his home in order to release equity and down size. By this time his sons had left home. The following month Colin and his wife moved into a residential caravan where they lived until they moved into their new home in April 2007. The selling of his home, which Colin had had built for the family, was a disappointment to both him and his wife:

I mean, you work hard ... you try to build something up. Then really to live as near normal as you can, not extravagant but, if that's what you have got to do, that's what you have got to do. There's no point in getting into debt.<sup>347</sup>

---

<sup>341</sup> Ibid, page 60

<sup>342</sup> Ibid, pages 60–62

<sup>343</sup> Ibid, page 61; Excerpts from the medical records recovered in respect of Colin

<sup>344</sup> Day 77, pages 62–63; Excerpts from the medical records recovered in respect of Colin

<sup>345</sup> Day 77, pages 63–64

<sup>346</sup> Ibid, page 64

<sup>347</sup> Ibid, page 67

**6.162** The new home Colin and his wife bought was a flat overlooking a river. It was not ideal for Colin, but he was so unwell by this time that he bought it for his wife. He wanted to ensure that, were he to die, his wife would not be left with any debt. By this time Colin was bed-ridden and he described this time as 'the grim period'.<sup>348</sup>

#### *Colin's assessment for liver transplant*

**6.163** In April 2007 Colin was referred to the Royal Infirmary of Edinburgh (RIE) for assessment for a liver transplant. In the following June he was admitted there for tests. Colin stated:

[I] knew that the only way for me to stay alive was to get a transplant. It was as simple as that. It was a daunting prospect but you have to be realistic and look at it and hope that all being well, that I would live through it.<sup>349</sup>

**6.164** Colin underwent numerous tests and scans:

What I wasn't prepared for was the answers on the Friday. I was – my wife was asked to come down, you are taken into a room. You have got all the senior people in front of you and the chap that spoke to me, he said, 'Well, there is no doubt about it, you need a liver transplant.' He said, 'You could get two years, you could live another two years, you might live a year, but I'll give you six months.' And at that you could have picked me up off the floor because although you know you are ill, you are not putting a term on your life ....<sup>350</sup>

**6.165** Colin was put on to the liver transplant list. He had to attend the RIE for regular review appointments. At a review appointment in August 2007, Colin was noted to be jaundiced with low grade encephalopathy.<sup>351</sup> He was also suffering from significant peripheral oedema and fluid retention. Colin had a long discussion at this appointment with the surgeon about the implications of being on the waiting list. Colin knew that there was no guarantee that there was going to be a liver which would be a match so 'it was a waiting game'.<sup>352</sup> He was told that he could not go further than half an hour away from his house. This was not a problem for Colin as he was so unwell by this time that he remained at home. The prospect of Colin being transplanted by means of a non-heart-beating donor (a donor who had just died and whose heart had stopped, as opposed to a donor whose heart beat was being maintained until shortly before the liver is removed) and also having a transplant from a relative was also discussed with Colin. He was unaware at the time but one of his sons asked to be tested by the hospital to find out if he could donate half his liver to his father. In the event these tests were not concluded before Colin received his liver transplant.

#### *Colin's liver transplant*

**6.166** In September 2007 Colin received a telephone call from the Transplant Unit at the RIE telling him that they had a liver available to transplant. He was taken immediately by ambulance to the hospital and prepared for surgery. He was ready to go to surgery when he was told that the liver had arrived and was unsuitable for transplant as it had been drug abused. Colin described this as 'very, very difficult' for him and his family.<sup>353</sup>

---

<sup>348</sup> Ibid, page 68

<sup>349</sup> Ibid

<sup>350</sup> Ibid, page 69

<sup>351</sup> Ibid, pages 69–70; Excerpts from the medical records recovered in respect of Colin

<sup>352</sup> Day 77, page 70

<sup>353</sup> Ibid, page 71

**6.167** Colin continued to deteriorate and in the last weeks of October 2007 he became delirious due to hepatic encephalopathy, secondary to dehydration. He was jaundiced and also had ascites. He had bilateral pitting oedema to mid-shin. On 24 October 2007 he was admitted to Ninewells Hospital where he was treated with intravenous antibiotics and an ascitic tap.<sup>354</sup> He remained in hospital until 29 October. During this period Colin's name was removed from the transplant list due the fact that he had an infection. Colin had not realised how jaundiced he was until he saw his skin next to the white shirt of one of the doctors: '[t]hat was when I realised how bad it was'.<sup>355</sup> The hospital wanted Colin to remain as an in-patient but Colin wished to go home as he did not want to die in the hospital. At this time, Colin's name was reinstated on the transplant list.

**6.168** At 9pm on Thursday 1 November 2007 Colin received another telephone call from the transplant unit at the RIE advising him that a liver was available. Colin asked if they could check that the liver was suitable as he did not think that he would survive the trip to Edinburgh and back. He was told that the liver was good. He was then taken to Edinburgh by a 'blue light' ambulance. Within three-quarters of an hour of arriving at the hospital Colin was in theatre. In the early hours of 2 November he received a graft from a non-heart-beating donor. Colin subsequently discovered that his new liver had come from the north of England as all the transplant units in that area were busy carrying out transplants, and so it was surplus: 'it was a lucky day for me'.<sup>356</sup>

**6.169** Colin became independent of infused Factor IX on 4 November and initially recovered 'extremely well'.<sup>357</sup> He felt fine. However, on 7 and 8 November there was deterioration in his liver function test results. Tests revealed that there 'was a kink in the recipient hepatic artery'. Colin's mental state deteriorated and he became quite confused. This gradually settled along with his abnormal liver function test results. Colin was discharged home on 18 November. During his admission it was noted that his glucose levels were elevated before meal times. Colin was told that, as with a number of people who undergo a liver transplant, he had developed type 2 diabetes. He was prescribed Gliclazide. In addition, Colin had to continue taking a number of medications including anti-rejection medications, anti-fungal medications and antibiotics.<sup>358</sup> He continues to take two anti-rejection medications.

**6.170** Colin felt very well after the liver transplant: '[i]t was a big change'.<sup>359</sup> He initially attended the Scottish Liver Transplantation Unit (SLTU) at the RIE weekly for review, then fortnightly and then monthly. He now attends the SLTU's Outbound Clinic at his local hospital every six months for review. He attends the RIE annually for a liver biopsy.

**6.171** In September 2008 Colin returned to work as a manager for a stocktaking company working in large stores. The work was flexible in that Colin was able to tell the company when he was available to work the following month. This could be three or four days a week. Colin loved the work, but as he was working in the management side he had to travel a lot. One day he could be working in Aberdeen, the next Berwick and then back in Aberdeen the following day. Colin started to suffer from joint pain again. He also began to feel unwell at times. Occasionally he had difficulty concentrating as he drove. His hands

---

<sup>354</sup> Ibid, pages 71–72; Excerpts from the medical records recovered in respect of Colin

<sup>355</sup> Day 77, page 73

<sup>356</sup> Ibid, pages 74–75

<sup>357</sup> Ibid, pages 75–76; Excerpts from the medical records recovered in respect of Colin

<sup>358</sup> Day 77, pages 77–78; Excerpts from the medical records recovered in respect of Colin

<sup>359</sup> Day 77, page 78

became blotchy, and his face puffed up. He found it stressful trying to manage 30 people when he felt unwell. Initially he cut his working hours down to 16 a week, but the travel remained difficult. He left this job to work in a supermarket as a night-shift shelf stocker. He initially worked three nights a week there but found that all he did between shifts was sleep. He then reduced his work to two nights a week. Two or three times he nearly collapsed at work, and so Colin realised 'enough was enough'.<sup>360</sup> He accepted medical advice that working night shifts was significantly contributing to his symptoms, and that he should retire. He retired in late 2010 at the age of 56. Given his strong work ethic, this was difficult for him: '[retirement] doesn't come easy, I can tell you that'.<sup>361</sup>

**6.172** A liver biopsy in November 2008 showed evidence of fatty change which may reflect metabolic causes, for example, diabetes or other causes, such as development of the Hepatitis C virus. It also showed no evidence of rejection. A liver biopsy in November 2009 showed no significant scarring, or fibrosis.<sup>362</sup>

### *Colin's current symptoms*

**6.173** Colin continues to suffer from aches and pains. He is prescribed Tramadol and takes paracetamol to alleviate these. These pains are mostly joint and muscle pains, particularly in his hands. At times they become very 'puffed up'.<sup>363</sup> Also, he stated:

My ankles puff up and it's hard to walk. Then you are not bothered with it, it will go away again. I have always got the shoulders and arm pains. They do not go away, they are there all the time but you get used to that, but to me that's not being ill. That's just having a pain. You just accept that and get on with it.<sup>364</sup>

**6.174** Colin continues to attend the haemophilia meetings, although he no longer has haemophilia. He does so in order that younger people attending the group may see the benefits of a liver transplant.<sup>365</sup>

**6.175** With regard to future treatment, Colin has been told that Ninewells Hospital has funding for the new treatments but that it is the decision of the RIE if he receives either of these treatments or not. The new treatments that Colin referred to are Boceprevir and Telaprevir.

**6.176** It is likely that the addition of these treatments will cause more severe side-effects for patients.<sup>366</sup> These new treatments are discussed in more detail in Chapter 13, *Knowledge of Viral Hepatitis Now*, paragraph 13.115.

**6.177** When Colin attended a review appointment at the RIE in about March 2011 he spoke to one of the doctors about these new treatments. The doctor seemed cautious about Colin receiving the treatment as 'we don't want to make you ill. We have just made you better'.<sup>367</sup> Colin believes that if he is going to try and eradicate the virus, it is better to take the treatment when he is well. He plans to discuss this again with the doctor at the RIE at his next appointment.

---

<sup>360</sup> Ibid, page 83

<sup>361</sup> Ibid, page 83

<sup>362</sup> Ibid, pages 79-80; Excerpts from the medical records recovered in respect of Colin

<sup>363</sup> Day 77, page 84

<sup>364</sup> Ibid, page 84

<sup>365</sup> Ibid, pages 84-85

<sup>366</sup> Professor Thomas – Day 53, page 52

<sup>367</sup> Day 77, pages 85-86

### *Specific impacts of Colin's infection with Hepatitis C*

**6.178** As a result of his infection with Hepatitis C, Colin feels that he has missed a large part of his children growing up. He knows that his daughter, the eldest, was very concerned about him. His sons used to see him in bed ill and bring him cups of tea. There were long periods of time when Colin was unable to do activities with them, such as skiing. He believes that his illness put 'a lot of stress on them'.<sup>368</sup>

**6.179** Colin's close friends knew about his infection with Hepatitis C. His illness had a big effect on his social life. For a number of years he was unable to socialise as he was not well enough to do so. He was unable to go on holidays. He was unable to pursue his hobbies of skiing, sailing, fishing and walking. Since Colin's health has improved he has managed to have a couple of sailing trips.<sup>369</sup>

**6.180** The financial impacts of Colin's infection with Hepatitis C have been described to a certain extent already. The greatest impacts were Colin having to stop working, and being forced to sell his family home to release some capital. In addition, Colin had a small pension. When he became unwell, and stopped working in the mid-1990s he made it 'fully paid up'.<sup>370</sup> Colin has life assurance which he took out before his diagnosis with Hepatitis C. It is a whole-of-life policy. He had a repayment mortgage which has not been affected by his diagnosis with Hepatitis C. He has taken out travel insurance since his diagnosis, but although he disclosed his haemophilia he did not inform the insurers that he had Hepatitis C. He has incurred travel expenses and parking charges, attending numerous hospital appointments both in Dundee and Edinburgh. He has received two payments from the Skipton Fund.<sup>371</sup>

### **Gordon**

**6.181** When Gordon gave evidence he was 65 years of age and he lived with his wife in England. Before he retired he was a senior academic.<sup>372</sup> Sadly, Gordon died in the summer of 2013.

**6.182** Gordon lived in Edinburgh between 1965 and 1985. He acquired Hepatitis C, Genotype 1, from one of a number of blood transfusions he received at the RIE in December 1975 and/or early 1976.<sup>373</sup>

### *Gordon's blood transfusions*

**6.183** In October or November 1975, when Gordon was 29 years old, he had a respiratory tract infection with pleural effusions.<sup>374</sup> On 1 December he was diagnosed with pericarditis (inflammation of the membranous sac surrounding the heart) and was admitted to the City Hospital, Edinburgh.<sup>375</sup> Constrictive pericarditis was diagnosed in mid-December. On 27 December he was transferred to the care of a Cardiothoracic Surgeon at the RIE, for an urgent pericardiectomy (surgical removal of the pericardium). His condition was sufficiently serious to warrant opening the cardiothoracic theatre which was usually closed between

---

<sup>368</sup> Ibid, pages 87–88

<sup>369</sup> Ibid, pages 89–90

<sup>370</sup> Ibid, pages 90–91

<sup>371</sup> Ibid, pages 92 and 94–95

<sup>372</sup> Ibid, page 97

<sup>373</sup> Ibid, page 98

<sup>374</sup> Gordon's Witness Statement; pleural effusions occur when excess fluid accumulates between the two pleural layers, the fluid-filled space surrounding the lungs.

<sup>375</sup> The pericardium is the fluid-filled sac surrounding the heart and the proximal ends of the aorta, vena cava and the pulmonary artery.

Christmas and New Year. Gordon underwent the pericardiectomy on 29 December. He suffered excessive blood loss in the early post-operative period, and required to undergo further surgery on about 29 or 30 December to rectify bleeding from the operation site. About 1.5 litres of blood and clot were removed from the pleural cavities. Gordon received a number of blood transfusions between 29 and 31 December. As Gordon stated, at that time, he was 'distinctly, critically unwell'.<sup>376</sup>

**6.184** Gordon's recovery was complicated by a number of conditions including septicaemia, cardiac arrest, low cardiac output, bilateral pneumothorax, renal failure and a gastric stress ulcer. In January 1976, while still a patient at the RIE, he received a further transfusion of whole blood and packed red cells after a series of haematemeses (vomiting of blood). He was eventually discharged home in mid-March, having first been transferred back from the RIE to the City Hospital, Edinburgh.<sup>377</sup>

**6.185** Gordon accepted that the operation and the associated blood transfusions were 'necessary and potentially life saving procedures'.<sup>378</sup> Although he discussed the risks of the pericardiectomy with the cardiothoracic surgeon, he very much doubted that there were any discussions about the risks associated with blood transfusions. Prior to his surgery, he expected that if he needed a blood transfusion then it would have been available to him.<sup>379</sup>

**6.186** Gordon was told by nursing staff and a number of people who visited him in hospital, including his late mother, that between the pericardiectomy on 29 December 1975 and the series of haematemeses in January 1976 he became severely jaundiced. One of the people from his work who visited him left the ward immediately after he saw him in this condition. His jaundiced state was also noted in a discharge letter from a Registrar to Gordon's GP: 'he developed severe jaundice which was progressive. However the aetiology of this remained obscure although halothane appears to be incriminated'.<sup>380</sup> Halothane was subsequently discounted as a cause for Gordon's jaundice.<sup>381</sup> A likely explanation for this episode of jaundice is that it was caused by 'shock liver', hypoperfusion (decreased blood flow) of the hepatic artery which kills liver cells. This condition often follows major cardiac surgery particularly when there is a very significant fall in blood pressure. Thus, it is unlikely to have been related to Gordon acquiring Hepatitis C from the blood transfusions.

### *Investigation of Gordon's abnormal liver function test results*

**6.187** Gordon's recovery from these operations and subsequent complications, was good. He returned to work in June 1976. He continued to see a General and Gastrointestinal Surgeon at the RIE in respect of gastric symptoms, from which he suffered following the surgery in January 1976. During these follow-up appointments Gordon's liver function tests were found to be abnormal. It was noted that before the pericardiectomy, apart from a minor elevation of alkaline phosphatase, Gordon's liver function tests were normal. In September 1976 the surgeon noted that Gordon's ALT level was raised, at 139. At the suggestion of the surgeon, Gordon subsequently abstained from alcohol for three months, but his ALT level remained elevated.<sup>382</sup>

---

<sup>376</sup> Day 77, pages 98–100

<sup>377</sup> Ibid, pages 99–100; Gordon's Witness statement

<sup>378</sup> Day 77, page 100; Gordon's Witness statement

<sup>379</sup> Day 77, page 100

<sup>380</sup> Ibid, pages 101–102; Excerpts from the medical records recovered in respect of Gordon

<sup>381</sup> Halothane is a general anaesthetic drug.

<sup>382</sup> Day 77, pages 103–105; Excerpts from the medical records recovered in respect of Gordon



**6.188** In early 1977, the surgeon referred Gordon to Dr Niall Finlayson, Consultant Physician at the RIE, for his opinion on the cause of Gordon's persistently abnormal liver function tests. Gordon attended to see Dr Finlayson in about March or April of that year. Gordon found Dr Finlayson to be very thorough. Dr Finlayson reviewed Gordon's case notes and examined him. Gordon gained the impression that he was puzzled about the liver function test results and keen to investigate their cause. Tests for Hepatitis B antigen and antibody were negative as were tests for other diseases – Q fever, toxoplasmosis and infectious mononucleosis. At this time Gordon was 'not terribly worried' about his abnormal liver function results although he was 'not entirely happy to see that he had persistent hepatitis'. He was energetic, back at work and 'generally enjoying everything [he] did'.<sup>383</sup>

**6.189** In September 1978 Gordon underwent a liver biopsy. This showed 'a mild persistent hepatitis'.<sup>384</sup> Gordon does not recall being told the results of the biopsy.<sup>385</sup> About this time, Dr Finlayson concluded that non-A, non-B Hepatitis was the most likely cause of Gordon's abnormal liver function test results as he had excluded all other known possible causes. Gordon remembers Dr Finlayson telling him about NANB Hepatitis which at that time was presumed to be viral. He remembers that Dr Finlayson mentioned to him that he was aware of recent research that an agent, just found to be transmissible in chimpanzees, was a possible/probable candidate.<sup>386</sup>

**6.190** Between 1977 and 1982 Gordon continued to attend appointments with Dr Finlayson for monitoring. During that period Gordon did not display any symptoms of NANB Hepatitis. In 1985 Gordon moved to England as he was offered a good position there. After he moved, there was no further monitoring of his condition by the NHS in Scotland. Gordon married in 1987. Before marrying his wife he told her that he had an illness and was not clear what the outcome of it was likely to be.<sup>387</sup>

**6.191** In March 1988, while carrying out an experiment as part of his work, Gordon measured his own blood ALT and found it to be high. He mentioned this to a personal friend, a Consultant Physician, who agreed to take a blood sample and check the ALT level. This doctor subsequently wrote to Gordon and stated that 'the hepatocellular enzymes are indeed quite high and I personally would be a little unhappy to ascribe them to chronic persistent hepatitis'. He suggested that Gordon seek further advice 'as at the very least, they require further monitoring'.<sup>388</sup> Gordon then attended his GP and asked him to refer him to Professor Losowsky, a Gastroenterologist and Hepatologist as well as Professor of Medicine at St James's University Hospital in Leeds. Gordon was acquainted with Professor Losowsky who had told Gordon that he would be delighted to see him. Gordon's GP refused to refer Gordon to Professor Losowsky, and instead advised him to abstain from alcohol. Unsurprisingly, this had no effect on Gordon's ALT levels and at that stage no monitoring of Gordon's liver function was undertaken.<sup>389</sup>

**6.192** Until 1995, Gordon continued in good health and felt remarkably well. He successfully developed his career which he obviously relished and he assumed more responsibilities at work. If he felt tired occasionally, he put this down to having a lot of

---

<sup>383</sup> Day 77, pages 105, 107, 109–110

<sup>384</sup> Excerpts from the medical records recovered in respect of Gordon

<sup>385</sup> Day 77, pages 110–111;

<sup>386</sup> *Ibid*, page 113; Gordon's Witness Statement

<sup>387</sup> Day 77, pages 114–115; Gordon's Witness Statement

<sup>388</sup> Excerpts from the medical records recovered in respect of Gordon

<sup>389</sup> Day 77, pages 115–117

commitments. He did not worry about his health. As he stated, 'I found plenty to fill every moment and every moment wasn't just for work'. He enjoyed fishing and photography too.<sup>390</sup>

### *Investigation of Gordon's symptoms of Hepatitis C and diagnosis with the virus*

**6.193** In early 1995 Gordon started to suffer from exhaustion. In addition, he lost a considerable amount of weight over two to three months. He attended his GP, who was by now a different GP to the one Gordon saw in 1988. This GP carried out some blood tests, including a liver function test. Gordon returned a week later for the results of these tests and was told that his liver function test results were highly abnormal. From his GP's demeanour, Gordon formed the impression that the doctor thought that the results were very bad indeed. His GP examined him and agreed with Gordon's suggestion that he be referred to Professor Losowsky. At the end of the appointment his GP gave him a strong handshake and it felt to Gordon as if he was saying a final farewell to him. Gordon was very surprised and very shaken by this reaction.<sup>391</sup>

**6.194** Following the referral to him, Professor Losowsky arranged for Gordon to be admitted to St James's University Hospital for full investigation of his weight loss and fatigue. Gordon was admitted there in April 1995 and remained an in-patient for about 19 days while wide-ranging investigations were carried out. As a result of these investigations, which included a liver biopsy, Gordon was told that he had acquired Hepatitis C and that he had cirrhosis of the liver. He 'was not unduly surprised or devastated ... by the Hepatitis C bit, but the fact that I had cirrhosis was very unpleasant ...'.<sup>392</sup> Gordon knew that cirrhosis was irreversible. He did not remember having any discussions with Professor Losowsky, or any other doctor, about the severity of the virus or about its health implications. He was not offered any counselling. Gordon did not feel that the doctors were deficient in this respect, and appreciated that his infection was acquired very early on in the timescale of knowledge of the Hepatitis C virus. Those treating Gordon were aware of his professional background and his ability to access medical information. Gordon would have felt patronised had they spent time explaining the virus to him.<sup>393</sup>

**6.195** The letter written on Gordon's discharge from hospital records that Gordon's alpha-fetoprotein level was found to be significantly elevated, at 200.9. It also records that at that time Gordon was drinking approximately 40 to 50 units a week.<sup>394</sup> Gordon accepted that he was a regular drinker, but considered that these figures were an overestimate of his weekly intake. On his discharge from hospital Gordon was told to abstain from alcohol, which he did for four years.<sup>395</sup>

**6.196** Following his discharge from hospital, Gordon attended out-patient appointments with Professor Losowsky for monitoring. He felt 'optimistic'.<sup>396</sup> In her statement to the Inquiry, Gordon's wife recalled being advised at a subsequent appointment which she attended with Gordon to consider having protected sex. Gordon does not recall this matter being discussed.<sup>397</sup>

---

<sup>390</sup> Ibid, page 118

<sup>391</sup> Ibid, pages 119–120

<sup>392</sup> Ibid, page 123

<sup>393</sup> Ibid, pages 120–125; Gordon's Witness Statement

<sup>394</sup> Excerpts from the medical records recovered in respect of Gordon

<sup>395</sup> Day 77, pages 120–124

<sup>396</sup> Ibid, page 125

<sup>397</sup> Ibid, pages 124–125; Gordon's wife's Witness Statement

### *Gordon's treatment with Interferon*

**6.197** In January 1996 Professor Losowsky offered Gordon treatment with Interferon. By this time his ALT level had increased and Gordon was continuing to feel tired. Professor Losowsky told Gordon that the likelihood of response to the Interferon was small 'in view of his age, duration of disease, presence of cirrhosis and relatively little inflammatory change on the liver biopsy'.<sup>398</sup> Gordon's alpha-fetoprotein level remained raised at 90. A further CT scan of his liver in February 1996 showed no lesions.<sup>399</sup>

**6.198** Gordon and Professor Losowsky agreed that, in order to cause the least disruption to Gordon's work, he should start treatment with Interferon during the Easter holidays. On 2 April 1996 Gordon was once again admitted to St James's University Hospital for a repeat liver biopsy and commencement of treatment with Interferon. The ultrasound-guided liver biopsy showed 'the presence of established micronodular cirrhosis with some portal inflammation consistent with Hepatitis C infection'.<sup>400</sup> The degree of inflammation had not changed since the previous biopsy in 1995. Gordon was commenced on three million units of Interferon, three times weekly. He initially suffered a slight temperature but no other complication was noted. Gordon was discharged home on the same dose of Interferon.<sup>401</sup>

**6.199** During the course of the treatment with Interferon Gordon suffered from substantial fatigue and flu-like symptoms. He found day-to-day living 'a struggle'.<sup>402</sup> The flu-like symptoms did not abate much during the course of the treatment because, as soon as Gordon felt he was recovering from a dose of Interferon, it was time to take the next dose. He 'ached and felt miserable'.<sup>403</sup> He continued to work throughout the course of the treatment. Gordon stopped taking the Interferon treatment after five months as his ALT level remained elevated and he remained HCV PCR positive.<sup>404</sup>

### *The period after Gordon's treatment with Interferon*

**6.200** Gordon continued to attend St James's Hospital for monitoring by Professor Losowsky, and then by his successor Dr Davies, a Consultant Hepatologist. Gordon described his life at this time as 'a progressive struggle' and 'a battle'.<sup>405</sup> He developed considerable tiredness and became more prone to minor infections, such as colds and spots on his skin. Gordon's ability to carry out all aspects of his work began to suffer. In order to fulfil his teaching commitments, Gordon had to reduce the amount of time he spent on research. This must have been very difficult for Gordon as he obviously took great pride in his work, and wanted to carry it out to the best of his ability. In her statement, Gordon's wife describes this period:

From 1995 to about 2001 my husband still managed to work but he suffered from extreme tiredness. He developed sleep problems in that, although he was tired, he was unable to stay asleep. It was a struggle for him to get up in the mornings but he did so in order to go to work as normal .... Intellectually he remained sharp but he was physically exhausted. His appetite was poor and

---

<sup>398</sup> Excerpts from the medical records recovered in respect of Gordon

<sup>399</sup> Day 77, pages 126–127

<sup>400</sup> Excerpts from the medical records recovered in respect of Gordon

<sup>401</sup> Day 77, pages 127–128; Excerpts from the medical records recovered in respect of Gordon

<sup>402</sup> Day 77, page 129

<sup>403</sup> Ibid, page 129

<sup>404</sup> Ibid, pages 129–130; Excerpts from the medical records recovered in respect of Gordon

<sup>405</sup> Day 77, page 131

he was run down and unable to keep warm, usually having cold hands and cold feet. His condition made spontaneous home and social life minimal. My husband's mood became more thoughtful and introspective but he remained confident, in control, analytical and stoic.<sup>406</sup>

**6.201** In 1996 and 1999 Gordon was found to have minor varices which were ligated or otherwise treated.<sup>407</sup>

**6.202** The possibility of Gordon receiving treatment with Interferon and Ribavirin was discussed with him in 1998 but it was decided that, as he had cirrhosis and had been a non-responder to Interferon, the risks of side-effects of this treatment would outweigh the chance of Gordon deriving any benefit from it. In about 1999 or 2000, Gordon attended an appointment with one of Dr Davies' registrars. Gordon indicated to the registrar that he 'was very tired and not really coping'.<sup>408</sup> Gordon's wife, who also attended that appointment, pressed the registrar about what she proposed to do about Gordon's condition. It seems that she felt a degree of frustration at the fact the doctors were simply monitoring Gordon's condition, and were not treating his symptoms. The registrar suggested to Gordon that, in light of his symptoms, he might require a liver transplant but Dr Davies contacted Gordon the following morning to advise him that the risks of such a procedure would outweigh the benefits. He did, however, make it clear that if Gordon's condition progressed to hepatocellular carcinoma or liver failure his advice would be reversed.<sup>409</sup>

#### *Gordon's diagnosis with hepatocellular carcinoma*

**6.203** In April 2001 an MRI scan and ultrasound revealed that Gordon had probably developed hepatocellular carcinoma. The report of the MRI scan dated 19 April 2001 revealed 'several (5 at least) hypervascular nodules suggestive of HCC'.<sup>410</sup> Gordon was initially told that hepatocellular carcinoma was strongly suspected, with about a 1 in 100 chance of the result having been wrongly interpreted. This was 'perhaps the most drastic thing' Gordon had ever been told about himself.<sup>411</sup> A number of factors mitigated the shock of this news – first, having been aware that his alpha-fetoprotein level was raised and having been referred for both MRI and ultrasound scanning, (which he felt would not have been arranged without some 'serious suspicion'), Gordon knew that hepatocellular carcinoma was 'a possible scenario' and so was 'a little bit prepared' in his mind; secondly, Dr Davies told Gordon about this possible diagnosis 'in a most kindly way'. He telephoned Gordon, saw him and his wife and arranged Gordon's admission to hospital in the same day. Gordon found Dr Davies to be 'incredibly efficient' and his 'middle of the road approach' in giving him this news gave him confidence and 'was a sort of calming influence'.<sup>412</sup>

**6.204** Gordon's wife's reaction to her husband's diagnosis with hepatocellular carcinoma was 'pretty bad'. She was very supportive of Gordon but this was an 'unhappy time' for her. She had been 'tense' since his diagnosis with Hepatitis C.<sup>413</sup>

---

<sup>406</sup> Ibid, pages 130–131; Gordon's wife's Witness Statement

<sup>407</sup> Gordon's Witness Statement

<sup>408</sup> Day 77, page 132

<sup>409</sup> Ibid, pages 132–133

<sup>410</sup> HCC is hepatocellular cancer; Excerpts from the medical records recovered in respect of Gordon

<sup>411</sup> Day 77, page 134

<sup>412</sup> Ibid, pages 133–135

<sup>413</sup> Ibid, page 135

### *Gordon's liver transplant*

**6.205** Four days after his diagnosis with hepatocellular carcinoma, Gordon was signed off work. On 8 May 2001 he was admitted to St James's Hospital for assessment for liver transplantation and remained there until 11 May. One test was problematic, and Gordon had to wait until a respiratory specialist returned to perform a bronchoscopy on 25 May. Gordon's wife described these weeks as 'harrowing' and added 'the "ifs" and "buts" were too hard for me. I felt helpless and unable to do anything which would change anything. It was like walking on eggshells'.<sup>414</sup> Her father had died of cancer previously which made this time harder for her. She stated:

We were waiting and hoping to be admitted to the transplant list. Another patient came back from seeing a consultant and said to my husband that they could not offer him a transplant and so he was being sent home to die.<sup>415</sup>

Gordon agreed with the proposition that this was a 'very difficult, emotive time' for him and his wife.

**6.206** On 8 June 2001 Gordon was admitted onto the transplant list. He was advised to live normally and keep his bag packed. He remained signed off work. On 30 August Gordon received a telephone call advising him that a liver was available and he was admitted to hospital that night, for surgery at 6 am the next morning. Immediately following the liver transplant Gordon suffered two complications. The first of these was internal bleeding post-operatively. The evening after the surgery, Gordon was 'in considerable pain' and had 'tremendous abdominal tenderness. [He] was just covered with a sheet and if anyone just touched the sheet, [He] would wince in pain...'.<sup>416</sup> An ultrasound scan revealed the cause of this and Gordon was re-admitted to theatre for tying off of some blood vessels and the removal of a blood clot. The second complication was breathing problems which Gordon developed a few days after the transplant. As a result of this, he was taken from the High Dependency Unit to the Intensive Care Unit and was given C-PAP (continuous positive airway pressure) ventilation for a period of time. Gordon stated that he 'did not like' that experience. His wife was 'frightened for him' when she saw him back in the Intensive Care Unit being treated with this form of ventilation. The diagnosis of hepatocellular carcinoma in his explanted liver was confirmed.<sup>417</sup>

**6.207** Thirteen days after the liver transplant, Gordon was discharged home. He was 'delighted to be alive' and 'overjoyed at the success of the operation'.<sup>418</sup> Although Gordon's wife expected him to be confined to his bedroom on his return from hospital, Gordon was keen to be up and about. He returned to work in April 2002. He was very glad to be back and was able to resume most of his work-related activities. At that time his liver function tests were virtually normal, but Gordon had been advised by Dr Davies that it was certain that the Hepatitis C virus would recur.<sup>419</sup>

**6.208** By 2003, Gordon's liver function tests had started to deteriorate and his energy levels were falling. A liver biopsy in October of that year revealed 'considerable portal fibrosis'.<sup>420</sup>

---

<sup>414</sup> Ibid, page 136; Gordon's wife's Witness Statement

<sup>415</sup> Day 77, pages 135–136; Gordon's wife's Witness Statement

<sup>416</sup> Day 77, pages 137–138

<sup>417</sup> Ibid, pages 137–139; Gordon's wife's Witness Statement

<sup>418</sup> Day 77, page 139

<sup>419</sup> Ibid, pages 139–140

<sup>420</sup> Ibid, page 140; Excerpts from the medical records recovered in respect of Gordon

### *Gordon's treatment with Pegylated Interferon and Ribavirin*

**6.209** On 30 January 2004 Gordon started treatment with Pegylated Interferon and Ribavirin. In order that Gordon was able to minimise time spent away from his work, one of the doctors arranged to see Gordon for his regular review appointments just before the start of the clinic at 2 pm. Gordon described the side-effects of this treatment as 'horrendous'.<sup>421</sup> Once again he experienced substantial fatigue which he found particularly troublesome, especially for the first two or three days after each weekly injection. He also suffered flu-like symptoms, nausea, headaches, shortness of breath and aches and stiffness in his knees. He developed a rash which required treatment by a dermatologist. His haemoglobin fell. He lost 7 kilograms in weight. He experienced two episodes of syncope (fainting) which he described as 'very humiliating'.<sup>422</sup> These happened at work in front of a large number of people. The first episode was 'absolutely frightening'. Gordon suddenly became unconscious and hit his head on a bench causing a cut on his head which, as he said, looked worse than it probably was. He was taken by emergency ambulance to the local hospital. A month later the second episode occurred. After this Gordon was told to stop driving until he was reviewed by a neurologist. In order to expedite this review, Gordon arranged to see a neurologist privately. The neurologist concluded that Gordon was unwell and 'the side effects from his treatment have affected him perhaps more than he thought'.<sup>423</sup> After seeing the neurologist Gordon was allowed to drive again. Gordon also attended an appointment with a cardiologist and underwent a 24-hour ECG to rule out the episodes having a cardiological cause.<sup>424</sup>

**6.210** With hindsight, Gordon later considered that he perhaps had misjudged how much he could do while he was taking the Pegylated Interferon and Ribavirin treatment. The episodes of syncope brought home to him what a precarious position he was in while he took the drugs, and the dangerous nature of the treatment. Gordon was also aware that there was some controversy at the hospital as to whether he should be receiving treatment at all, being a non-responder to previous treatment and having received a liver transplant.<sup>425</sup>

**6.211** As there was no drop in Gordon's Hepatitis C viral count, he stopped taking the Pegylated Interferon and Ribavirin treatment after 24 weeks, in summer 2004. He thought that he had recovered fairly quickly from the side-effects of the treatment. As soon as he stopped taking the treatment his weight started to increase and he was 'able to get back to a reasonable life'.<sup>426</sup>

### *The period since Gordon's treatment with Pegylated Interferon and Ribavirin*

**6.212** In 2005, at the age of 59 years, on the advice of those treating him, Gordon took early retirement on the ground of ill-health. It is to his credit that he had managed to continue to work except during his few hospitalisations. Due to the symptoms he suffered, particularly the fatigue, he was unable to fulfil aspects of his work, which damaged his opportunities for career advancement. By 2005 it was clear to Gordon that he 'was not functioning as was essentially required of [him]'.<sup>427</sup> His early retirement, and the fact that

---

<sup>421</sup> Day 77, page 142

<sup>422</sup> Ibid, page 142

<sup>423</sup> Ibid, page 144; Excerpts from the medical records recovered in respect of Gordon

<sup>424</sup> Day 77, pages 142–143

<sup>425</sup> Ibid, pages 142–144

<sup>426</sup> Ibid, page 146

<sup>427</sup> Ibid, page 147

the last 10 years of his employment were much less productive than he would have liked, was a matter of 'considerable disappointment' and frustration to him. The outlet for his intellectual interests was largely abolished. He found it very hard to adjust after having had a reasonably prolonged career in one area of work, finding that he missed both the work and contact with people in the same field.<sup>428</sup>

**6.213** Since 2005 Gordon had continued to suffer from fatigue, loss of stamina, loss of muscle strength and arthritis and arthralgia. Due to the immunosuppressant treatment he was required to take since the liver transplant, he had suffered some severe dental infections and teeth were extracted as a result of this. In 2007 he was found to have impaired glucose tolerance and, in June 2010, he was diagnosed with diabetes. This is thought to be a consequence of both Gordon's immunosuppression and the Hepatitis C virus. In about 2011, Gordon was diagnosed with interstitial lung disease and the immunosuppression treatment, tacrolimus, was suggested as a possible factor in Gordon's development of this disease. He suffered from breathlessness and, in 2010, had suffered a number of moderately severe chest infections and lost a lot of weight. At the time he gave evidence Gordon was being investigated for pulmonary hypertension. As Gordon stated 'there always seems to be something looming on the horizon, which does seem to have some links going back to either the Hepatitis C virus ... and/or the immuno-suppressant agent'.<sup>429</sup>

**6.214** Gordon continued to attend St James's University Hospital for monitoring. A liver biopsy in August 2010 reported 'recurrent Hepatitis C infection with fibrosis stage 4 and necroinflammatory grade 3'.<sup>430</sup> A Specialist Registrar on the Liver Unit stated in a letter to Gordon's General Practitioner in October 2010 that the Stage 4 fibrosis was unchanged from 2003. He noted that Gordon had moderate inflammation at Grade 4 but overall the biopsy was reassuring and that there has been no progression over the past seven years to cirrhosis. He stated that it was agreed that Gordon would undergo an annual biopsy follow-up although, until he saw a copy of this letter, Gordon was unaware of this.<sup>431</sup>

**6.215** With regard to his prognosis, Gordon was told by Dr Davies when he developed cancer in 2001 that unless he received a successful liver transplant, his condition would be terminal. The prognosis for Gordon's recurrent Hepatitis C was never explained to him except that he was told that it is a progressive disease. Gordon did not ask about his prognosis as he suspected 'the answer is not known ... I feel that nobody knows and nobody will be too surprised if I had an early demise or if I carried on for quite a few years yet'.<sup>432</sup> Gordon had been told about the advent of the new generation of protease inhibitors but at the time he gave evidence had not been told if he was considered a candidate for them. He expected there to be a discussion about this in the near future although he wondered what impact his failure to respond to previous treatment and his age would have had on this.<sup>433</sup>

---

<sup>428</sup> Ibid, pages 146–147 and page 165; Gordon's Witness Statement

<sup>429</sup> Day 77, pages 147–149; Excerpts from the medical records recovered in respect of Gordon

<sup>430</sup> Ibid. The METAVIR score helps interpret a liver biopsy. This scoring system assigns two standardised numbers: one to represent the degree of inflammation and the other the degree of fibrosis.

<sup>431</sup> Excerpts from the medical records recovered in respect of Gordon

<sup>432</sup> Day 77, page 151

<sup>433</sup> Ibid, pages 150–151; Gordon's Witness Statement

### ***Specific impacts of Gordon's infection with Hepatitis C***

**6.216** One of the greatest impacts of Gordon's infection with Hepatitis C has been the effect of this on his wife. She has suffered from depression and anxiety since Gordon's diagnosis with hepatocellular carcinoma and his subsequent liver transplant in 2001.<sup>434</sup> Gordon spoke very eloquently and honestly about this. Understandably, he wished part of his evidence on this sensitive matter to be kept confidential, and so not all of what he said is narrated here although it has been considered by the Inquiry.

**6.217** With the benefit of hindsight, Gordon and his wife could see that every individual episode Gordon had experienced as a result of Hepatitis C had imposed an incremental psychological stress on her. This resulted in 'a big change in all sorts of aspects of her behaviour'.<sup>435</sup> Gordon described her experiencing episodes of agitation and becoming jittery, uptight and angry on occasion. She worried and was often quite tearful. There were times when Gordon was an in-patient when he was 'torn because [he] was looking forward to having her as a visitor, very keen to see her, but also dreading that she would react ....'<sup>436</sup> While he liked to read literature about Hepatitis C and followed the progress of this Inquiry, she found this upsetting and it made her feel very anxious. Good friends of theirs noticed the change in her behaviour.<sup>437</sup>

**6.218** In her statement to the Inquiry, Gordon's wife described in detail the distress and anxiety she experienced during each stage of Gordon's illness and, in particular, during the process involved in his liver transplant. At that time, she did not receive any support and she felt ignored because it was her husband who was ill. Each time her husband had an investigation she would become anxious about the procedure and the result. She candidly stated that she had episodes of moodiness and behaved inappropriately at times. 'I fear I embarrass him by my forthright actions sometimes. It is my way of coping ....'<sup>438</sup> She stated:

The care I feel that my husband needs from me is more emotional support than physical help, but I am short-tempered with him and react angrily when events that others see as insignificant happen, and this distresses him further ... I feel that I have lost the ability to support him properly.<sup>439</sup>

**6.219** She acknowledged having felt so low that she did not care if she did not wake up the following day. She stated, 'That is hard to say, think and acknowledge to someone who has been through the diagnosis of Hepatitis C, cancer and a transplant'.<sup>440</sup> Gordon described the times when she expressed an attitude of 'I have had enough. I don't care about anything'. He found it difficult to know how to respond to these episodes.<sup>441</sup>

**6.220** Gordon's wife has been prescribed medication by her GP, undergone a course of cognitive behavioural therapy from a clinical psychologist and attended sessions with a psychiatrist. At the time of the public hearings she was taking a high dose of one antidepressant medication and a moderate dose of another. If she ever forgot to take the medications, 'she [was] really unable to function coherently and very agitated and

---

<sup>434</sup> Day 77, page 151

<sup>435</sup> Ibid, page 152

<sup>436</sup> Ibid, page 156

<sup>437</sup> Ibid, pages 152–155

<sup>438</sup> Ibid, page 157; Gordon's wife's Witness Statement

<sup>439</sup> Ibid

<sup>440</sup> Ibid.

<sup>441</sup> Day 77, page 158



tearful, very tearful'.<sup>442</sup> All the medical professionals Gordon's wife has seen considered that Gordon's medical history has been a key feature in her depression. Gordon met with his wife's psychiatrist who was of the view that his wife's depression 'was very intimately linked' with Gordon's illness.<sup>443</sup> He also commented to Gordon and in a letter to Gordon's GP that he thought Gordon, too, was suffering a degree of reactive depression although not such as to require intervention. Gordon's wife noticed that his self-confidence was reduced and this too affected Gordon's quality of life. Gordon realised that the events he had experienced as a result of his infection with Hepatitis C have presented a prolonged psychological challenge and he struggled to cope.<sup>444</sup>

**6.221** Gordon's wife's depression had 'an ongoing significant effect' on their quality of life.<sup>445</sup> As Gordon stated 'we have got ... really quite a complicated situation which is not really getting better'.<sup>446</sup>

**6.222** Gordon's wife has had a varied and good career which was affected both by Gordon's illness and by her own depression. She left one job as it involved too much travel and she wanted to remain closer to Gordon. As she began to suffer symptoms of depression, Gordon's wife found her work increasingly difficult. One job ended 'essentially, in tears' as she was not coping and her employers were very unsympathetic.<sup>447</sup> This was clearly a very difficult and stressful time for both of them. At present Gordon's wife is working in a part-time teaching post 'which she is mainly coping with but occasionally, when the going gets tough, she is quite agitated'. This work may be the subject of cut-backs.<sup>448</sup>

**6.223** With regard to the financial impacts of his infection, while he continued to work Gordon did not incur any loss of earnings. This was due both to his admirable strength in continuing to work when he was more than likely unfit to do so, and to the goodwill of his employers. He considered that, but for his illness and the effect of this on his ability to carry out all aspects of his work, he would have had several increments in his salary. Had he been fit to do so, Gordon would have liked to continue working until he was 65 or possibly 67 years old; the latter being an option under his work contract. His pension income was substantially less than his earned income would have been had he been able to continue working. He calculated this cumulative difference to be at least £152,450, not taking account of any increments he might have been awarded. He acknowledged that it was very difficult to assess this loss reliably although considered this figure was likely to be an understatement. At the age of 65 onwards, his superannuation pension was expected to be about £3200 per annum less than it would have been had he been able to continue working.<sup>449</sup>

**6.224** Gordon had also incurred the costs of his own private referral to the neurologist and his wife's private psychiatric referral. He incurred expenses in travelling to the numerous hospital and other appointments he was required to attend. He received both available payments from the Skipton Fund. His mortgage and associated endowment policy were both initiated before his diagnosis with Hepatitis C so these were not affected.<sup>450</sup>

---

<sup>442</sup> Ibid, pages 151–152 and page 154

<sup>443</sup> Ibid, page 153; Gordon's Witness Statement

<sup>444</sup> Ibid

<sup>445</sup> Day 77, page 152

<sup>446</sup> Ibid, pages 153–154

<sup>447</sup> Ibid, page 161

<sup>448</sup> Ibid, pages 160–162

<sup>449</sup> Ibid, pages 162–164; Gordon's Witness Statement

<sup>450</sup> Day 77, page 164

**6.225** Gordon had found that relatively few travel insurance companies were willing to consider insuring someone with his medical history, which obviously included his medical history prior to his diagnosis with Hepatitis C. He found it problematic finding insurance but managed to obtain cover although at a much greater premium than his wife. On one occasion his travel insurance for one week's travel within the UK or Europe was £130 more than his wife's for the same trip.<sup>451</sup>

**6.226** The impacts of Gordon's early retirement have already been stated above. Also, Gordon's activities in retirement reduced from what he had expected due to his limited energy and general arthralgia. This became a further source of disappointment to him. Gordon's hobbies were fly fishing, post vintage and classic cars, photography and Hebridean history. Instead of managing a full day's fishing, he found himself restricted to one or two hours of fishing on rivers and loch banks. He could no longer walk to remote hill lochs to fish. He readily felt the cold and this restricted his outdoor activities. He found it difficult to crawl under his vintage car for basic maintenance, but was able to do some work provided that he rested afterwards. His use of the car was reduced in comparison to before.<sup>452</sup>

**6.227** Gordon wished to put on record that he greatly valued the conscientious attention he received from most of his doctors. He recognised that his survival at 10 years post-transplant was a tribute to a great deal of NHS expertise.<sup>453</sup>

## **Laura**

**6.228** Laura was 47 years old when she gave evidence. She is married with two children and lives in Edinburgh. Her children were born in 1987 and 1992. Laura acquired Hepatitis C from her husband. He has mild Haemophilia A with a Factor VIII level of 32%. Over the years he has been treated with plasma, cryoprecipitate and Factor VIII. As a child, Laura's husband was treated at the Royal Hospital for Sick Children, Edinburgh, and as an adult at the RIE.<sup>454</sup>

### *Laura's husband's diagnosis with Hepatitis C*

**6.229** In 1993 Laura's husband received a letter from the Haemophilia Centre at the RIE advising him that he might have been infected with a virus. Laura's husband had no idea what this letter might be about. He attended the hospital for tests and, at a follow-up appointment in August 1993, was told that he had acquired Hepatitis C. Tests revealed that he had antibodies to Hepatitis C in his blood, but the PCR test did not show the presence of the virus. Laura's husband was told that he had cleared the virus, but continued to attend the hospital for blood tests.<sup>455</sup>

**6.230** At the time he was diagnosed with Hepatitis C, Laura asked her husband if it was possible for the virus to have been passed on. Laura's husband was unsure about this and posed the question to Professor Ludlam, Consultant Haematologist, at the RIE. Professor Ludlam told Laura's husband that the virus 'probably' could not be passed on. His response was in keeping with the state of knowledge at the time about the risk of transmission of the virus. Laura was not offered testing for the virus by the Haemophilia Centre.<sup>456</sup>

---

<sup>451</sup> Ibid, page 165

<sup>452</sup> Ibid, page 165; Gordon's Witness Statement

<sup>453</sup> Day 77, page 166

<sup>454</sup> Day 79, pages 2-4

<sup>455</sup> Ibid, pages 5-6

<sup>456</sup> Ibid, pages 6-7

### *Laura's diagnosis with Hepatitis C*

**6.231** A few weeks after her husband's diagnosis with Hepatitis C, Laura attended an appointment for one of their children with the family GP. During this appointment, the GP asked Laura generally how the family was. Laura told her about her husband's diagnosis with Hepatitis C. Laura's impression was that the GP did not know much about the virus, but offered her a blood test to put her mind at ease so Laura gave a sample for testing.<sup>457</sup>

**6.232** Laura did not receive the result of this blood test until she attended a routine appointment with her GP about four to six weeks later. At this appointment, she mentioned that she had had the blood test and had not heard anything. The GP replied, 'Oh yes, it came back positive'.<sup>458</sup> Laura was shocked that she had not been informed of the result of this test. She asked the GP about Hepatitis C as she had never heard of it before her husband's diagnosis. Her GP told her that Hepatitis C was known as non-A, non-B Hepatitis but this did not mean much to Laura. She told Laura that the virus could be present in the body for some time before it came to light, but was unsure about treatments for the virus. Laura felt that her GP was not clear what the implications of the virus were. The GP suggested to Laura that she contact the Haemophilia Centre as they might be able to give her more information.<sup>459</sup>

**6.233** Laura took her GP's advice and telephoned the Haemophilia Centre at the RIE. She had known the staff there for some time but she cannot remember who she spoke to on this occasion. Laura informed the person she spoke to that she had tested positive for Hepatitis C. When Laura explained that she thought she had contracted the virus from her husband, that person seemed sceptical and told Laura that this was unlikely. Although the person with whom Laura spoke gave the impression that Laura's infection with Hepatitis C was nothing to do with the Haemophilia Centre, Laura was invited to attend the Centre for a further blood test to 'double-check'.<sup>460</sup> She felt that the Haemophilia Centre was doing her a favour.<sup>461</sup>

**6.234** Laura underwent both a Hepatitis C antibody and PCR test with both coming back as positive. On 17 August 1993 Laura and her husband attended an appointment with Professor Ludlam and Professor Hayes, Senior Lecturer at the Liver Clinic. They explained to her that the virus could cause damage to her liver and Laura agreed to undergo an endoscopy, laparoscopy and liver biopsy. She understood that the liver biopsy would show what effect the virus had had on her liver.<sup>462</sup>

### *Investigations of the source of Laura's infection with Hepatitis C*

**6.235** The Haemophilia Centre undertook further investigations to ascertain if Laura had acquired Hepatitis C from her husband. These investigations included ascertaining her virus genotype to see if it matched her husband's and contacting the Edinburgh and South East Scotland Blood Transfusion Service to ascertain whether she had received a transfusion when she sustained severe lacerations to her hand in 1983. The outcome of the latter investigation was negative. Laura had never heard of genotypes of Hepatitis C and is unaware which genotype of the virus she has. It is not specified in her medical records which the Inquiry recovered. In response to questions by the doctors, Laura told

---

<sup>457</sup> *Ibid*, pages 7–8

<sup>458</sup> *Ibid*, page 8

<sup>459</sup> *Ibid*, pages 8–9

<sup>460</sup> *Ibid*, page 10

<sup>461</sup> *Ibid*, pages 9–10

<sup>462</sup> Excerpts from the medical records recovered with respect of Laura

them that she had had no other sexual partners nor could she have acquired the virus by 'household spread', ie by sharing razors or toothbrushes. Following these enquiries, the source of her infection was not discussed again with Laura but it 'niggled at the back of [her] mind'.<sup>463</sup> In about 1997, Laura asked a Clinical Assistant to Professor Ludlam about how she might have contracted the virus. At that time, the doctor told Laura that they were now aware of a few other cases where the Hepatitis C virus had been transmitted sexually to a partner and so they now realised that 'it was more than likely ... that that was how [she] had contracted it'.<sup>464</sup> This doctor subsequently confirmed on Laura's application form to the Skipton Fund that she had contracted Hepatitis C from her husband.<sup>465</sup>

### *Testing of Laura's children for Hepatitis C*

**6.236** At the time of her diagnosis, Laura and her husband were very concerned that the virus might have been transmitted to their children. This was exacerbated by the uncertainty about how Laura had acquired the virus, and the fact that they knew from their discussions with the doctors that the virus could be transmitted by, for example, the sharing of toothbrushes. Although they did not share toothbrushes, as she said, 'young children sometimes help themselves to things'.<sup>466</sup> Furthermore, their youngest child was only one year old at the time Laura was diagnosed and Laura was worried that she had the virus while she was pregnant. She felt that no-one seemed to know, at that stage, whether in these circumstances there was a risk to her youngest child.<sup>467</sup>

**6.237** At the appointment on 17 August 1993 Laura and her husband asked for their children to be tested for Hepatitis C and the Haemophilia Centre arranged for this to be done. Obtaining a blood sample from Laura's youngest child proved difficult so she was transferred to the special baby unit, at the Simpson Memorial Maternity Hospital, Edinburgh, for this to be carried out. Both children were very upset when their blood samples were taken and Laura and her mother, who took them to these appointments, found the whole experience distressing. Both children were negative for the virus.<sup>468</sup>

### *Laura's symptoms of Hepatitis C*

**6.238** Looking back, Laura thinks she may have been experiencing some symptoms of Hepatitis C in 1992 and 1993. She feels that, following the birth of her second child in 1992, she did not recover or regain the energy levels the way she would have expected to.<sup>469</sup> She felt 'quite run down' during the summer of 1993.<sup>470</sup> She put it down to having a young child at the time.

**6.239** In January 1994 Laura was admitted to the RIE where she underwent an upper GI endoscopy and a laparoscopic liver biopsy. Laura remembers that the endoscopy was 'particularly horrible'. The liver biopsy was 'uncomfortable' and she had mild sedation for this. She remembers being in the theatre for these procedures and she found the whole experience 'quite traumatic'. She was worried about the outcome of both.<sup>471</sup>

---

<sup>463</sup> Day 79, page 17

<sup>464</sup> Ibid, page 17

<sup>465</sup> Ibid, pages 12–18

<sup>466</sup> Ibid, page 18

<sup>467</sup> Ibid, page 18

<sup>468</sup> Ibid, pages 18–19

<sup>469</sup> Ibid, page 19

<sup>470</sup> Ibid, page 20

<sup>471</sup> Ibid, pages 19–20

**6.240** The endoscopy revealed no evidence of varices. The laparoscopy revealed that the liver was slightly increased in bulk, with yellow areas, suggesting fatty infiltration. The liver biopsy reported 'focal fatty change and a periportal chronic inflammatory infiltrate ... with piecemeal necrosis'.<sup>472</sup> Laura was told these findings at a combined liver clinic with Professor Hayes and Professor Ludlam on 10 February 1994. She remembers that she was told that these findings meant that it was likely that she had been infected with the virus 'for some time'. This upset her. She had previously been told that 'the sort of life expectancy, if you like, from contracting the virus to ... a critical stage was 10 to 15 years'.<sup>473</sup> As these findings suggested that she had had the virus for a while, she felt that her life expectancy was much less than 10 to 15 years. This caused her a lot of distress because she had a young family. She does not remember discussing this with the doctors at that time although she believes that it was apparent to them that she was upset.<sup>474</sup>

### *Laura's treatment with Interferon*

**6.241** The doctors told Laura that Interferon was the only course of treatment available but, given the extent of their understanding about the effectiveness of this treatment at that time, they were unable to give her any guarantees about it. Laura asked what the worst case scenario was if the Interferon did not work. She was told that, in certain cases, if the virus continued to develop that a liver transplant might be necessary.<sup>475</sup> It was agreed that Laura would start treatment with Interferon at a dose of 3 million units three times a week. She was warned to expect flu-like symptoms following the first six to eight injections. She was told that it was usually better to inject the treatment in the evening and to take a couple of paracetamol tablets at the same time in the hope that the symptoms would have subsided by the morning. Laura was warned that a mild degree of depression occurs in some patients but that hair loss is not a problem with such a low dose of Interferon.<sup>476</sup>

**6.242** Laura commenced treatment with Interferon in February 1994. Prior to this she attended the Haemophilia Centre for pre-treatment blood tests and to be shown how to give herself injections of Interferon. As she stated 'the thought of injecting yourself, I don't think appeals to anyone' and she found the treatment 'quite scary'.<sup>477</sup> This was exacerbated by the fact that in order to administer the treatment, she had to break open a glass vial of sterile water. Since sustaining a severe laceration when she put her hand through glass when she was younger, Laura has had 'a bit of a thing about glass'.<sup>478</sup> As a result she was not confident in handling glass. When she was being taught to administer the treatment to herself, she was very nervous opening the vial and cut her finger quite severely. She then had to be 'rushed over' to another part of the hospital for treatment of the finger.<sup>479</sup> Laura found the staff very helpful, and she made the decision that she had to learn to take the treatment and she did so.<sup>480</sup>

---

<sup>472</sup> Excerpts from the medical records recovered in respect of Laura

<sup>473</sup> Day 79, page 21

<sup>474</sup> Ibid, pages 21–22

<sup>475</sup> Ibid, pages 22–23

<sup>476</sup> Excerpts from the medical records recovered in respect of Laura

<sup>477</sup> Day 79, pages 24–25

<sup>478</sup> Ibid, page 24

<sup>479</sup> Ibid

<sup>480</sup> Ibid, pages 24–25

**6.243** While being treated with Interferon, Laura felt extremely tired. She physically ached, had no appetite and lost weight. She suffered from headaches for which she was prescribed co-codamol. She also suffered from thinning of her hair. She felt generally miserable and depressed, describing herself as feeling 'completely flat'.<sup>481</sup> She 'found everything quite an effort' and she remembers her daughter's birthday party as an example of this.<sup>482</sup> On one occasion her menstrual period was late and the hospital gave Laura a pregnancy test which was negative. As the safety of Interferon for pregnant women was not established, it was recommended that patients use contraceptives while taking it.<sup>483</sup>

**6.244** The treatment had a significant impact on Laura's life. During this time, she was trying to look after her two children, who were then aged about five years and one year, as well as running her own business.<sup>484</sup> She had started this business in the year before her second child was born. She did not want to work full-time, and the business allowed her to work while her husband was at home so that they did not need to find childcare for their daughter. Laura had studied for 18 months and taken the necessary exams to qualify for the work. 'I was so excited about qualifying, just because it was something I had achieved that I had always wanted to do and I enjoyed it'.<sup>485</sup> Laura had built up a good client base for the business by the time she started treatment. The effects of the treatment meant that she found the work 'very difficult'. On one occasion, while with a client, she found herself nodding off, which put both of them at risk. She was very scared and found it frightening 'to be supposedly in control and knowing that you are not in control at all'.<sup>486</sup> Laura's ability to concentrate was also affected by the treatment, and she found it very difficult to maintain her concentration during her work.<sup>487</sup>

**6.245** Laura was certified by her GP as unfit for work from 30 May 1994.<sup>488</sup> Despite this Laura continued to work. She was concerned about financial commitments in respect of her business and the family finances. Laura's husband was working full-time. He realised that she needed more help and found it increasingly difficult to cope. There were times, at weekends, when Laura asked her husband to take the children out swimming or on another activity so that she could have a rest. Laura's parents both worked full-time but they and Laura's sisters tried to help when they could, especially with the children.<sup>489</sup> Looking back at this period now, Laura thinks that she 'wasn't a fun mum at the time. I wasn't very good at maybe spending time with them because I just didn't feel I had the energy ... I did what I had to do ...'.<sup>490</sup>

**6.246** As was standard practice, Laura's Hepatitis C PCR level and liver function were monitored during the treatment. There was usually a delay in receiving the results of these tests and Laura found this a nerve-racking time.<sup>491</sup> Initially, Laura had a good response to treatment – her ALT level halved after two weeks of treatment and then further reduced after four weeks of treatment. However, there was no change to Laura's viral load. Laura recalled that initially it seemed that she had a good response to treatment and she was quite optimistic. However, after eight weeks of treatment Laura's ALT levels rose. There

---

<sup>481</sup> Ibid, page 25

<sup>482</sup> Ibid

<sup>483</sup> Excerpts from the medical records recovered in respect of Laura

<sup>484</sup> Laura wished the nature of this business to be kept confidential in order to preserve her anonymity.

<sup>485</sup> Day 79, page 26

<sup>486</sup> Ibid, page 26

<sup>487</sup> Ibid, pages 25–27; page 66

<sup>488</sup> Ibid, page 28

<sup>489</sup> Ibid, pages 27–28

<sup>490</sup> Ibid, page 32

<sup>491</sup> Ibid, page 53

was no reduction in quantitative Hepatitis C PCR and after 12 weeks she developed a binding and a neutralising antibody to Interferon.<sup>492</sup> Due to her failure to respond to the treatment, Laura's treatment was stopped after 27 weeks, on 30 August 1994.<sup>493</sup>

**6.247** Laura was devastated that the Interferon treatment had failed and she found this news very difficult to cope with. She felt that, although she was young and had a young family, she was living 'on borrowed time to a certain extent'.<sup>494</sup> No one was able to tell her when another treatment might become available and so she felt that nobody was able to offer her 'a solution or a treatment to give me some sort of hope'.<sup>495</sup> After the treatment stopped, Laura continued to feel 'very low'. She felt unable to shake off a feeling of dread that she felt all the time.<sup>496</sup> She considers that she is quite an optimistic person but 'that was quite a dark time'.<sup>497</sup> She was prescribed anti-depressant medication, Amitriptyline and then Prozac, by her GP to help her sleep. Laura found that that the anti-depressant medication helped a little. A record of Laura's attendance at a clinic appointment in November 1994, three months after she finished Interferon, noted that Laura was tired and seemed down. It noted she had had a lot to cope with over the past year and was working very hard.<sup>498</sup>

#### *The period after treatment and the effect of Laura's symptoms on her business*

**6.248** After finishing the Interferon treatment Laura attended the Haemophilia Centre for regular monitoring. She continued to have both good and bad spells, both physically and emotionally. She was told that she needed to build up her immune system. At these appointments, Laura was advised to give up work to give her body a chance to fight the virus, especially if new treatments became available. Although it was not specifically stated to her, she felt that there was an implication that she had not given the Interferon treatment a chance due to working so hard and being so busy. Laura's parents were also very concerned about her and they, too, tried to encourage her 'to ease up on work' and offered to try to help out financially.<sup>499</sup>

**6.249** Laura continued to work part-time due to financial commitments. However, her condition worsened as time went on and, in 1996, she gave up her business completely. This was a very stressful time for her and her husband. By this time, Laura's business was unable to make the necessary repayments to the finance company which had financed one of her business assets. Laura and her husband were struggling to pay domestic bills and their outgoings exceeded their income. Laura had always been in charge of the family finances and took pride in ensuring bills were paid on time and everything was in order. Other than having a mortgage, she and her husband had never been in debt before, and they found it very distressing to be in debt. Over a number of months Laura negotiated with the finance company with regard to the return of the business asset. She found that this company was not very understanding of her position. It seemed, to her that the company did not want to know what she was going through and the reason she found herself unable to make the payments. When the asset was subsequently repossessed Laura found it 'just terrible'. She felt that she had let everyone down.<sup>500</sup>

<sup>492</sup> Sometimes patients develop a neutralising antibody to Interferon which counteracts its possible beneficial effects.

<sup>493</sup> Day 79, pages 29–30; Excerpts from the medical records recovered in respect of Laura

<sup>494</sup> Ibid, page 30

<sup>495</sup> Ibid

<sup>496</sup> Ibid, page 31

<sup>497</sup> Ibid, page 32

<sup>498</sup> Ibid, page 32; Excerpts from the medical records recovered in respect of Laura

<sup>499</sup> Day 79, pages 33–34

<sup>500</sup> Ibid, pages 34–36

### *Laura's treatment with Wellferon*

**6.250** In February 1996, at a clinic appointment with Professor Ludlam, two options were discussed with Laura. The first of these was that her Hepatitis C status be monitored every few months and further treatment considered when new drug regimes became available. The second option was for Laura to start on a course of Wellferon, a mixture of alpha interferons. It was noted that there was some evidence that Wellferon was useful in individuals like Laura who developed anti-interferon antibodies. Laura was warned that the side-effects were likely to be similar to her previous treatment.<sup>501</sup> Laura was keen to start treatment as soon as possible so she did not care about the side-effects. 'I would have put up with anything just to be able to start some sort of treatment'.<sup>502</sup>

**6.251** There was a slight delay in starting the treatment to allow Laura time to stop taking Prozac. She was never happy taking Prozac and worried that the longer she took it, the harder it would be to stop taking it. Also, she was concerned that it would interfere with the Wellferon treatment. However, her attempts to stop taking it, at this time, were unsuccessful. 'I wasn't a very nice person when I wasn't on them because I was so down'.<sup>503</sup> So she continued to take this medication.<sup>504</sup>

**6.252** In March 1996 Laura commenced treatment with Wellferon. Once again, she had to inject herself with the medication three times a week. She injected herself in her stomach area, and in her legs, but over time found that she ran out of areas to use. She found the injections increasingly uncomfortable, particularly putting the needle through the skin. She asked the hospital for EMLA cream and found that this helped.<sup>505</sup>

**6.253** Laura felt 'dreadful' during this treatment. She 'functioned on auto-pilot and at times could not get out of bed'.<sup>506</sup> She was constantly tired and irritable. She suffered aches and pains in her neck and shoulders. Eight weeks after she had started treatment, in May 1996, Laura's blood test results were very encouraging. Her ALT had returned to normal and the Hepatitis C virus was undetectable by quantitative PCR test. Laura was aware that the test results were looking positive and that the doctors were pleased with these results. However, by July 1996, her blood test results revealed that she had relapsed. Professor Ludlam and Professor Hayes believed that Laura might benefit from combination therapy of Interferon and Ribavirin. At that time ethical approval was still awaited for the use of Ribavirin in such circumstances. Laura was understandably keen to try this combination therapy.<sup>507</sup>

### *Laura's treatment with Ribavirin and Interferon*

**6.254** In August 1996 Laura commenced treatment with Ribavirin and Interferon as part of a clinical trial. At the same time, Laura stopped taking Prozac for a while as she feared an interaction between it and this new treatment. By this time, Laura had obtained part-time clerical work. Due to their financial situation, Laura felt that she had to earn an income but wanted to find work which was not too big a commitment. This position was a temporary job and was mornings only. Her family helped out with child care.<sup>508</sup> When

---

<sup>501</sup> Excerpts from the medical records recovered in respect of Laura

<sup>502</sup> Day 79, pages 37–38

<sup>503</sup> Ibid, page 41

<sup>504</sup> Ibid, pages 39 and 41

<sup>505</sup> Ibid, pages 40–41. EMLA is an anaesthetic cream.

<sup>506</sup> Day 79, page 40

<sup>507</sup> Ibid, pages 41–42

<sup>508</sup> Ibid, pages 40–42 and 44–45



she started this treatment, Laura was aware that the side-effects of it were likely to be similar to those she had experienced from her earlier treatment.

**6.255** Those treating Laura were obviously aware of Laura's mental state and were concerned about this. In a letter to Laura's GP, Professor Ludlam stated that if Laura were to become more depressed on this treatment then 'we must seriously review her Interferon therapy. The difficulty is that she is keen to proceed with treatment and her worry is related to the state of her liver'.<sup>509</sup>

**6.256** In September 1996, Professor Ludlam's Clinical Assistant referred Laura to a consultant psychologist, for psychological help through relaxation and stress management. Laura described her two main problems to the psychologist as being unable to relax, and becoming emotional when she spoke about Hepatitis C.<sup>510</sup>

**6.257** A further matter Laura discussed with the psychologist was the effect of her diagnosis with Hepatitis C on her relationship with her husband. Laura's husband was involved in a serious road traffic accident in about 1988. As a result of this his memory was impaired and, initially, he only trusted Laura. Gradually he recovered, but Laura felt that one of the lasting effects of the accident was that her husband became less responsible. After her diagnosis with Hepatitis C, Laura felt angry that her husband had not asked more about Hepatitis C when he was diagnosed with it. She thought that he should have asked more about what his diagnosis meant and how it could affect her. Also, she considered that he should have asked more questions about his treatment for haemophilia and the implications of it. As a result of this, for a while, Laura blamed her husband for the fact that she had acquired Hepatitis C and thought that perhaps it could have been avoided, had he been better informed about his haemophilia treatment.<sup>511</sup>

**6.258** Laura felt that her husband did not cope well when she was first diagnosed with Hepatitis C:

He kind of stuck his head in the sand and he didn't really want to know. He couldn't cope with it, and I felt I was having to cope on my own and cope with the children and cope with the financial worries as well. And for all those reasons I was quite angry with him at the time. I felt quite let down.<sup>512</sup>

**6.259** Also, Laura felt that she did not get the support she needed from him. For example, she usually cooked all the family meals and her husband does not cook. On the occasions when she did not feel well enough to cook for the family, he did not know what to do, and in the end she had to cook. Laura felt that this, taken together with having had to cope with the after-effects of her husband's road traffic accident, had a major effect on their relationship.<sup>513</sup> In his written statement to the Inquiry, Laura's husband described the strain of Laura's diagnosis with Hepatitis C as having had 'a devastating effect on our relationship'.<sup>514</sup> He stated that 'the guilt I felt for being the one to infect her was almost impossible for both of us to come to terms with'.<sup>515</sup> This guilt must have been compounded by the fact that Laura's husband cleared the virus spontaneously and never suffered any symptoms of it.<sup>516</sup>

---

<sup>509</sup> Ibid, pages 42–43; Excerpts from the medical records recovered in respect of Laura

<sup>510</sup> Day 79, pages 43–44; Excerpts from the medical records recovered in respect of Laura

<sup>511</sup> Day 79, pages 46–47

<sup>512</sup> Ibid, page 48

<sup>513</sup> Ibid, pages 48–49

<sup>514</sup> Laura's husband's Witness Statement

<sup>515</sup> Ibid

<sup>516</sup> Ibid

**6.260** Another factor contributing to the strain Laura was under was the fact that she did not talk about her condition or treatment to anyone. Other than her parents and sisters, Laura did not tell anyone that she had Hepatitis C or about the treatment she was receiving. Laura felt that if there was anything in the media about Hepatitis C, people often confused it with HIV. People seemed not to know about Hepatitis C and she did not want to start explaining it to people. A further concern to her was that people had the wrong idea about how the virus could be passed on, and she was concerned that this lack of understanding might result in her losing her job.<sup>517</sup>

**6.261** Laura met with the psychologist on a few occasions when she attended clinic appointments. Laura felt that she was not good at accepting counselling as she found it hard to talk to people but benefited from the relaxation tape which the psychologist gave her.<sup>518</sup>

**6.262** The side-effects Laura experienced of Interferon and Ribavirin were 'flu-like symptoms'. She became susceptible to colds. Once again she lost weight.<sup>519</sup> Laura's Hepatitis C RNA became undetectable after starting treatment with Interferon and Ribavirin. By December 1996 her liver function tests were normal. Having relapsed previously after three or four months of treatment, Laura was concerned that this might happen again. However, her blood test results remained normal and when the Interferon and Ribavirin treatment finished, in July 1997, her Hepatitis C PCR remained negative. At this time Laura was told that she was now clear of the Hepatitis C virus. She was told that she would continue to be monitored so that if the virus returned, it could be dealt with. Initially Laura was monitored by the Haemophilia Centre every month, then every three months, then every six months until latterly she was monitored annually.<sup>520</sup>

**6.263** The side-effects of the treatment persisted for a while after Laura had finished it. For a long time after the treatment, Laura felt tired. During the treatment she had restarted Prozac and she continued to be prescribed Prozac. The family's financial situation continued to worry her.<sup>521</sup>

**6.264** At a review appointment in April 2000, Laura was told that her blood test results remained encouraging, 'but that we still do not have enough knowledge about the natural history of hepatitis C to say with complete confidence how the disease may progress in the future'.<sup>522</sup> This uncertainty about the future was always 'in the back of [Laura's] mind'.<sup>523</sup> Despite this, Laura tried to bring some sort of normality back to family life. In particular, feeling more energetic than she had done previously, she made an effort to do more activities with their children.<sup>524</sup>

### *The period since Laura's treatment with Interferon and Ribavirin*

**6.265** In 2000, Laura was diagnosed with breast cancer. She was treated for this at the Western General Hospital, Edinburgh. Laura was told that the cause of the cancer was unclear. She had no family history of this type of cancer. She was told that hormones and stress could have contributed to this diagnosis. Laura had concerns that the treatment for

---

<sup>517</sup> Day 79, page 51

<sup>518</sup> Ibid, page 52

<sup>519</sup> Ibid, page 43

<sup>520</sup> Ibid, pages 53–54

<sup>521</sup> Ibid, page 55

<sup>522</sup> Ibid, page 57; Excerpts from the medical records recovered in respect of Laura

<sup>523</sup> Day 79, page 57

<sup>524</sup> Ibid, page 57

Hepatitis C, and the stress she suffered, contributed to her diagnosis with breast cancer. She mentioned this at one of her appointments at the hospital and nobody said that this could not have contributed to it. This concerned her.<sup>525</sup>

**6.266** Laura was treated with a mastectomy, reconstructive surgery, chemotherapy and five years of hormone drug treatment. Those treating Laura were aware of her previous diagnosis with Hepatitis C and the virus was taken account of when treatments for the breast cancer were being considered. Laura's Oncology Consultant discussed matters with Professor Ludlam's Clinical Assistant and with Professor Hayes. She was told that despite Laura being Hepatitis C PCR negative, Laura should still be considered 'at risk during surgical procedure'.<sup>526</sup> Professor Hayes was also asked whether chemotherapy would reactivate her Hepatitis C. His response to this was that as Laura was PCR-negative:

[W]e would hope that she is cured of hepatitis C and therefore if the virus has gone she would not reactivate even if this is immunosuppressed. However, of course a certain number of people do relapse after treatment and it is possible, although we cannot detect it that she might still be harbouring hepatitis C somewhere.<sup>527</sup>

He suggested that Laura undergo a PCR test every two to three months. Laura was unaware that these matters were being discussed by her doctors. Although there was a note in Laura's medical records of her concern about the impact of the chemotherapy treatment on the Hepatitis C virus, Laura does not remember being overly anxious about this.<sup>528</sup>

**6.267** Laura completed her chemotherapy treatment in about April 2001. It had no effect on her liver function. At a review appointment at the Haemophilia Clinic on 30 April, Laura was noted to be keen to have a quantitative Hepatitis C PCR test. Laura was advised by letter dated 18 June that year that this test, and her ALT, was normal. Laura's treatment for breast cancer was successful.<sup>529</sup>

**6.268** Laura continued to attend the Haemophilia Clinic for review annually. After the doctors there had taken the advice of Professor Hayes, Laura was discharged from this clinic in November 2006.<sup>530</sup>

**6.269** More recently Laura has developed inflammatory bowel disease. Once again, while being treated in hospital, 'there was a lot of talk in hospital about the fact I have had Hepatitis C'.<sup>531</sup> She has been treated for her bowel disease with steroids. She was unable to take another medication for this as there was concern about the effect it might have on Laura's immune system, due to her previous diagnosis with Hepatitis C.<sup>532</sup>

---

<sup>525</sup> Ibid, pages 57–58; page 61

<sup>526</sup> Excerpts from the medical records recovered in respect of Laura

<sup>527</sup> Ibid

<sup>528</sup> Day 79, pages 58–62; Excerpts from the medical records recovered in respect of Laura

<sup>529</sup> Day 79, pages 63–64

<sup>530</sup> Ibid, page 64

<sup>531</sup> Ibid

<sup>532</sup> Ibid, pages 64–65

### *Specific impacts of Laura's infection with Hepatitis C*

**6.270** Laura believes that one consequence of her infection with Hepatitis C is that her children are more protective of her. At the time she took her treatment for the virus, she was very careful to hide it from the children. She hid the needles she used to inject herself. They were unaware that she was taking treatment. However, she considers that her son was old enough to sense that his mother was unwell and that 'things weren't quite right'.<sup>533</sup> He is now very protective of her. As a toddler, her daughter was loath to let her mother out of her sight and she is much more insecure than Laura expected her to be.<sup>534</sup>

**6.271** Laura considers that her infection with Hepatitis C had the greatest effect on her relationship with her husband. Although Laura and her husband tried to keep the strain in their relationship from the children, Laura believes that the children sensed it anyway and 'were inevitably going to be affected by it'.<sup>535</sup>

**6.272** As detailed in paragraphs 6.257 to 6.259 above, Laura's diagnosis with Hepatitis C, and the consequences of it, had a significant and detrimental impact on her relationship with her husband for a number of years. In about 2008, Laura and her husband attended a series of couple counselling sessions: 'our problems reached a point where it was either a case of we gave up on our relationship or we went for counselling'.<sup>536</sup> She stated that neither of them was inclined to give up too easily which she believes is a reason why they remained together. Another reason was that, for a time, they could not afford to separate due to the debts they had incurred. Initially Laura's husband found it difficult to accept the idea of counselling. During the counselling sessions Laura and her husband talked a lot about how they both felt 'during ... the Hepatitis C period'.<sup>537</sup> Laura stated:

[I] learned a lot about how he felt and I think that helped me to sort of accept that it wasn't all his fault. And I knew deep down it wasn't but I think his way of handling the situation also contributed to the problems and we both ... faced up to things and our relationship is much, much better now and back on track. It has just taken a long time. That has been a lot of years before we reached that point.<sup>538</sup>

**6.273** Laura feels that it would certainly have helped her husband to have been offered counselling sooner, perhaps when she received counselling from a psychologist, but this was not offered to him.<sup>539</sup>

**6.274** Some of the financial impacts of Laura's infection with Hepatitis C have already been stated in paragraph 6.249 above. As a result of the debts the family incurred when Laura had to wind up her business, the family acquired a bad credit rating. They had planned to move from their two-bedroom flat to a house to give their children more space, but this was delayed by about five years. Due to their bad credit history, they found it difficult to obtain a mortgage. A local broker assisted them with this but the mortgage they obtained had a slightly higher interest rate than the average. Laura was unable to obtain new life assurance to cover the mortgage. She had a policy which she had acquired prior to her diagnosis with

---

<sup>533</sup> Ibid, page 66

<sup>534</sup> Ibid

<sup>535</sup> Ibid, page 67

<sup>536</sup> Ibid

<sup>537</sup> Ibid, page 67

<sup>538</sup> Ibid, page 68

<sup>539</sup> Ibid, page 69

Hepatitis C. Furthermore, she was unable to afford the premiums quoted to her for income protection insurance, due to her infection with Hepatitis C, and so her husband obtained this and she did not. In addition, Laura has incurred inflated travel insurance premiums due to her infection with Hepatitis C. She has also incurred travel expenses attending regular appointments at the hospital and prescription charges. Laura and her husband remain in debt: 'We have never really managed to get back on track ...'.<sup>540</sup>

**6.275** As a result of the stigma attached to the Hepatitis C virus, Laura still has not told many people that she had it. Her current employers do not know that she had the virus. She found it difficult to take time off work to attend hospital appointments during her treatment with Interferon and Ribavirin but her employers were understanding and did not ask about the reason for the appointments.<sup>541</sup>

**6.276** On one occasion, Laura had to attend hospital for a tooth extraction. Although she was one of the first patients to arrive for the procedure that day, she was kept waiting until the end of the day. When she enquired why she was having to wait so long she was told by a nurse that it was due to her having Hepatitis C. The operating list was rearranged so that Laura was last as she was deemed a risk in the theatre. She understood that the theatre required to be disinfected after her procedure. She was shocked and upset by this. In addition, Laura was given a paper gown although everyone else that day wore a cloth one. This made her feel as if she had a 'horrible disease' and that nobody wanted to come near her.<sup>542</sup>

**6.277** In describing the effects of her infection with Hepatitis C on her and her family, Laura said, 'This whole period in my life was a nightmare for me and my whole family. It has taken many years to recover from most of the effects, and some effects we will never recover from'.<sup>543</sup>

## Anne

**6.278** At the time of giving evidence, Anne was 57 years old. She lives in Ayrshire and works as an administrator.<sup>544</sup>

### *Anne's blood transfusion*

**6.279** Anne contracted Hepatitis C, Genotype 2b, from a blood transfusion she received in a local hospital in January 1986. At that time Anne was 31 years old. She was admitted to hospital for a myomectomy (surgical removal of fibroids) and as a result of this procedure, Anne required a blood transfusion. Anne is uncertain how many units of blood she received, but she thinks that it was more than three units. This is the only blood transfusion which Anne has ever received. Anne was a blood donor prior to receiving this blood transfusion but, due to low haemoglobin levels, did not donate afterwards.<sup>545</sup>

### *Anne's diagnosis with Hepatitis C*

**6.280** In 1995 Anne's sister, who provided a statement to the Inquiry, had a routine appointment with her GP. This GP was also Anne's GP. He asked Anne's sister to ask Anne to make an appointment to see him but did not explain why. Anne's GP had been advised by

---

<sup>540</sup> Ibid, pages 69–72

<sup>541</sup> Ibid, pages 72–73; Laura's Witness Statement

<sup>542</sup> Ibid, pages 73–74

<sup>543</sup> Ibid, page 74; Laura's Witness Statement

<sup>544</sup> Day 79, page 77

<sup>545</sup> Ibid, pages 77–78

the Scottish National Blood Transfusion Service (SNBTS), by letter dated 16 October 1995, that Anne had been transfused with 'a presumed hepatitis C positive blood component' in January 1986.

**6.281** Anne's sister conveyed this request to Anne. Anne considers that this was 'a very strange way' for her GP to initiate 'such important contact with [her]'.<sup>546</sup> Anne made an appointment to see him on 24 November. At the time of this appointment, Anne was 41 years old. She did not feel unwell. Anne's memory of exactly what happened at the appointments with her GP around this time is understandably hazy in view of both the time which has elapsed since, and the impact of the news she received. Having considered her medical records as well as Anne's evidence, it appears that at the appointment on 24 November, Anne's GP told her that it was likely that she had acquired Hepatitis C and a blood sample was taken to confirm this.<sup>547</sup> At the following appointment her GP confirmed her Hepatitis C diagnosis. Anne's GP gave her the impression that Hepatitis C was nothing to worry about. He said to her 'not to worry about it because it didn't really mean anything'.<sup>548</sup> Anne had never heard of Hepatitis C.<sup>549</sup> She did not receive any advice from him about the implications of a positive result. She did not receive any counselling or advice about her future health. Her liver was not discussed. All he told her was 'Don't drink, and tell your dentist'.<sup>550</sup> Anne believes that her GP did not realise the seriousness of the virus.<sup>551</sup>

**6.282** Despite her GP's assessment of her diagnosis, Anne realised it was something to be concerned about and she was worried about it: '[I]f you have a virus, it's obviously something'.<sup>552</sup> She made contact with the local hospital to try to obtain an explanation as to how she had become infected and what her prognosis was. Sometime in 1996 she met with a representative of the SNBTS and a hospital representative at the local hospital. She did not find the meeting helpful. She found the attitude of the hospital representative upsetting, although the doctor from the SNBTS was helpful.<sup>553</sup>

### *Anne's treatment for Hepatitis C*

**6.283** Anne's GP referred Anne to Dr Mills' Hepatitis Clinic at the Gartnavel General Hospital in Glasgow. On 12 March 1996 Anne attended her first appointment there. She was seen by a Senior Registrar. On examination Anne was found to look well and there were no signs of chronic liver disease. The doctor had a long talk with Anne about the implications of Hepatitis C infection. This included the prognosis for someone with Hepatitis C, the risks of liver disease, sexual transmission and treatment options; namely Interferon. Anne was 'gobsmacked' as this was the first time she understood the full implications of the virus. She was told that 'anything that was likely to happen would probably be about 20 years down the line'.<sup>554</sup> This worried her as she realised that she had already had the virus for about nine or ten years. The doctor suggested that Anne have a liver biopsy.<sup>555</sup>

---

<sup>546</sup> Anne's Witness Statement

<sup>547</sup> Excerpts from the medical records recovered in respect of Anne

<sup>548</sup> Day 79, page 82

<sup>549</sup> Ibid, page 87

<sup>550</sup> Ibid, page 83; Anne's Witness Statement

<sup>551</sup> Day 79, page 84

<sup>552</sup> Ibid, page 90

<sup>553</sup> Ibid, pages 91–92

<sup>554</sup> Ibid, page 93

<sup>555</sup> Ibid, pages 93–94; Excerpts from the medical records recovered in respect of Anne

**6.284** Anne felt shocked after this appointment. She returned home and relayed the information she had been given to her mother and sister. They did not know anything about the virus either, and they all started to try to find out more about it.<sup>556</sup>

**6.285** On 26 June 1996 Anne underwent an ultrasound-guided liver biopsy. She found this a very invasive and painful procedure: 'I am not a coward but I found this very hard'.<sup>557</sup> The biopsy revealed 'a mild hepatitis consistent with Hepatitis C'.<sup>558</sup> It was suggested to Anne that she start treatment with Interferon. Anne knew that she had to take treatment for the virus. At the time she was experiencing flu-like symptoms.<sup>559</sup>

**6.286** Since her diagnosis with Hepatitis C she has had five liver biopsies. Anne subsequently became aware of the risks associated with liver biopsies and believed that this 'amplifies the actual and real risks' which she has been subjected to as a result of the virus.<sup>560</sup>

### *Anne's treatment with Interferon*

**6.287** Anne started Interferon treatment on 29 January 1997. Prior to starting this treatment Anne was taught how to inject herself. She was warned about the side-effects of the treatment. She was warned that she might experience flu-like symptoms, hair loss, tiredness, depression, dry mouth and bone marrow suppression.<sup>561</sup> Anne had to inject herself three times a week.<sup>562</sup> It was noted in Anne's medical records two weeks after she started treatment that on the first day of treatment she experienced 'slight flu symptoms with a headache persisting all next day. Cold during the night.'<sup>563</sup> It was noted after Anne had completed four weeks of treatment that she was suffering from 'slight flu symptoms, easily coped with. Cramp in legs during night'.<sup>564</sup> After eight weeks of treatment the leg cramps had settled, but the headaches and slight flu symptoms persisted. These symptoms were worse the day after Anne injected herself and settled with paracetamol. Twelve weeks after starting treatment Anne continued to suffer from headaches, and was tired especially after injections. She also suffered from hair loss. At this time Anne was noted to be Hepatitis C PCR-negative with a reduction in serum transaminases to normal. At this time Anne was told that she had cleared the virus although she was also told that the virus could 'hide and come back again'.<sup>565</sup> Unfortunately, after 24 weeks of treatment, Anne was once again PCR-positive with an elevated AST. At this time Anne was also found to have hypothyroidism, a known side effect of Interferon treatment. Anne started treatment with thyroxine, which she continues to take now.<sup>566</sup> Anne's dose of Interferon was increased at this time. After a further 12 weeks of treatment at this level, Anne's dose of Interferon was reduced for the final 12 weeks of treatment. She stopped taking treatment 48 weeks after starting it.<sup>567</sup>

---

<sup>556</sup> Day 79, page 94

<sup>557</sup> Ibid, page 95; Anne's Witness Statement

<sup>558</sup> Day 79, page 95; Excerpts from the medical records recovered in respect of Anne

<sup>559</sup> Day 79, page 95

<sup>560</sup> Anne's Witness Statement; the risks associated with a liver biopsy include a risk of haemorrhage and death. The risks are stated in more detail in Chapter 13, *Knowledge of Viral Hepatitis Now*, paragraph 13.91.

<sup>561</sup> Day 79, page 97; Excerpts from the medical records recovered in respect of Anne

<sup>562</sup> Anne's Witness Statement

<sup>563</sup> Day 79, page 97; Excerpts from the medical records recovered in respect of Anne

<sup>564</sup> Ibid

<sup>565</sup> Ibid, page 99

<sup>566</sup> Ibid, page 100

<sup>567</sup> Ibid, pages 100–101

**6.288** Anne gained about half a stone in weight during the Interferon treatment.<sup>568</sup> She managed to keep working throughout the course of treatment. She had to attend the hospital for appointments and initially these were once a week to collect the Interferon to bring home and keep in her fridge. She used flexi-time to allow her to do this. This added to the pressure of the treatment on her.<sup>569</sup>

**6.289** On 17 December 1997 Anne underwent a further liver biopsy. The features of this biopsy were similar to the previous one.<sup>570</sup> Anne was told that the Interferon treatment had not been successful and that there was no real change in the state of her liver. She was told that she would attend the hospital annually and that 'probably there would be treatment in the future, but obviously that would be a few years down the line'.<sup>571</sup> Anne was glad that the treatment was over. The side-effects of it persisted for a further few months.

**6.290** At a review at Dr Mills' clinic in December 1999, it was noted that Anne remained well, apart from 'some slight discomfort in the muscles of her upper legs'.<sup>572</sup> Dr Mills discussed possible improvement in treatment for Hepatitis C but noted in a letter to Anne's GP that 'It seems likely that it will be at least three years away until the next generation of treatment becomes available for her'.<sup>573</sup>

**6.291** Anne continued to attend Dr Mills' clinic annually for review. In July 2002 Anne was noted to be in 'reasonably good health' although she was complaining of having more flu-like symptoms than previously, having headaches in the morning and feeling tired each day at about three o'clock. The possibility of Anne being treated again with combination Pegylated Interferon and Ribavirin was discussed, but Anne decided to postpone this treatment. She reached this decision as, having found the treatment so invasive the first time, she wished to carry on for a further year without it and to keep working.<sup>574</sup>

**6.292** At the review the following year, Anne was noted to be remaining well, although she was occasionally tired and went to bed an hour and a half earlier than usual. Once again, she decided to postpone treatment for the same reasons as before. She knew that at some point she would have to undergo further treatment but she still wanted to put it off.<sup>575</sup>

**6.293** In October 2004 Anne underwent a further liver biopsy to aid the decision as to whether she required to make a further attempt at treatment. Once again, this showed similar appearances to the previous biopsies and no evidence of progression. Her liver function tests remained normal and she had no particular symptoms of the virus.<sup>576</sup> On the basis of this, once again, Anne decided to postpone treatment. She continued to attend for annual review.<sup>577</sup>

**6.294** Gradually Anne began to suffer more symptoms of Hepatitis C. She began to suffer flu-like aches and pains, constant tiredness, intermittent insomnia and alopecia. At

---

<sup>568</sup> Ibid, page 103

<sup>569</sup> Ibid

<sup>570</sup> Ibid, pages 101–102; Excerpts from the medical records recovered in respect of Anne

<sup>571</sup> Day 79, page 102

<sup>572</sup> Ibid, page 104; Excerpts from the medical records recovered in respect of Anne

<sup>573</sup> Day 79, page 104; Excerpts from the medical records recovered in respect of Anne

<sup>574</sup> Day 79, pages 105–106; Excerpts from the medical records recovered in respect of Anne

<sup>575</sup> Day 79, pages 106–107; Excerpts from the medical records recovered in respect of Anne

<sup>576</sup> Day 79, pages 107–108; Excerpts from the medical records recovered in respect of Anne

<sup>577</sup> Day 79, page 108



a clinic appointment in December 2008, Anne stated that she had noticed that her fatigue had become more pronounced and as a result she was no longer able to attend the gym. Prior to this Anne had for many years gone to aerobic classes at the gym. As she stated, it was 'a big deal when I had to stop that'.<sup>578</sup> An ultrasound scan of Anne's abdomen on 14 April 2009<sup>579</sup> revealed that Anne's liver was mildly enlarged. Anne was told this but was not told what it meant. Anne was also told that there was no tumour on the liver.

**6.295** As a result of the impact of her symptoms on her daily life, Anne felt that the time had come to start considering treatment for the virus. She considered that starting treatment was 'a big commitment' which impacted on both her working and private lives.<sup>580</sup> One factor Anne took account of in deciding when to start treatment was the impact of this on her job. Anne was warned by management at work of the risk of potential redundancy. As a result of this she decided to put off the treatment as long as possible so as not to jeopardise her employment.<sup>581</sup> The threat of redundancy remains to this day due to changes in Anne's area of work.<sup>582</sup> A further difficulty for Anne in receiving treatment was that, although she could drive, she did not drive to the hospital due to the effects of the treatment, especially the fatigue. This meant that she was required to take two trains there, and back, amounting to a three hour return journey. Anne stated that she is a private person and would rather not have told her employers that she was undergoing the treatment. However, due to the length of time involved in attending clinics and regular reviews, she felt that she had to tell her employer's Human Resources manager about the treatment.<sup>583</sup>

#### *Anne's treatment with Pegylated Interferon and Ribavirin*

**6.296** On 16 September 2009 Anne started a six-month course of Pegylated Interferon and Ribavirin. This involved Anne injecting herself with Interferon and taking Ribavirin orally in tablet form. Anne deliberately arranged to start this treatment on the Wednesday before a holiday weekend so that it would not impact on her work. She took annual leave on the Thursday of that week as she knew from her previous treatment that she would experience bad side-effects. In fact, Anne found the side-effects worse than she had remembered. She suffered from very bad flu-like symptoms and had to spend the rest of the holiday weekend indoors. She felt that her holiday weekend 'was completely wasted'.<sup>584</sup>

**6.297** Anne developed a routine during the course of her treatment whereby she took her Interferon injection on a Wednesday evening. In order to allow herself more time to recover from the injection and to enable her to cope with her 45-minute commute to work, Anne obtained permission from her employer to start work three and half hours late on a Thursday, and finish early on a Friday. On a Thursday she did not take any breaks and worked right through the day. She found that reducing her hours helped her manage to continue working while taking the treatment. She had to attend regular clinic appointments during the course of the treatment, initially fortnightly and then monthly, and so missed further time at work. Her reduced working hours and her absences due to clinic appointments did not affect her pay.<sup>585</sup>

<sup>578</sup> Ibid, page 109

<sup>579</sup> Excerpts from the medical records recovered in respect of Anne

<sup>580</sup> Day 79, page 111

<sup>581</sup> Anne's Witness Statement

<sup>582</sup> Day 79, pages 109–111

<sup>583</sup> Ibid, pages 111–112; Anne's Witness Statement

<sup>584</sup> Day 79, pages 112–113

<sup>585</sup> Ibid, pages 113–114

**6.298** This second course of treatment with Interferon and Ribavirin affected Anne greatly. She suffered both physical and psychological symptoms which she described as 'intense'.<sup>586</sup> With regard to the physical effects, she had continuous flu-like symptoms. During the first three weeks of the treatment, she took no fewer than six paracetamol tablets daily and thereafter took paracetamol regularly. She described some of the other side effects as follows:

My temperature fluctuated. I felt cold and clammy. I was shivery. I felt hot. I had a dry mouth. I produced less saliva due to interferon treatment. I had dry skin and suffered alopecia. I saw my hair on the pillow and in the shower. I suffered from poor concentration. In the first two months of treatment my concentration was exceptionally low. On a scale of one to ten, it was zero to one only. Towards the end of the treatment I was living with concentration levels at, say, five out of ten. My immunity to fighting infection was compromised. I had a non-productive dry cough for the first six weeks of treatment followed by a serious chest infection which lasted four weeks requiring antibiotics. My appetite was suppressed. I did not feel hungry. I had to force myself to eat. In the early weeks of Interferon treatment I skipped many meals and ate tiny portions. I was unable to eat starchy foods such as potatoes.<sup>587</sup>

**6.299** Initially, Anne lost weight during the treatment but, due to a craving she developed for ice cream, she regained this prior to finishing the treatment. During the treatment Anne never had a good night's sleep. She often had vivid nightmares which caused her to wake early, about 4 am, and remain awake for the rest of the night. She used to take a nap during the day which she never did before starting treatment. Anne's stamina was reduced. She estimated that, on a scale of one to ten, her stamina was only three. If she went shopping with her sisters, she had to sit down for 20-minute spells at least three times during the course of an outing. In September 2009, she had to stop swimming which she had previously enjoyed.<sup>588</sup>

**6.300** In addition to these physical symptoms, as a result of the treatment, Anne was diagnosed with symptoms consistent with Interferon-induced mood disorder and associated insomnia. Although she did not notice it at the time, her mood and personality began to alter as the treatment progressed. She became irritable and anxious. She suffered from panic attacks. She experienced episodes when she lost her self-control. At times she shouted, 'Get out of here' or 'Please go away' to people.<sup>589</sup> She spent one weekend in bed communicating with no one. She experienced a form of claustrophobia as she was unable to cope if she found her immediate doorway or exit being blocked. In such situations she had to pinch herself to try to make these feelings subside. She developed a strategy of taking herself for a walk to calm down and used this many times both at home and at work. At one point, Anne told her sister that she could understand how someone might be driven to suicide. Now that her mental state has improved, Anne cannot believe that she said this.<sup>590</sup>

---

<sup>586</sup> Ibid, page 121; Anne's Witness Statement

<sup>587</sup> Day 79, page 122; Anne's Witness Statement

<sup>588</sup> Day 79, pages 122–123

<sup>589</sup> Ibid, page 115

<sup>590</sup> Ibid, pages 114–115 and 118

**6.301** Anne's sister provided a statement to the Inquiry.<sup>591</sup> It was provided eight months after Anne commenced this second course of treatment and so the events she described in her statement were recent. Anne's sister was on holiday at the time Anne started the drug regime. Before she left, Anne was very tense about starting the treatment. On her return from holiday Anne's sister immediately noticed changes in Anne's personality and became very worried about her:

Anne was irritable and narky. I could not say anything to her without her reacting in an extremely confrontational manner. She was twisted and volatile and really hard to live with. It was a very difficult time. [Anne] had episodes of daily anger .... [Anne's] behaviour was really destructive. I worried about how I would speak to her because she became hypersensitive. She became a 'monster'. In a rage she would behave with eyes flaring and voice blaring. I became really worried and had to keep a daily eye and check on how things were .... [Anne] was out of control, snapping and being like a huffy, moody teenager. My son who is a loving nephew aged 20 years old avoided [Anne] for months ....<sup>592</sup>

**6.302** The description Anne's sister gave of Anne during the treatment was hard to reconcile with the person who appeared in the witness box at the Inquiry hearings. This highlighted the extreme psychological effect the Interferon had on her. Anne's sister described the change in her sister in September and October 2009 as 'very frightening'. Anne's sister stated:

The Interferon treatment was horrendous for [Anne]. The side effects of the drugs have placed the entire family under pressure. We could not possibly have envisaged the violent effects of this medication. It is upsetting today to recall all of this.<sup>593</sup>

**6.303** Anne's behaviour had a significant impact on her 85-year-old mother with whom she lived. Anne's mother felt threatened and vulnerable living with Anne during this period. On one occasion Anne's other sister witnessed 'a huge volatile row' between Anne and her mother and had to intervene to protect their mother. Anne is aware that her mother bore the brunt of living with her, the symptoms she suffered from Hepatitis C and the Interferon and Ribavirin treatment. Anne's sister stated that she knows that Anne's behaviour has 'deeply upset' Anne herself.<sup>594</sup>

**6.304** On one occasion Anne was so consumed with 'uncontrollable and involuntary anger' that, to prevent herself kicking her mother, Anne kicked a door.<sup>595</sup> She was so ashamed of her actions that she 'jumped in [her] car and took a long drive in tears'.<sup>596</sup> Shortly after this episode Anne attended a review appointment at the hospital at which she was asked to complete a questionnaire on how she was feeling. Anne reacted to this by having 'a mini breakdown' and she told the nurse how bad she felt. Anne felt that the nurse understood her problems and told her that she considers the psychological side-effects of Interferon very seriously. This was the first time Anne connected how she was feeling to Interferon, although she had been warned that the treatment might affect her

---

<sup>591</sup> Anne's sister's Witness Statement

<sup>592</sup> Day 79, pages 119–121; Anne's sister's Witness Statement

<sup>593</sup> Day 79, page 129; Anne's sister's Witness Statement

<sup>594</sup> Day 79, pages 119–120; Anne's sister's Witness Statement

<sup>595</sup> Day 79, page 116; Anne's Witness Statement

<sup>596</sup> Ibid

mood.<sup>597</sup> The nurse suggested two options to Anne – the first being to attend her GP and to ask for anti-depressant treatment, the second being to speak with the psychiatrist at the Brownlee Centre, Gartnavel Hospital, Glasgow.

**6.305** Anne decided to follow the second option and so, in October 2009, attended an appointment with a psychiatrist at the Gartnavel General Hospital. The psychiatrist considered that Anne's clinical presentation with regard to her mood and sleep disturbance was entirely in keeping with a diagnosis of Interferon-induced mood disorder and associated insomnia. Anne was prescribed anti-depressant therapy. It took three weeks for this medicine to improve Anne's symptoms. Anne attended a number of appointments with the psychiatrist. He noted that Anne continued to experience intermittent bouts of anxiety until the completion of her treatment in March 2010. In the last two to three weeks of the treatment her sleep pattern again deteriorated, with nocturnal disturbance secondary to disturbing dreams.<sup>598</sup> The psychiatrist suggested that Anne stop taking the antidepressant medication at the end of her treatment, but the nurse attached to the Hepatitis C clinic considered that it was too soon for Anne to stop it. Anne continues to take this medication and is 'not too anxious to come off it'.<sup>599</sup>

**6.306** To her credit, despite the severity of the side-effects of the Interferon and Ribavirin treatment, Anne continued to work during it.<sup>600</sup> Anne had been told by the Specialist Nurse that there was an 80% success rate of the treatment in those people, like her, who had Genotype 2 of the virus. Anne was 'exceptionally hopeful' that the treatment would be successful. She nearly gave up taking the treatment, due to the effect of it on her mood, but the antidepressant medication enabled her to continue with it.<sup>601</sup> One month after she started the treatment, blood tests revealed that Anne was Hepatitis C negative.<sup>602</sup> However, a blood test taken when Anne finished the treatment in March 2010 revealed that she was Hepatitis C positive. Anne discovered on 30 March 2010 that the treatment had failed. Understandably she was very upset. The Specialist Nurse was shocked that the virus was detectable so soon after she finished treatment. A further blood test in September that year confirmed this positive result. Anne has been classed as 'a non-responder to combination anti-viral therapy'.<sup>603</sup>

**6.307** Anne's sister described in her statement how upset the family was that the treatment did not work:

[N]o one envisaged the treatment failing so quickly. My sister and mother are very upset. My mother continues to worry about [Anne]. Her life has been so challenging. We have all been affected with the effects of Hepatitis C in some way.<sup>604</sup>

Anne too realises that her mother worries about her. She added that her mother has worried about her for 25 years and 'that is most unfortunate'.<sup>605</sup>

---

<sup>597</sup> Day 79, pages 116–117; Anne's Witness Statement

<sup>598</sup> Excerpts from the medical records recovered in respect of Anne

<sup>599</sup> Day 79, pages 125–126

<sup>600</sup> Ibid, page 123

<sup>601</sup> Anne's Witness Statement

<sup>602</sup> Day 79, page 114

<sup>603</sup> Ibid, pages 123–124 and page 128; Excerpts from the medical records recovered in respect of Anne.

<sup>604</sup> Anne's sister's Witness Statement

<sup>605</sup> Anne's sister's Witness Statement

### *Anne's present symptoms*

**6.308** For a couple of months after the treatment finished Anne continued to suffer from some anxiety and panic attacks, but these have now resolved. Anne continues to suffer from flu-like symptoms and aches and pains. Her stamina remains poor, and she has been unable to return to her hobbies of aerobics and swimming. She continues to suffer from fatigue and goes to bed earlier than before. According to Anne's sister's statement, 'She is ill just now. She tires very easily. She cannot even cope physically with going shopping and has to sit down every hour for a long rest'.<sup>606</sup>

**6.309** Anne now attends the liver clinic annually for monitoring.<sup>607</sup> With regard to her prospects Anne states, 'I do not know what my future holds for me. My future is very uncertain'.<sup>608</sup> Anne understands that there may be more treatment for Hepatitis C in a few years but she is unaware what that treatment may be.<sup>609</sup>

### *Specific impacts of Anne's infection with Hepatitis C*

**6.310** Anne described the impacts of her infection with Hepatitis C as follows:

[It] has had a profound impact upon my life. This has reduced my life opportunity in terms of maintaining personal relationships, obtaining employment chances and the subsequent economic disadvantage suffered by me as a result. In my opinion this is why I remained single and did not progress or encourage potential marriage options. I was a young woman when this happened to me. I did not encourage any long-term relationships. You have to draw the risk of transmission of this virus to someone's attention right away. My confidence to do so was non-existent. I have missed out with the opportunity of potentially raising a family of my own.<sup>610</sup>

**6.311** Her infection with Hepatitis C has exacerbated Anne's anxiety about her work situation. Anne has worries about how she would be able to obtain a new job in light of her condition and, for example, whether she would need to declare to any new employer that she had Hepatitis C. 'My age together with Hepatitis C will rule out many employment options available to me.'<sup>611</sup> At present her work situation has settled but, as she stated, the threat of redundancy 'raises its head every now and again ...'.<sup>612</sup>

**6.312** With regard to financial consequences of her infection with Hepatitis C, Anne has a mortgage but she did not have to disclose her diagnosis to her mortgage provider. She worries about being unable to pay the mortgage were she to lose her present job. She has no life assurance as she does not wish to discuss her diagnosis with potential insurers. She has obtained travel insurance, but has not divulged the fact that she has Hepatitis C to the insurers. She has incurred travel expenses attending many clinic and other appointments at the hospital. She received the first Skipton Fund payment in 2004. When her GP signed the Skipton Fund application form for her, he remarked that only three of his patients had Hepatitis C and they were all drug users. It appeared to Anne that he did not differentiate her status, as having acquired it through no fault of her own, from theirs.<sup>613</sup>

---

<sup>606</sup> Day 79, page 129; Anne's sister's Witness Statement

<sup>607</sup> Day 79, pages 126–127 and 129

<sup>608</sup> *Ibid*, page 127; Anne's Witness Statement

<sup>609</sup> Day 79, page 129

<sup>610</sup> *Ibid*, page 130; Anne's Witness Statement

<sup>611</sup> Anne's Witness Statement

<sup>612</sup> Day 79, page 131

<sup>613</sup> *Ibid*, pages 133–134; Anne's Witness Statement

**6.313** Anne is concerned about the stigma attached to the Hepatitis C virus. She likes to keep such a personal matter to herself and is keen to preserve her privacy. She lives in a small community. She has told very few people about her diagnosis.<sup>614</sup>

### **Alex**

**6.314** Alex is presently in his mid-20s.<sup>615</sup>

**6.315** Alex has severe Haemophilia A and was infected with Hepatitis C, Genotype 1a, from his treatment with blood products.<sup>616</sup> He was infected with the virus when he was very young and he was assisted in the evidence he provided to the Inquiry by his father, who also provided the Inquiry with a witness statement,<sup>617</sup> and by referring to reports and notes which were kept by his late mother.

### *Alex's diagnosis with haemophilia and his treatment for this*

**6.316** Alex is the youngest of four children. He has two brothers and one sister. As a child Alex's family lived in a remote part of Scotland. In October 1986, when Alex was about six months old, he developed a swollen right thigh and was distressed. His GP referred him to a local hospital. Initially it was thought that Alex had developed osteomyelitis (bone infection) and he was treated with medication for this. On 22 October Alex was referred to a regional hospital. There, a coagulation screen revealed that Alex had Haemophilia A. It was noted that this appeared to be the result of a spontaneous mutation as the Factor VIII levels in Alex's mother, and in his two brothers, were normal. As there was no family history of haemophilia, Alex's parents had no knowledge or experience of haemophilia. The discharge document from Alex's admission to the regional hospital states that '[Alex] was given an infusion of cryoprecipitate before going home so that his parents could see what was involved, although he did not have any bleeding disturbances at that time'.<sup>618</sup> Alex's father remembers this first treatment very well, although until he saw the discharge letter recently, he thought that Alex's first treatment was with Factor VIII concentrate. Alex's father stated that nothing was discussed with him or his late wife about the treatment Alex was given. He remembers a doctor coming into the ward to see them and saying that they needed to treat Alex with Factor VIII as this was all they could do for haemophilia. At that time Alex's parents did not know what haemophilia was. The doctor said that they would give him a dose of Factor VIII, and that Alex would probably need to take Factor VIII for the rest of his life.<sup>619</sup> It is possible that this is how the doctor referred to the cryoprecipitate since it contains Factor VIII.

**6.317** Alex's parents clearly found this first admission to the regional hospital a traumatic experience. It took eight days for Alex to be diagnosed with haemophilia.<sup>620</sup> During this period Alex gave a number of blood samples for tests. Each time he was taken away from his parents and they would hear him screaming while the sample was being taken. He returned to them with bruises on his arms.<sup>621</sup>

---

<sup>614</sup> Day 79, page 134; Anne's Witness Statement

<sup>615</sup> Day 81, page 3

<sup>616</sup> Ibid, page 4

<sup>617</sup> Alex's father's Witness Statement

<sup>618</sup> Excerpts from the medical records recovered in respect of Alex

<sup>619</sup> Day 81, pages 8–10

<sup>620</sup> Alex's father's Witness Statement

<sup>621</sup> Day 81, pages 11–12

**6.318** In January 1987, Alex developed swelling of his left thigh. Initially he was admitted to a local hospital where he was treated with three doses of Factor VIII concentrate. The swelling did not improve, and so the local hospital decided to refer him to a larger hospital for further review. At Alex's parents request this referral was made to the Royal Hospital for Sick Children (Yorkhill) in Glasgow instead of the regional hospital.<sup>622</sup> Alex was admitted to Yorkhill Hospital on 22 January 1987. He was treated daily with cryoprecipitate. This resolved the bleed and Alex was discharged home on 28 January. During his admission Alex's Factor VIII level was checked again, and was found to be less than 1%, indicating severe haemophilia.<sup>623</sup> Alex's mother, who accompanied him during this admission, was provided with further information about haemophilia and was introduced to parents of older children with the condition.

**6.319** In March 1987 Alex fell and cut his tongue on his teeth. Initially he was treated at home with Factor VIII, but this failed to stop the bleed. So he was admitted to Yorkhill where he was treated with two bags of cryoprecipitate and then tranexamic acid (a drug used in the control of bleeding). It was noted in the discharge letter from this admission that Alex's parents were under considerable stress. Alex's father explained in his evidence to the Inquiry that their stress was due to Alex's diagnosis with haemophilia, and the fact that they lived in such an isolated place. 'We had nobody in our area with the same problem and there was nobody we could discuss it with'.<sup>624</sup> With the help of their GP Alex's parents found out about two other families in their local area who had experience of mild haemophilia. One was an 80-year-old man, and the other was a family who had lost their son before Alex was born. They did not wish to discuss haemophilia with Alex's parents. According to Alex's father there was stigma about haemophilia, which is likely to have been due to the publicity surrounding HIV at that time.<sup>625</sup>

**6.320** Alex usually attended his GP if he had a bleed. He attended Yorkhill for review appointments every three or four months. One of his parents accompanied Alex to these appointments, while the other parent stayed at home to look after their other children. Each appointment usually involved a round trip of two days, and staying overnight in Glasgow. Alex did not enjoy staying in the city. At one point Alex's parents considered moving to Glasgow to be nearer Yorkhill.<sup>626</sup>

**6.321** At each of Alex's review appointments he underwent a blood test. Alex's parents were told that these tests were to check his factor levels and his liver function. At some point Alex's parents were told that he was being tested for 'non-A, non-B' but they did not know what it was.<sup>627</sup> It was not explained to them. Alex's father recalled asking on one occasion what non-A, non-B was and he was told 'It is just a test that we do'.<sup>628</sup> He knew that everyone with haemophilia was being tested for this. Alex's parents were not told the results of these tests. In April 1991 Alex underwent an abdominal ultrasound, the results of which were normal.<sup>629</sup>

---

<sup>622</sup> Excerpts from the medical records recovered in respect of Alex; Day 81, pages 11–13

<sup>623</sup> *Ibid*, pages 14–15; Excerpts from the medical records recovered in respect of Alex

<sup>624</sup> Day 81, page 20

<sup>625</sup> *Ibid*, pages 21–22

<sup>626</sup> *Ibid*, pages 21 and 23–24

<sup>627</sup> *Ibid*, page 26

<sup>628</sup> *Ibid*, page 26

<sup>629</sup> *Ibid*, page 37

**6.322** Alex started prophylactic treatment with Factor VIII concentrate in about October 1990 when he was four years old. It was usually Alex's mother who gave him the injections of Factor VIII, but if she was unable to access a vein, or it was 'a struggle', the GP would administer the treatment. Alex hated the injections: 'I understood why I had to get them but it just wasn't very nice having to have a needle stuck into your arm'.<sup>630</sup> This home treatment was obviously distressing for Alex and his family, in particular his mother. Alex continued to attend Yorkhill every three months for monitoring, which included blood tests.<sup>631</sup> These blood tests included liver function tests. It seems that, at this time, Alex's parents were unaware that his liver function was being monitored.<sup>632</sup>

**6.323** Alex started school in August 1991. He suffered recurrent bleeds once or twice a week. These were usually in his ankles and knees. When they occurred Alex was unable to weight bear for several days, and had to be carried everywhere by his mother. As a result of these bleeds Alex missed a considerable amount of schooling.<sup>633</sup> Alex was provided with a wheelchair to use when he had a bleed. This was used both at home and at school. Alex's school installed stair lifts to allow Alex to access the upstairs classrooms. Alex hated his wheelchair: 'it wasn't very cool to go to school in a wheelchair ... I would have to get pushed around as well and it wasn't very pleasant'.<sup>634</sup>

### *Alex's diagnosis with Hepatitis C*

**6.324** Alex's father was unsure when he and his wife discovered that Alex had acquired Hepatitis C. He thinks that it may have been roughly a year before Alex started treatment with Interferon: he started this treatment in April 1994.<sup>635</sup> He remembers his wife returning from one of Alex's review appointments in Glasgow, and relaying the news to him that Alex had Hepatitis C. His wife was very upset and so was he. They did not know what Hepatitis C was, and Alex's father stated that no explanation about the virus was given to his wife at that time. They eventually discussed it with Alex's GP who was very good to the family over the years. He explained to Alex's parents 'what Hepatitis C meant, what the implications were, the long-term and it wasn't nice'.<sup>636</sup> Alex's parents were not given any advice on how, and if, to tell Alex of his diagnosis. They were not offered counselling. None of the family was offered testing for the virus.<sup>637</sup>

**6.325** Alex was about seven years old at the time his father believes they found out he had Hepatitis C. Alex does not remember being told that he had Hepatitis C: 'there was never one point where I was sat down and told, it was always just kind of there. I had haemophilia, I had Hepatitis C'.<sup>638</sup> Alex remembers asking his mother on the way to one of his review appointments what Hepatitis C was, and why he needed treatment for it. She told him that it was like a scar on his liver and that it was not very good that he had it.<sup>639</sup> Alex's parents only told a few members of his immediate family about his diagnosis with Hepatitis C: 'it has been kept very, very secret, within the family ...'.<sup>640</sup> They considered that there was already a stigma in respect of Alex having haemophilia and they did not wish to add to it. They believed that living in a small community made this worse.

---

<sup>630</sup> Ibid, pages 33–34

<sup>631</sup> Alex's Witness Statement

<sup>632</sup> Day 81, page 34

<sup>633</sup> Ibid, page 46; Excerpts from the medical records recovered in respect of Alex

<sup>634</sup> Day 81, page 47

<sup>635</sup> Ibid, pages 42–44

<sup>636</sup> Day 81, page 43

<sup>637</sup> Ibid, pages 45–46

<sup>638</sup> Ibid, page 44

<sup>639</sup> Ibid, page 45

<sup>640</sup> Ibid, page 44



### *Alex's treatment with Interferon*

**6.326** It appears that Interferon treatment was first discussed with Alex's mother in around 1993.<sup>641</sup> Alex and his father recalled that Alex's mother wished him to receive treatment for Hepatitis C, but she was apprehensive about the benefits and negatives of it.

**6.327** In January 1994, it was decided that Alex would start treatment with Interferon during the Easter holidays. Other than abnormal liver function test results, Alex was not displaying any symptoms of Hepatitis C although, looking back, now Alex feels that he suffered from bouts of tiredness, 'At the time ... I would never have associated the two but looking back, it did seem a bit strange that I would go a couple of days where ... I would just want to stay in bed. I guess for a young child I was quite tired'.<sup>642</sup> His parents were advised that the reason for starting the treatment was to delay the progression of the virus.<sup>643</sup> It was arranged that Alex would spend two weeks in Glasgow at the start of the treatment. Although Alex was supposed to be taking prophylactic treatment for his haemophilia, by this time he was not taking as much treatment as was prescribed. He was 'always quite resistant' to taking this treatment, and this was difficult for both Alex and his parents.<sup>644</sup> As the Interferon treatment was going to involve further injections, and in the hope that compliance with Interferon would be better, Professor Gibson, Consultant Haematologist, did not reinstate prophylactic treatment in January 1994.<sup>645</sup>

**6.328** Alex's parents felt that they were given 'sparse' information about the treatment by Yorkhill, so Alex's mother contacted the Haemophilia Society and enrolled to attend a symposium in Glasgow on Hepatitis in early 1994.

**6.329** On 30 March 1994 Alex underwent an abdominal ultrasound scan. The result of this revealed mild hepatomegaly (enlarged liver) but was otherwise normal.<sup>646</sup>

**6.330** On 1 April 1994, when he was eight years old, Alex started treatment with Interferon. His treatment with Interferon was given as part of a study entitled 'A Prospective Study of the Efficacy of Human Alfa [sic] Interferon in the Treatment of Chronic Liver Disease in Haemophilia'.<sup>647</sup> Over the months leading up to the trial, the implications of treatment for Alex and his family were discussed by Professor Gibson and the Haemophilia Nurse Specialist with Alex's mother, and a plan was made, including training, to deal with these. Alex's mother signed the consent form for this study after these discussions. The consent form records that the nature of the study and the side-effects of Interferon were explained to Alex's mother. Alex's father believes that his son was the youngest person in Scotland to become infected with Hepatitis C from blood products, and to receive Interferon treatment.<sup>648</sup>

**6.331** Alex's GP was obviously keen to support the family during the treatment. By letter dated 31 January 1994, Alex's GP wrote to Professor Gibson stating that he understood that Alex was due to start treatment with Interferon at the end of March. The GP asked Professor Gibson for 'any further information regarding Interferon treatment which you may be able to send me, and [I] would also appreciate copies of any information which

---

<sup>641</sup> Professor Gibson wrote to Alex's GP on 6 July 1993, and commented that she had discussed Interferon treatment 'in a preliminary fashion' with Alex's mother; Excerpts from the medical records recovered in respect of Alex.

<sup>642</sup> Day 81, page 53

<sup>643</sup> Ibid, page 52

<sup>644</sup> Ibid, page 51

<sup>645</sup> Ibid, page 50

<sup>646</sup> Ibid, page 56; Excerpts from the medical records recovered in respect of Alex

<sup>647</sup> Day 81, pages 51–52; Excerpts from the medical records recovered in respect of Alex

<sup>648</sup> Day 81, page 53

is provided to [Alex's parents] in order to facilitate any discussion with [them]'.<sup>649</sup> In her reply to this letter, dated 3 February, Professor Gibson wrote 'If the decision is taken to go ahead with Interferon therapy for [Alex] then I will keep you very informed of the risks and side effects'.<sup>650</sup> As stated above, Alex started this treatment on 1 April 1994. Professor Gibson did not keep Alex's GP informed about this treatment. On 16 August 1994 Alex's GP wrote to Professor Gibson that '[Alex's mother] tells me that he has been back to Yorkhill several times as his Interferon treatment continues. The last typed letter I have from yourself is dated 3 February 1994 and I wonder if it is possible to have an update on [Alex's] treatment since then?'.<sup>651</sup> In her reply to this letter dated 23 August, Professor Gibson stated that Alex tolerated the treatment 'very well' and that they had seen Alex at monthly intervals.<sup>652</sup> She noted that Alex had minimal local inflammation at the injection site but no other side-effects. She noted that there had been a little improvement in Alex's recent AST and ALT results but that they remained above the normal range.

**6.332** The injections of Interferon were administered to Alex by the community nurse at his house. When asked how he found taking the Interferon treatment Alex stated:

I hated it. I couldn't stand it. And I did feel sick from it. I just felt drained. [A]fter my first treatment I was really sick. I had ... extreme flu symptoms and hot sweats. It was never as bad as the first time but it was bad enough carrying on, and I also – because I hated going to the hospital so much, I hated having to go for my appointments – I never wanted to make a big deal about it in the hospital. I always tried to play down any illness I had.<sup>653</sup>

**6.333** The reason Alex did not stress these symptoms to the hospital was that he was worried that if he did, he would have to stay at the hospital: 'it was always such a horrible place to be'.<sup>654</sup> Alex remembers also feeling generally unwell. Alex's first treatment was around the time of his birthday. When he returned home after this he had a birthday party. Alex remembers that he did not wish to be around anyone. He did not wish to have to play with anyone and he stayed in his room. Alex's father stated that although the side-effects of the treatment had been explained to Alex's mother it was 'awful' when Alex received the treatment: 'I can't even go into the detail of what it was like. It was horrible, absolutely horrible to give it to a young child, these injections, the district nurse used to come in every day and every one of the family used to cringe to hear'.<sup>655</sup> When describing the effect of the Interferon treatment on Alex, his father stated '[I]t doesn't bear to think about what he went through'.<sup>656</sup>

**6.334** Alex's transaminase levels became normal within eight weeks of starting Interferon, and remained normal for the following month.<sup>657</sup> However, this improvement was transient, and by October 1994, six months after he had started the treatment, both his AST and ALT levels were elevated. Alex was consistently Hepatitis C PCR positive on all but one occasion in the first six months of his treatment; the one occasion apparently being of doubtful significance. As his liver function test results were abnormal at weeks 20 and

---

<sup>649</sup> Excerpts from the medical records recovered in respect of Alex

<sup>650</sup> Ibid

<sup>651</sup> Day 81, pages 55 and 58

<sup>652</sup> Ibid, page 58; Excerpts from the medical records recovered in respect of Alex

<sup>653</sup> Day 81, page 59

<sup>654</sup> Ibid, page 60

<sup>655</sup> Ibid, page 54

<sup>656</sup> Ibid, page 65

<sup>657</sup> Ibid, pages 60–61; Excerpts from the medical records recovered in respect of Alex

24, he fulfilled the criteria for trial failure and withdrawal from the trial. Alex's mother was informed at a review appointment in October 1994. She was understandably very disappointed by this, and after discussion with Professor Gibson it was agreed to continue Alex's treatment with Interferon for a further month. In fact, Alex's treatment continued until 17 February 1995. One of the reasons it was continued this long was that Alex's HCV RNA was negative in December 1994, but unfortunately it became apparent that this was another 'one off' result. At some point Alex's parents were told that with hindsight it might have been better had his treatment been stopped after six months.<sup>658</sup>

**6.335** Alex believes that he was 'quite happy' to stop the treatment as it meant that the injections stopped. At his age, the fact that the treatment had not worked did not mean much to him. He knew that having Hepatitis C was bad and that he needed to get rid of it.<sup>659</sup> He described his understanding about Hepatitis C as being 'a long period of discovery'.<sup>660</sup> Alex's father described the failure of the treatment with Interferon as '[V]ery, very disappointing, very hard to deal with, because there was no improvement whatsoever. He was still the same as he was before he started his interferon'.<sup>661</sup>

#### *Alex's condition after the Interferon treatment and the effect of both his haemophilia and Hepatitis C on his schooling*

**6.336** After his treatment with Interferon was stopped, Alex continued to attend Yorkhill Hospital for monitoring and annual ultrasound scans. His liver function test results remained mildly abnormal, but not sufficiently to cause concern. In 1996 there was some discussion among the doctors there about whether Alex would benefit from further treatment with Interferon at a higher dose, but these proved inconclusive.<sup>662</sup> In January 1997 Alex's mother, who was keen to pursue treatment options for the virus, was told by Professor Gibson that it was unlikely that Alex was eligible for the combined Interferon and Ribavirin trial which was about to start, as this was principally for patients who had become Hepatitis C negative during their treatment with Interferon, and had subsequently relapsed following its withdrawal. After his experience taking Interferon, Alex was not keen to take further treatment for Hepatitis C. In fact he continued to be reluctant to accept prophylactic treatment for his haemophilia.<sup>663</sup>

**6.337** In the late 1990s Alex started secondary school. His school was aware that he had haemophilia but did not know that he had Hepatitis C. When asked to describe how he found starting secondary school Alex stated:

I found it pretty hard. I found it quite hard to make friends. I never really had any best friends because I always felt like I had a tonne of secrets and baggage that I had to carry around .... It was hard enough to tell people that I had haemophilia let alone anything else. I felt quite withdrawn because of that, because I knew I had something to hide and I never really felt like I could open up or explain why I was going away every other month or what I was doing. I still do to this day. I am still quite closed.<sup>664</sup>

---

<sup>658</sup> Day 81, page 62

<sup>659</sup> Ibid, page 66

<sup>660</sup> Ibid, page 67

<sup>661</sup> Ibid, page 65

<sup>662</sup> Ibid, pages 67-69

<sup>663</sup> Ibid, pages 69-71

<sup>664</sup> Ibid, page 71

**6.338** Alex's bleeds changed at this time, and he found that he could go to school when he had a bleed although he probably should not have done so. He chose not to use his wheelchair: 'I didn't like being the disabled boy at school. I felt like I was labelled with that anyway because I was the only one with [haemophilia]'.<sup>665</sup> When Alex had a bleed, instead of going to school in a wheelchair, he often rested at home and then returned to school. He continued to miss a lot of school due to his bleeds. His target joints were developing and he had persistent bleeding into his right knee and his left ankle. In the event of Alex having a bleed at school, the school contacted Alex's parents either by the home telephone, or via a pager which the parents carried. They would then collect Alex and take him home for treatment there.<sup>666</sup> At one point Alex's school insisted that he wore a helmet to participate in gym lessons. Alex felt stigmatised by this and a doctor from Yorkhill Hospital wrote to the school advising that this was unnecessary.

**6.339** When Alex was younger and in primary school he did not think that having Hepatitis C was 'a big deal' and so he probably mentioned it to everyone. In secondary school Alex only told his best friend that he had the virus due to the stigma surrounding it. He felt isolated at school and ashamed of his condition.<sup>667</sup>

**6.340** In November 2000, when Alex was 14 years old, his Consultant Haematologist at Yorkhill sought the advice of Dr Morris, Consultant Gastroenterologist, on further treatment of Alex's Hepatitis C. Alex and his mother attended Dr Morris' clinic on 19 February 2001. At this appointment Dr Morris discussed the possible benefits of combined therapy with them and told them that it was their policy to consider liver biopsy in patients they intended to treat with this therapy. It was agreed that Alex and his mother would consider the pros and cons of further therapy and the potential risks of liver biopsy, before returning to the clinic in three months.<sup>668</sup> At this time Alex did not want a liver biopsy and was not keen on treatment:

At that time I didn't want [a liver biopsy]. I didn't see the point. I didn't feel like I had any main symptoms from it. To be honest, I just kind of ignored it. I didn't think about it too much. I didn't feel like I was sick at that point. So there wasn't anything to treat almost. I was also – I was quite worried about having a liver biopsy as well, obviously being a haemophiliac, and also I kind of heard that the combination of ribavirin and interferon, the side effects can be quite extreme. So ... I just didn't really consider it.<sup>669</sup>

**6.341** As he grew older Alex began to consider what the virus might mean for him and so he started on 'a personal quest for information'. He was scared of what he was going to find out. He obtained booklets from the hospital.<sup>670</sup> He gained the impression that those infected with Hepatitis C generally lived for 15 to 20 years. He saw other haemophilia patients dying. As a result of this, he did not think that he would live long past his teen years. He stated:

[I]t is hardly surprising that I lacked the motivation and ambition to work hard and gain qualifications for a 'future' that no-one could assure me I would have

---

<sup>665</sup> Ibid, page 72

<sup>666</sup> Ibid, page 73

<sup>667</sup> Ibid, page 74; Alex's additional Statement

<sup>668</sup> Day 81, pages 75–77; Excerpts from the medical records recovered in respect of Alex

<sup>669</sup> Day 81, page 78

<sup>670</sup> Ibid, page 74

.... So I just didn't try. I gave up before I had even started and at the age of 16 dropped out of education with few standard grades and no ambition.<sup>671</sup>

### *The period after Alex left school*

**6.342** Alex started to attend Dr Morris' Liver Clinic annually. An abdominal ultrasound in August 2001 was normal.<sup>672</sup> In 2002, at the age of 16, Alex began a course at his local college. He spent less than a year on this course and then moved to Glasgow to study on another course. He completed the first year of this course. He found it difficult being away from home and thinks that he was perhaps too young to have moved away from home. At his annual reviews at Dr Morris' clinic his position with regard to treatment remained the same:

I was quite happy just to go in and ... get them done and leave really. Also, I didn't find I had any problems relating to my Hepatitis C at that point. I wasn't really interested in treatment or exploring anything any further. I did look into treatment myself a little bit but I didn't want to pursue it.<sup>673</sup>

Throughout this period Alex suffered from fatigue. He would suddenly become 'really, really tired' but he did not associate it with Hepatitis C.<sup>674</sup>

**6.343** Over time Alex became more concerned about the progression of the virus. When asked what caused this he stated:

I think it was a combination of a lot of things. I was finding it quite hard living in Glasgow and getting around the city, just even my joints and things were starting to seize up. My knee was getting especially bad and I think I – over a short period of time I just started to care a bit more that I had Hepatitis C and I started to almost think about it and research it. And I guess over a period of time it just hit me that it is actually really serious.<sup>675</sup>

**6.344** During his research Alex found something on the internet or elsewhere that said that patients with Hepatitis C can expect to live for 20 years. As he was nearing his 20th birthday he thought that his 'time was getting kind of close'.<sup>676</sup> Also at this time Alex's mother became unwell. Alex voiced his concerns to an Associate Specialist in the haemophilia and thrombosis centre at Glasgow Royal Infirmary. In April 2007, this doctor wrote to Dr Morris and asked him to see Alex ahead of his next appointed clinic time, with a view to discussion of possible biopsy and treatment. Unfortunately, Dr Morris was about to take a sabbatical and so was unable to see Alex until the appointed clinic in October 2007. When Alex attended this appointment he was seen by a junior doctor. During this appointment Alex asked this doctor some questions. A number of times the doctor left the room to discuss Alex's questions with Dr Morris, who was in the room next door. Having reconsidered the possibility of treatment, Alex would have liked to have had the opportunity to speak to Dr Morris personally on this occasion. At this appointment it was decided that Alex should undergo an ultrasound-guided liver biopsy which required him to be admitted beforehand to correct his clotting, and then afterwards for observation.<sup>677</sup>

---

<sup>671</sup> Alex's additional Statement

<sup>672</sup> Day 81, page 77; Excerpts from the medical records recovered in respect of Alex

<sup>673</sup> Day 81, page 80

<sup>674</sup> Ibid, page 81

<sup>675</sup> Ibid, page 82

<sup>676</sup> Ibid

<sup>677</sup> Excerpts from the medical records recovered in respect of Alex

**6.345** Later in 2007 Alex attended the Glasgow Royal Infirmary (GRI) to undergo the liver biopsy. Before attending for this procedure Alex researched it on the internet. He found a lot of information but was unsure which details were correct, 'But I had made a mental decision that maybe now is the time to do something about it and if I have to get a biopsy to get the treatment, maybe it's worth it'.<sup>678</sup> Having been admitted to the hospital for the procedure, and had a cannula inserted into his hand, Alex changed his mind about having a liver biopsy. One reason for this was that the liver specialist nurse came to speak to Alex to make sure that he wanted to go ahead with it. She asked Alex if he knew what genotype of the virus he had, and Alex told her that he did not know. She told Alex that the genotype of the virus he had would have 'a massive impact on the treatment and the success rate'.<sup>679</sup> She went away to find out his genotype. On her return she told Alex that he had Genotype 1 and so he had a much lower chance of clearing the virus than if he had one of the other genotypes. Another factor which contributed to Alex's decision to postpone the procedure was that his Haemophilia Consultant came from upstairs to check on Alex. He told him that it was a fairly serious procedure for a person with haemophilia to undergo, and seemed to want to make sure that Alex understood fully the implications of having a liver biopsy. Alex believes that, until his discussion with the Haemophilia Consultant, he had not fully appreciated the risks of a liver biopsy. The fact that two people checked on him and asked him if he wished to continue with the procedure scared Alex: 'At that point [he] said, "Maybe I need to think about this. Maybe I need to think whether I'm doing the right thing"'.<sup>680</sup> He left the hospital without undergoing the procedure.

**6.346** In February 2008 Alex moved from Glasgow to another city in the UK. By this time Alex had managed to complete only two years of his college course in Glasgow. Alex's attendance on the course was poor. He believes that this was due to his haemophilia and the fact that, during this period, he became preoccupied with the fact he had Hepatitis C. He also found it difficult to concentrate.<sup>681</sup> He found it hard to get close to people and was quite withdrawn.<sup>682</sup> Alex decided to move to this new city as his girlfriend at the time lived there, and he knew that there was a good hospital there. On moving Alex started attending a joint hepatology and haemophilia clinic at the local hospital every six months. He believes he receives good care there. This care includes Fibroscans. These scans use transient elastometry to measure the amount of liver stiffness, from which the level of fibrosis can be assessed. His Fibroscan result in 2010 was 6.8kPa.<sup>683</sup>

**6.347** His blood test results from April 2010 revealed an albumin 46g/L, alkaline phosphatase 77iu/L, AST 62 iu/L, ALT 107 iu/L and bilirubin 10 mmol/L. His viral load was 1.7 million, suggesting that that there was not major liver fibrosis, that the liver was functioning well, but that the virus was still actively reproducing.

### *The present position*

**6.348** Alex has been advised by the doctors in this new hospital that he should consider treatment for the Hepatitis C virus while he is healthy enough to withstand the side-effects. Understandably this change in advice has caused Alex to become confused about what

<sup>678</sup> Day 81, page 87

<sup>679</sup> Ibid, page 86

<sup>680</sup> Ibid, page 86

<sup>681</sup> Alex's Witness Statement

<sup>682</sup> Day 81, page 90

<sup>683</sup> Excerpts from the medical records recovered in respect of Alex; a score of over 7.2kPa indicates higher likelihood of significant fibrosis.

would be the best course of action for him. Some time in 2011, Alex was offered treatment with Interferon and Ribavirin and was on the verge of accepting it. His doctor then advised him that he might be better waiting for the new treatment of protease inhibitors.<sup>684</sup>

**6.349** Alex believes that he has suffered from symptoms of Hepatitis C throughout his life although 'sometimes [he] did not realise the full extent of them'.<sup>685</sup> He has often been depressed, angry, tired and lethargic. Alex has never received treatment for depression although he did once mention how he felt to his GP in Glasgow.<sup>686</sup> Alex's father stated that after Alex started his treatment with Interferon he:

[W]as just going away all on his own, wouldn't come out. He would spend days and he would hardly eat and we just thought, well, it's just the effect of the interferon that's causing it, but obviously it wasn't. It was just an ongoing thing right up until he moved away from home ....<sup>687</sup>

He told the Inquiry that he found it hard to speak to his parents or anyone else because 'all my experiences of going to the hospital were very negative, so everything surrounding having haemophilia and Hepatitis C was all really negative'.<sup>688</sup> He tried on occasion to speak to his mother about it but 'it wasn't a very nice thing to do. I always found it ... really hard'.<sup>689</sup> Alex's family, especially his mother, cared for him extensively as he grew up and Alex now relies heavily on his girlfriend.

**6.350** Alex has been given limited advice about the prognosis for his condition. He has tried to research it himself but has never fully understood it.<sup>690</sup> He believes that:

[I]t is so complicated to even consider having children that I just don't bother. The risk of passing on an infection and then the thought of not being around to see my children grow up really prevents me from planning any kind of family life.<sup>691</sup>

He has discussed this with his doctor and has been told that there is a risk of passing on the Hepatitis C virus. He understands that there are alternatives, such as IVF, which would lower the risk of infecting his partner but, although Alex would love to have children when he is older, he is not considering it at present.

### *Specific impacts of Alex's infection with Hepatitis C*

**6.351** Alex's father stated that the family is very close and that it has been 'heart breaking' that one of the five of them has had Hepatitis C. It had a 'huge' effect on Alex's late mother, and Alex appreciates that his having haemophilia and then Hepatitis C was 'a lot to go through'.<sup>692</sup> He feels responsible for having put his parents through this. It was apparent from Alex's evidence that his diagnosis with haemophilia and then Hepatitis C has put a strain on both his parents, in particular his mother as his main carer, and his family life. Although they are close, Alex described himself as 'quite closed' and stated that '[A]s a family we generally don't talk about it. It's always there, obviously, but it's hard to talk about'.<sup>693</sup>

---

<sup>684</sup> Day 81, pages 93–94; Excerpts from the medical records recovered in respect of Alex

<sup>685</sup> Day 81, page 94

<sup>686</sup> Ibid, page 96

<sup>687</sup> Ibid, page 95

<sup>688</sup> Ibid

<sup>689</sup> Ibid

<sup>690</sup> Ibid, page 97

<sup>691</sup> Ibid, page 98

<sup>692</sup> Ibid, pages 98–99

<sup>693</sup> Ibid, pages 99–100

**6.352** The diagnosis with Hepatitis C has affected his social life. He finds it difficult to get close to people because then he feels that he needs to tell them about his condition:

It's this whole big thing that you have to explain. It's not like you can tell every person you meet and have a quick explanation of 'Oh, that's a shame. It's terrible that could have happened'. You have this whole other big baggage of information that you have to carry and explain. I almost feel like I have to defend it if I do tell anybody, which is why I generally choose not to.<sup>694</sup>

**6.353** As a result of this he does not have a large circle of friends and does not become involved in community life. Alex worries that he may sustain an injury causing him to bleed, and then he will have to tell people he has Hepatitis C.<sup>695</sup>

**6.354** In 2009 Alex underwent an arthroscopy to repair damage to his right knee, one of his target joints. This had a good effect. Alex is generally confined to non-physical activities which is due both to his haemophilia and Hepatitis C. He is unable to play impact sports of any kind. He finds it difficult to do activities which keep him fit as he finds that he tires easily.<sup>696</sup>

**6.355** After Alex left Glasgow he started studying again. Now he has part-time, unpaid work, the nature of which he wishes to remain confidential. This work is relaxed in that he can take breaks when he wishes and he can work from home. The people he works with are accommodating with regard to his haemophilia. Alex told his employers about this when he started working there. He hoped that his work there would become full-time within the next month or so. In the past Alex has found it difficult to sustain any level of work. His lack of qualifications on leaving school limited the career options open to him. During the time he was at college Alex tried to work in bars and coffee shops but he found such jobs difficult to maintain due what he described as 'the immense bouts of fatigue' from which he suffered and the unpredictability of them.<sup>697</sup> He stated that, on occasion, he has had to turn down or leave other work due to his symptoms of Hepatitis C.<sup>698</sup> As a result of this Alex felt that he was unreliable in the work place and not the best kind of employee. 'I feel like a bit of a failure on the work front and it is always difficult when I compare myself with friends my age who seem to be progressing with their lives'.<sup>699</sup> Due to his uncertainty about his future, motivation has been hard for him.

**6.356** For number of years Alex has had to rely on benefits. Nobody else in his family has ever claimed benefits and the fact that he does so is something he feels guilty about: 'I have never enjoyed it or been proud of it'.<sup>700</sup> Over the years Alex has accumulated debts, including an overdraft and credit card bills, amounting to about £18,000. He stated that he was reckless with money as he was immature and did not think he was going to live long enough to have to pay these debts off. At one time he was called by debt collectors almost every day and this caused him a lot of anxiety. He has now consolidated his debts and feels that he is more in control of his finances. He has started to make payments to reduce the debt and hopes eventually to repay it. In 2004 Alex received £20,000 from the Skipton Fund, and he paid off some debts, gave some money to his family and paid rent on his accommodation in Glasgow.

---

<sup>694</sup> Ibid, pages 100–101

<sup>695</sup> Ibid, page 102

<sup>696</sup> Ibid

<sup>697</sup> Ibid, page 103

<sup>698</sup> Alex's additional Statement

<sup>699</sup> Day 81, page 104

<sup>700</sup> Ibid, page 105



**6.357** Alex believes that his diagnosis with Hepatitis C precludes him from obtaining a mortgage and so he is unable to consider buying a house. He has never applied for a mortgage but has researched obtaining one. The expense of travel insurance, and Alex's financial situation makes it difficult for him to travel abroad. On one occasion Alex travelled to the USA with his parents. His parents' travel insurance cost £32, but Alex's cost £109 due to his haemophilia and Hepatitis C. He wishes he was able to travel more.<sup>701</sup>

**6.358** When Alex was a child, the costs of his travel to the Haemophilia Unit at Yorkhill, and that of the parent who accompanied him, were paid for by the Health Board. They usually stayed with Alex's aunt. They were given an allowance of £28 a night for accommodation. This was insufficient to cover the cost of this, particularly if they were unable to stay with a relative. Alex's parents paid the rest of their costs of these trips from their savings. Alex's father stated: '[I]t was quite a big chunk of any savings that we had'.<sup>702</sup> A disadvantage for Alex of staying with his aunt was that after each hospital visit he had to answer her questions, and explain what had happened, at the appointment. He found this difficult and gave the impression he would have preferred not to have had to speak about his appointments.

**6.359** Alex feels the cold and has bad circulation in his toes and fingers. This may be a symptom of Hepatitis C. As a result of this he has incurred increased heating costs. Occasionally when Alex's symptoms of Hepatitis C are severe, he employs a cleaner and a handyman. He bears the cost of this. He stated that his girlfriend often has to look after him now.<sup>703</sup>

**6.360** In a written statement to the Inquiry about the financial effects of his infection with Hepatitis C, Alex wrote:

I feel like I have lost my future. I find it hard to assess exactly how much financial hardship I have faced as a result of my illness because it is difficult to measure potential. I can compare myself to my siblings and peers, all of whom have successful jobs, own their own houses and have a good quality of life. At the age of ... I have none of these things and I can only put this down to being different and the difference is my illness. I know I am intelligent, I know there are a lot of things I would have loved to have done, but my illness, and in particular the lack of support and information I was given growing up, has prevented me ever achieving anything. I can't hold down a job as I am just not reliable, I would not employ me and I [am] embarrassed that as a ... year old man I have never really achieved anything. I just want a fresh start but I feel trapped in my situation – I rely on benefits and don't have the finances to re-enter education and start my life again. I feel I will always be reliant on others for my life and the burden of that makes me just want to give up.<sup>704</sup>

## Christine

**6.361** Christine's son contracted HIV from contaminated blood products and she gave evidence during the Oral Hearing in support of Chapter 5, *The Effect of Infection with HIV, Including the Effects of Treatment, on Patients and their Families*. Christine herself contracted

---

<sup>701</sup> Ibid, pages 107–108

<sup>702</sup> Ibid, page 109

<sup>703</sup> Alex's additional Statement

<sup>704</sup> Alex's additional Statement

the Hepatitis C virus from blood products, and her account of some of the effects of this on her, and her family, is narrated below. It is likely that these are understated as Christine's evidence to the Inquiry mainly focused on her son's infection with HIV. In order to gain a fuller appreciation of the impacts of Christine's infection with Hepatitis C, what is written below should be considered together with the evidence narrated at paragraphs 5.5 to 5.62.

### *How Christine acquired Hepatitis C*

**6.362** At the date of the hearing Christine was in her mid-50s.<sup>705</sup> She had a family history of haemophilia, with her two brothers, a cousin and an uncle being diagnosed with it.<sup>706</sup> In 1975 following the birth of her son, who was referred to in evidence as 'John', and his diagnosis with Haemophilia A, Christine was investigated and found to be a carrier of Haemophilia A.<sup>707</sup>

**6.363** As a result of being a carrier of Haemophilia A, Christine decided to undergo sterilisation. She found this a very difficult decision to make. The surgery was carried out in December 1981 at a hospital elsewhere in the west of Scotland. Prior to the surgery, Christine's Factor VIII levels were checked by her son's Consultant Haematologist at Yorkhill Hospital and were found to be 26%. She had never had any bleeding problems.<sup>708</sup> But when she regained consciousness after the operation, Factor VIII was being administered to her. Christine asked the medical staff to stop this treatment. She felt that they were 'making a mountain out of a molehill'.<sup>709</sup> Christine made her unhappiness clear and was told that she had signed a waiver consenting to the administration of any treatment thought necessary.<sup>710</sup> She later learned that the administration of Factor VIII had been at the suggestion of the Haemophilia Unit at Yorkhill, with the Factor VIII being sent over in a taxi from Yorkhill at the time of her operation.<sup>711</sup> It was 2800 units of Armour Factor VIII, batch number VC2103, which proved to have been infected with Hepatitis C.<sup>712</sup> This was the only time Christine received human Factor VIII concentrate.<sup>713</sup>

**6.364** Immediately following the sterilisation procedure, Christine had acute jaundice and felt extremely nauseous for a week. She was treated for this by her GP. Having not been warned specifically of any risks associated with Factor VIII, she did not think there was any link between it and her symptoms. Christine was told by one of the nurses that, as a result of her having suffered jaundice, the batch of Factor VIII which she had received was withdrawn from use as a safety precaution.<sup>714</sup> The cause of Christine's episode of jaundice was investigated by her GP, and markers for Hepatitis A and B were negative. There was no further follow-up of liver function tests or other viral markers.<sup>715</sup>

**6.365** In December 1981 Christine was referred to the Haemophilia Unit at the Glasgow Royal Infirmary to be registered as a haemophilia carrier. She has attended the Haemophilia Unit annually for routine blood tests. Since 1981 she has had synthetic desmopressin (DDAVP) cover for all major and minor surgery, including for a hysterectomy in November 1988.<sup>716</sup>

---

<sup>705</sup> Day 28, page 3

<sup>706</sup> Ibid, page 6

<sup>707</sup> Ibid, page 7; Excerpts from the medical records recovered in respect of John

<sup>708</sup> Day 28, pages 25–26

<sup>709</sup> Ibid, page 27

<sup>710</sup> Ibid, pages 27–28

<sup>711</sup> Ibid, page 27

<sup>712</sup> Ibid, page 30

<sup>713</sup> Christine's Witness Statement

<sup>714</sup> Day 28, pages 29–30

<sup>715</sup> Ibid, page 30; Excerpts from the medical records recovered in respect of Christine

<sup>716</sup> Day 28, pages 31–32; Christine's Witness Statement

### *Christine's symptoms of Hepatitis C*

**6.366** After 1981 Christine suffered from skin itching, arthritis and painful feet. She had episodes of insomnia and extreme tiredness but generally kept good health. She attributed her tiredness to a combination of factors, namely caring for her elderly mother and working hard, as she did.<sup>717</sup> Later she had also to deal with the challenges presented when her son was diagnosed with HIV.

### *Christine's diagnosis with Hepatitis C*

**6.367** Christine did not find out that she was infected with Hepatitis C until 1991. A couple of weeks after giving blood at a mobile blood transfusion centre she was asked to attend a meeting at the Glasgow offices of the SNBTS. She did not know what the meeting was about. At this meeting she was told by an unidentified individual that, having tested her blood donation, it had been discovered that she was positive for Hepatitis C. Christine could not believe this and was in shock. After she was questioned about whether she had taken any drugs or medication, it was suggested to her that she could have acquired the virus from the Factor VIII she was given in 1981. It was never confirmed to her that this was the source of her infection. She does not recall being given any information at this meeting about the virus except that she was told that she should not donate blood again and not to consider organ donation. She stated that if she was given any more information than that, she was in too much of a shock to absorb it. She was advised to attend her GP.<sup>718</sup>

**6.368** Christine believes that she was not properly counselled when she was told she had Hepatitis C. She was not told to practise safe sex and she was not warned that she could be at risk of HIV from the Factor VIII she received in 1981. She believes that had she not donated blood, she would not have discovered that she had the virus.<sup>719</sup>

### *Christine's treatment for Hepatitis C*

**6.369** As suggested to her, Christine attended her GP and he referred her to the Hepatology clinic of Dr Mills, Consultant Hepatologist at the Gartnavel General Hospital, Glasgow. Christine attended this clinic in 1991. There she was advised by Dr Mills to start treatment with a 48-week course of Interferon and she did so. During the treatment she suffered side-effects and described the treatment as 'horrible'.<sup>720</sup> Immediately after taking the treatment she felt very ill. She suffered from flu-like symptoms, her joints were sore and she became very tired. She was working full-time and in order to cope with the treatment, she used to inject herself with the Interferon in the early evening, and then immediately go to bed. Unfortunately, tests 12 weeks after the treatment started showed that it had been ineffective and so, in accordance with practice at the time, the treatment was stopped. Christine was very disappointed.<sup>721</sup>

**6.370** Thereafter, Christine continued to attend the liver clinic for monitoring once a year. Liver biopsy was considered to be too risky for her. She has had annual liver function tests and Hepatitis C RNA tests. She has a two-yearly liver scan performed. In January 2010 Christine underwent a new sonar pulse scan which produced a 3D picture of her liver. She was told that her liver was no more affected than to be expected for a person of her

---

<sup>717</sup> Ibid

<sup>718</sup> Ibid, pages 33–34

<sup>719</sup> Ibid, pages 33–34; Christine's Witness Statement

<sup>720</sup> Christine's Witness Statement

<sup>721</sup> Day 28, pages 35–36

age. Later in 2010, Christine started a 48-week course of treatment with Interferon and Pegylated Interferon. The side-effects of this were similar to those she experienced during her previous course of treatment. She felt very tired and she felt sick.<sup>722</sup> She stated, 'I must have been a nightmare to live with because I felt as if I was living a nightmare'.<sup>723</sup> Christine completed this course of treatment shortly before she gave evidence to the Inquiry in June 2011. At the end of the treatment she was negative for the virus, but was warned that the virus could still return.

**6.371** Christine received a payment of £20,000 from the Skipton Fund.<sup>724</sup>

### **Patients' experience – Conclusion**

**6.372** Chapters 4, 5 and 6 have dealt with the experiences of the patients and relatives. In conclusion the Inquiry is very grateful to the many witnesses who came forward and provided evidence about the effects of their own or their relative's infection with HIV and/or Hepatitis C.<sup>725</sup> At the heart of this Inquiry lies the fate of people who, simply by accepting treatment for a medical condition, contracted either HIV or Hepatitis C, or both these viruses. In many cases the infections were acquired because of treatment for a blood coagulation disorder, such as Haemophilia A or Haemophilia B. Those with these disorders had already suffered to varying degrees as a result of their underlying conditions. Others became infected as a result of a single blood transfusion, sometimes being unaware until later that they had even been transfused. Whatever the route of transmission, suffering resulted – whether to the patients themselves or to their relatives. The pain they felt cannot be quantified. Many people have had their lives shaped and overshadowed by a loved one's illness. Many people have had to watch their loved ones, including children, suffer. In some cases, they have had to watch them decline and die.

**6.373** The stigma which some feel persists, even today, in relation to both viruses, made it particularly difficult for some witnesses to contact the Inquiry. These witnesses had to overcome fear of disclosing their own identity in order to do so. The Inquiry put in place a number of measures to maintain confidentiality. These are described in Appendix 2 to this Report.

**6.374** Hearing the personal stories was a fundamental part of the Inquiry and it would not have been possible without the witnesses being so willing and open. For many, giving statements was their first opportunity to share the experiences of what had happened to them in the course of NHS treatment. Some told of adverse consequences which they had not disclosed to even their closest family members. It is hoped that by telling their stories to the Inquiry and making them available for publication these witnesses felt that they had been heard.

**6.375** As was stated at the start of this section of the Report, the evidence of the patient and relative witnesses makes its own impact and it would be inappropriate to single out particular aspects for comment. What can be said is that the Inquiry heard many tales of truly extraordinary bravery in the face of adversity. There were also tales of resignation and tales of rage. For all patients and relatives the consequences of infection were at least distressing, for many they were devastating and, for some, tragic.

---

<sup>722</sup> Ibid, pages 36–37; Christine's Witness Statement

<sup>723</sup> Day 28, page 37

<sup>724</sup> Ibid, page 108; Christine's Witness Statement

<sup>725</sup> The process involved in providing a witness statement to the Inquiry is described in Appendix 2

**6.376** The Inquiry is particularly indebted to those witnesses who agreed to give oral evidence to the Inquiry. In doing so, these witnesses opened their lives up to intense scrutiny by others. As will be apparent from the narration of their evidence, each of these witnesses was both candid and brave. In recounting their stories they required to revisit very difficult, painful and sad times in their past as well as recounting ongoing effects which, understandably, they might be trying to forget. Some of the witnesses became visibly distressed when giving their evidence while others showed quiet stoicism. The impact of their evidence was felt by all those present and everyone was moved by it. It is hoped that the narration of the evidence of each of these witnesses in such detail is able to convey, as closely as possible, the power of it. This evidence illustrated just how far into a person's life the impacts of infection could reach. Of course it must be remembered that for each of these stories there are others, every one unique and compelling in its detail.

**6.377** Finally, it is a matter of sorrow to the Inquiry team that some of the witnesses who provided statements and Gordon, who gave oral evidence to the Inquiry, died before this report was published. Gordon impressed all those who heard his evidence as a dignified and intelligent man. Like others, he took a great interest in the work of the Inquiry and he did all he could to assist with its task.

## CHAPTER 7

### AN INVESTIGATION INTO THE DEATHS OF THE REVEREND DAVID BLACK, MRS EILEEN O'HARA, MR ALEXANDER BLACK LAING AND MR VICTOR TAMBURRINI

#### Introduction

**7.1** The matters which the Inquiry was asked to investigate and report upon were set out in the Terms of Reference issued up by the Cabinet Secretary for Health and Wellbeing, following consultation. Term of Reference 6 required the investigation of the deaths of certain named individuals with particular reference to the circumstances in which they became infected with Hepatitis C, HIV or both. In the event, none had acquired infection with HIV.

Term of Reference 6.

To investigate the deaths of Reverend David Black, Mrs Eileen O'Hara, Alexander Black Laing and Victor Tamburrini, with particular reference to the circumstances in which they became infected with the Hepatitis C virus, HIV or both.

**7.2** Originally, the Inquiry was required to investigate the deaths of Reverend Black and Mrs O' Hara only. Those particular deaths were selected as the personal representatives of the two deceased had raised proceedings in the Court of Session to challenge decisions made by the Lord Advocate and the Scottish Ministers, respectively, not to investigate the circumstances of those deaths. In February 2008 the Court of Session quashed the Lord Advocate's decision. The Scottish Ministers' decision was not then quashed having regard, amongst other things, to the fact that on 16 June 2007 the Scottish Government had re-affirmed its commitment to hold 'a general Public Inquiry' to 'find out why people were infected with Hepatitis C through NHS treatment'. Upholding that commitment, on 23 April 2008 the Scottish Ministers set up this Inquiry under the Inquiries Act 2005. On 13 November 2009, the Scottish Ministers added three further deaths for investigation: Mr Laing, Mr Tamburrini and Mr Neil Mullen. On 22 February 2011, however, at the request of his family, Mr Mullen's name was removed from the list of deaths to be investigated. As noted above, none of the individuals whose deaths the inquiry was asked to investigate was infected with HIV.

**7.3** As the personal representatives of the deceased were expected to have a key role during the Inquiry, they applied for and were designated as Core Participants. In addition, they were awarded funding for their legal representation, which was provided through Thompsons, Solicitors. The four personal representative Core Participants were:

- Mrs Jean Black as the personal representative of the Reverend Black.
- Mrs Roseleen Kennedy as the personal representative of Mrs O'Hara.
- Mrs Annie Laing as the personal representative of Mr Laing.
- Mrs Jean Tamburrini as the personal representative of Mr Tamburrini.

**7.4** An important early step in the investigation process was the obtaining of the medical records of the deceased. Principals were obtained where they existed. Records were recovered from the relevant Health Boards and the Crown Office and Procurator Fiscal Service. Documents were also recovered from the Scottish National Blood Transfusion Service (SNBTS).

**7.5** Suitable medical experts were identified and instructed to provide independent, expert reports in order to help focus the issues for investigation into each of the deaths. The expert reports were circulated for observation and comment to the legal representatives of all the Core Participants which, in addition to the personal representatives, included Haemophilia Scotland, the Scottish Ministers, the SNBTS,<sup>1</sup> the 14 Scottish Area Health Boards and 15 individuals as representative of classes of patient interests.

**7.6** Written statements were taken from the personal representatives of the deceased and other individuals.

**7.7** The public hearings began with the taking of detailed evidence relating to each of the deaths. This approach was adopted in order to ensure that any issues which arose in the course of those investigations and which had significance beyond the individual death under consideration could be noted and explored subsequently in the course of the topic-based investigations. Accordingly, information obtained as a result of the intense scrutiny to which each death was subjected assisted in understanding important systemic issues which were of relevance in the later consideration of many of the additional terms of reference. Evidence on the deaths was heard over four days, from 8–11 March 2011 and 12 witnesses appeared in order to assist the Inquiry in this matter.

**7.8** Immediately following the conclusion of this evidence, a public session was held at which Senior Counsel for the Inquiry and Counsel representing the Core Participants sought to identify systemic issues arising from the evidence. In the event, no issues additional to those already scheduled to be covered in hearings arose from evidence in relation to the specific deaths.

**7.9** Before the conclusion of the Oral Hearings phase of the Inquiry, all Core Participants' legal representatives were invited to make written submissions on what they considered to be the questions and issues arising from the evidence. They were also permitted to comment upon the written submissions of other Core Participants.

**7.10** The personal representatives of the deceased, Haemophilia Scotland and the patient interest Core Participants, who were all legally represented by Thompsons, Solicitors, jointly made written submissions in relation to the deaths. The SNBTS and the Health Boards, jointly represented by the Central Legal Office of the Common Services Agency, provided comments in relation to the submissions on the Reverend Black and Mr Laing.

**7.11** Having considered all the evidence before the Inquiry, this chapter sets out the Inquiry's findings in relation to each of the deaths.

## **Reverend David Black**

**7.12** Mr Black was born on 1 May 1937. He died on 31 October 2003 at Strathcarron Hospice, Stirlingshire. The cause of death was registered as hepatocellular cancer in a transplanted liver, Hepatitis C, transfusion of blood products and haemophilia.<sup>2</sup>

---

<sup>1</sup> The SNBTS is one of the health support services provided by the Common Services Agency (CSA) for the Scottish Health Service. The CSA is the designated Core Participant on behalf of the SNBTS.

<sup>2</sup> Death Certificate [BLA.001.2118]

## Mr Black's early medical history in relation to haemophilia

**7.13** There was a history of haemophilia in Mr Black's family.<sup>3</sup> He was diagnosed as having the disease in the early 1940s when he was five.<sup>4</sup> A possible alternative diagnosis of von Willebrand's disease<sup>5</sup> was considered in the early 1970s.<sup>6</sup> However, his von Willebrand Factor antigen was 65% of normal, the relevant bleeding time test was normal and the correct diagnosis was almost certainly Haemophilia A.<sup>7</sup> When his condition was investigated, it was found that he had a resting Factor VIII level of between three and seven international units per decilitre (3–7%).<sup>8</sup> Along with his history of treatment, that was consistent with mild to moderate Haemophilia A.<sup>9</sup> For the purposes of this Report, that diagnosis is accepted.

**7.14** Mr Black's early medical history was typical of a child with relatively mild haemophilia. He did not have haemarthrosis (bleeding into his joints) or spontaneous bleeding. He required occasional treatment with blood, blood components and blood products in response to specific events, however. Mr Black was probably first treated aged five when he had a haemorrhage; thereafter, on his own account, he was given 'transfusions', mainly for procedures such as tooth extractions from time-to-time.<sup>10</sup> His early records were incomplete: it was recorded that he had been given blood or plasma once at Edinburgh Sick Children's Hospital and twice at Glasgow Western Infirmary.<sup>11</sup> In October 1965, it was recorded that he had received plasma once at the Glasgow Royal Infirmary (GRI), in 1957, when he had a sudden episode of haematuria (blood in the urine).<sup>12</sup> He was treated at various times at Professor Alexander Douglas' clinic and by Dr Paul Davis, Dr Colin Prentice and Professor Gordon Lowe (who would become Co-Director of the Glasgow Hemophilia Centre in 1988).

**7.15** More detailed records were available from the 1960s and Mrs Black was able to supplement these from her own recollection. Mr and Mrs Black met in 1961.<sup>13</sup> Mrs Black had been a nurse and was more familiar than some with the diseases and terminology relevant to the Inquiry.<sup>14</sup> The account of Mr Black's medical history reflects her evidence in addition to evidence drawn from Mr Black's medical records. Mrs Black was rather frail at the date of the Inquiry's Oral Hearings. So far as her positive recollections are concerned, her written witness statement is accepted as generally true and reliable. Not surprisingly, there are omissions from her account and some of these at least were made good by the medical records.

**7.16** Mr Black was admitted to the GRI on 20 October 1965, then aged 28, for a tooth extraction. He was given four flasks of antihæmophilic globulin (AHG), an early form of NHS Factor VIII concentrate prepared in Edinburgh.<sup>15</sup> AHG was a crude plasma product

---

<sup>3</sup> Family history in Glasgow Royal Infirmary (GRI) records [BLA.001.2121] to [BLA.001.2123] and [BLA.001.2126]

<sup>4</sup> Dr Colvin – Day 2, page 76; GRI pro forma for assessment of haemophilia etc [BLA.001.2164]

<sup>5</sup> A different blood coagulation disorder. See the Preliminary Report at paragraphs 3.15–3.17

<sup>6</sup> Letter from GRI to GP dated 3 June 1971 [BLA.001.2149]

<sup>7</sup> Dr Colvin's report [BLA.001.2281] at 2284; Letter from GRI to GP dated 9 April 1971 [BLA.001.2151]

<sup>8</sup> Factor VIII level is a measure of coagulant activity. See Chapter 2, *Patients at Risk*, paragraph 2.26 for discussion of relative levels of severity.

<sup>9</sup> Dr Colvin – Day 2, pages 79–84; Dr Colvin's report [BLA.001.2281] at 2283

<sup>10</sup> GRI pro forma for assessment of haemophilia etc [BLA.001.2164]; RIE clinical note dated 20 March 1996 [BLA.001.1740]; Dr Colvin – Day 2, page 78

<sup>11</sup> GRI pro forma for assessment of haemophilia, etc [BLA.001.2164]

<sup>12</sup> Extract from GRI medical notes dated 20 October 1965 [BLA.001.2213]

<sup>13</sup> Witness statement of Mrs Black [PEN.001.0011]

<sup>14</sup> Statement by Counsel to the Inquiry – Day 2, page 69

<sup>15</sup> GRI report to GP dated 11 November 1965 [BLA.001.2204]; GRI Haematology form dated 22 October 1965 [BLA.001.2200]. Bottles identified as 3019C; 2727C; AF3097; 3013B without further description. The product was prepared by Cohn fractionation. The process is described in Chapter 20, *Haemophilia Therapy – The Period up to the Early 1980s*.



and Mr Black was given phenergan and cortisone, probably to reduce or eliminate the risk of an allergic reaction to the treatment. In the event, the extraction was without difficulty and bleeding was not troublesome.<sup>16</sup>

**7.17** The next recorded hospital visit was in May 1969 when he again required dental treatment.<sup>17</sup> On this occasion he was probably treated with cryoprecipitate, a frozen plasma product derived from a single donor's blood. AHG was by this point in short supply; by that date, treatment with cryoprecipitate was in general use throughout the UK.<sup>18</sup>

**7.18** Mr Black also received treatment abroad. Though specific instances are recorded, there is inevitably a lack of certainty about his history of treatment in other countries. He was a Baptist minister and worked both in the USA and in developing countries. At one point he worked for Oxfam. After their marriage, he, Mrs Black and their family travelled widely. Inevitably, there is a risk that his Scottish medical records do not reflect all of the treatment he received and some of his known history depends solely on Mrs Black's recollection.<sup>19</sup>

**7.19** Mrs Black said that her husband received blood products in San Jose, California, in 1970 when treated for a kidney stone.<sup>20</sup> He was working in South Korea at the time and was treated en route to or from there.<sup>21</sup> At this time, US pharmaceutical companies were in the vanguard in developing large-pool concentrates (concentrates, that is, prepared from a large number of donations from a large number of donors). Clinicians there were ahead of UK doctors in the use of concentrates: Dr Brian Colvin<sup>22</sup> said that he and his colleagues at the London Hospital were just beginning to use them in 1970. He thought that it was entirely possible that treatment received by Mr Black in the USA in 1970 would have involved an American large-pool concentrate.<sup>23</sup> A positive finding to that effect cannot be made, however, as cryoprecipitate continued to be the therapeutic material of choice for some clinicians at this time. Mr Black was treated by Dr Judith Pool in Stanford Medical Centre.<sup>24</sup> Dr Pool, noted by Dr Colvin as the 'founding mother' of modern haemophilia care, described the preparation of cryoprecipitate in 1964 and 1965<sup>25</sup> and reported use of that product in 1966.<sup>26</sup> It is not unlikely that she would have continued to use cryoprecipitate, the product she had devised and developed, even though early forms of large-pool concentrates were becoming available. It is not possible to resolve the issue of which product she may have used to treat Mr Black in 1970.

**7.20** For a period after 1970, Mr Black had no treatment in the UK. He was referred to the GRI following his treatment in the USA<sup>27</sup> and had tests in April and May 1971.<sup>28</sup> In April, he reported no haemostatic problems and the examination disclosed no other problems at that time apart from some slight tenderness over the left renal angle (the area

---

<sup>16</sup> GRI report to GP dated 11 November 1965 [BLA.001.2204]

<sup>17</sup> Letter from GRI to Mr Black dated 23 April 1969 [BLA.001.2154]

<sup>18</sup> Dr Colvin – Day 2, page 92

<sup>19</sup> Witness statement of Mrs Black [PEN.001.0011]

<sup>20</sup> Ibid [PEN.001.0011] at 0012

<sup>21</sup> GP request to GRI for out-patient consultation dated 22 March 1971 [BLA.001.2153]

<sup>22</sup> At that time a junior doctor in haematology and latterly Director of the Haemophilia Centre at Barts and The London Hospital.

<sup>23</sup> Day 2, page 119. Commercial Factor VIII was licensed in the UK in 1972. Until then it was available only for clinical trials and for routine treatment on a named patient basis. Before the Oral Hearings Dr Colvin had not been aware of Mr Black's treatment in the US.

<sup>24</sup> Letter from GRI to Dr Pool dated 7 April 1971 [BLA.001.2152]

<sup>25</sup> See Chapter 20, *Haemophilia Therapy – The Period up to the Early 1980s*, paragraphs 20.21–20.22

<sup>26</sup> *New England Journal of Medicine*, 1966; 275:966: letter commenting on use [PEN.018.1455]

<sup>27</sup> GP request to GRI for out-patient consultation dated 22 March 1971 [BLA.001.2153]

<sup>28</sup> Letter from GRI to Dr Pool dated 07 April 1971 [BLA.001.2152]; letter from GRI to GP dated 9 April 1971 [BLA.001.2151]; and see Mr Black's hospital notes [BLA.001.2218]

of the lower back around the site of the kidney).<sup>29</sup> In May, he was seen by Dr J F Davidson, who reported that Mr Black was still complaining of vague ill-health, with an ache in his right lumbar region, and that they could find no cause for his backache.<sup>30</sup> On 7 February 1973, the Regional Haemophilia Centre wrote to him asking him to attend in order to bring his records up to date, as he had not been reviewed at the Centre for four years.<sup>31</sup> In February 1974 he had chest pains and was referred to the GRI.<sup>32</sup> In May 1974, he reported that he had been keeping fairly well and had not had bleeding problems, although he again expected to need dental treatment.<sup>33</sup> Mr Black appears to have changed GPs about mid-January 1975. A letter dated 17 January 1975 was sent to his new GP informing him of the Haemophilia Centre's interest. The letter commented that Mr Black did not appear to have any problems except when faced with a haemostatic challenge (such as trauma, surgery and dental extractions); when that occurred, he would require active Factor VIII replacement therapy.<sup>34</sup> That was consistent with his recorded history up to that point.

**7.21** On 26 and 27 June 1975, Mr Black attended the GRI with pain in his left knee. On clinical examination this was thought to relate to a haematoma (subcutaneous clotted or partially clotted blood) rather than a haemarthrosis. He had factor replacement therapy at that stage, probably with large-pool concentrate.<sup>35</sup> In May 1978 he required SNBTS Factor VIII concentrate and cryoprecipitate to support a tooth extraction.<sup>36</sup> In February 1979, Mr Black again had cryoprecipitate prior to a dental extraction and, on this occasion, also to deal with post-extraction bleeding.<sup>37</sup>

## Evidence of Hepatitis C infection

**7.22** Mr Black was reviewed in the autumn of 1976<sup>38</sup> and in the spring of 1978.<sup>39</sup> He did not report any bleeding problems but on the second visit complained of chest and abdominal pains. Tests were negative for abnormalities of the oesophagus, stomach and duodenum (the first section of the small intestine) and there was no evidence of a peptic ulcer.<sup>40</sup> In September 1978, his condition was unchanged and he reported no new problems.<sup>41</sup> There were no recorded signs of hepatitis infection at that time, although, in retrospect, his blood test results can be associated with Hepatitis C infection.

**7.23** On 14 December 1979, elevated liver function test results were recorded for the first time when his transaminase GOT<sup>42</sup> was 97.<sup>43</sup> The majority of his liver function test results after this date were abnormal.<sup>44</sup> As the natural history of the disease is now understood, this was typical of Hepatitis C infection, then covered by the umbrella term 'non-A non-B Hepatitis' (NANB Hepatitis). There were few diagnoses of NANB Hepatitis in Scotland

---

<sup>29</sup> Letter from GRI to GP dated 9 April 1971 [BLA.001.2151]

<sup>30</sup> Letter from GRI to GP dated 3 June 1971 [BLA.001.2149]

<sup>31</sup> Letter from GRI to Mr Black dated 7 February 1973 [BLA.001.2146]

<sup>32</sup> Letter from GRI to GP dated 22 February 1974 [BLA.001.2145]

<sup>33</sup> Letter from GRI to GP dated 30 May 1974 [BLA.001.2142]

<sup>34</sup> Letter from GRI to GP dated 17 January 1975 [BLA.001.2139]. The word 'change' in the letter should be read as 'challenge.'

<sup>35</sup> Letter from GRI to GP dated 30 June 1975 [BLA.001.2137]; Dr Colvin – Day 2, page 95

<sup>36</sup> GRI Haemophilia Centre Treatment Sheet [BLA.001.2231]; Dr Colvin's report [BLA.001.2281] at 2284

<sup>37</sup> GRI Haemophilia Centre Treatment Sheet [BLA.001.2231]

<sup>38</sup> Letter from GRI to GP dated 22 October 1976 [BLA.001.2135]

<sup>39</sup> Letter from GRI to GP dated 26 May 1978 [BLA.001.2134]

<sup>40</sup> Letter from GRI to GP dated 9 June 1978 [BLA.001.2133]

<sup>41</sup> Letter from GRI to GP dated 6 September 1978 [BLA.001.2132]

<sup>42</sup> 'Transaminase GOT' is Glutamic-oxaloacetic transaminase, a blood enzyme. GPT (Glutamic-pyruvate transaminase), another blood enzyme, was also elevated. According to Dr Colvin (Day 2, page 97) normal levels for both are about 40. Other 'liver function tests' more frequently referred to in the records are Alanine Aminotransferase (ALT) and Alkaline-phosphatase tests. They have broadly the same significance in the diagnosis of hepatitis.

<sup>43</sup> GRI Blood Investigation Sheet [BLA.001.2232]

<sup>44</sup> Dr Colvin's report [BLA.001.2281] at 2284

before the late 1980s.<sup>45</sup> In Mr Black's case, however, it was recognised by 1985 that he had NANB Hepatitis, for which no treatment was then available.<sup>46</sup> There was also evidence of previous exposure to Hepatitis B but not of ongoing infection.<sup>47</sup>

**7.24** Mr Black had a bleed into the tibial muscles of his right leg in about April 1981. On review on 9 April 1981, the last previous episode reported was of bleeding into the renal tract while in America.<sup>48</sup> When he was seen for routine review in September 1984, there was mild crepitus (a 'crackling' sound) in his right knee, suggestive of some underlying arthritis. He also complained of occasional lower back pain. Clinical examination was not remarkable and his liver function tests were normal.<sup>49</sup> In December 1985, liver function test results were again significantly elevated.<sup>50</sup> Dr Colvin thought that it was difficult to make much of the increase, however, as fluctuating transaminase results are typical of NANB Hepatitis/Hepatitis C. Inflammation of the liver varies from time to time and it was necessary to look at a sequence of results to tell whether the patient truly had an increase in transaminases.<sup>51</sup>

**7.25** In 1987, Mr Black was in Fort Pierce, Florida. He was admitted to hospital there on 30 September complaining of black stools, generalised weakness and lethargy. He was given packed red cell support and cryoprecipitate. He had a Computerised Tomography (CT) scan which proved to be negative for retroperitoneal haematoma or any other intra-abdominal pathology.<sup>52</sup> Upper endoscopy revealed Grade 1 oesophageal varices.<sup>53</sup> This was the first significant episode of clinically apparent liver disease. Liver damage causes a build-up of pressure in the portal venous system which backs up into the stomach and oesophagus and causes internal varicose veins (oesophageal varices) to develop.<sup>54</sup> Though not specifically related to Hepatitis C, in that the condition can have other causes, oesophageal varices associated with liver damage are a frequent complication of cirrhosis.<sup>55</sup> The doctors in Fort Pierce apparently suggested to Mr Black that there was an underlying cause of the varices and that his liver damage was potentially virus-related.<sup>56</sup>

**7.26** On return to Scotland, Mr Black was admitted to the GRI in October 1987, where he gave an account of his experience in the USA. On examination, the US findings of varices were confirmed. Mr Black had an old Mallory-Weiss tear (scarring at the gastro-oesophageal junction), a condition usually associated with vomiting.<sup>57</sup> By 1987, the liver and spleen were palpable (noticeable to the touch in examination) and there was evidence of chronic liver disease.<sup>58</sup> Mr Black was informed that the virus could have caused his diseased liver to become cirrhotic.<sup>59</sup> Portal hypertension and the oesophageal varices

---

<sup>45</sup> Professor Hayes – Day 78, pages 46–48; Professor Hayes' report [PEN.018.0240] at 0240–0241. See Chapters 14–16, *Knowledge of Viral Hepatitis 1 to 3*.

<sup>46</sup> Letter from GRI to GP dated 16 December 1985 [BLA.001.0863]

<sup>47</sup> Dr Colvin's report [BLA.001.2281] at 2284

<sup>48</sup> Letter from GRI to GP dated 10 April 1981 [BLA.001.0869]

<sup>49</sup> Letter from GRI to GP dated 4 September 1984 [BLA.001.0867]

<sup>50</sup> Letter from GRI to GP dated 16 December 1985 [BLA.001.0863] Bilirubin and alkaline phosphatase were slightly elevated, while transaminases were markedly elevated.

<sup>51</sup> Day 2, pages 99–101

<sup>52</sup> Discharge Summary from Lawnwood Regional Medical Center after discharge on 3 October 1987 [BLA.001.0861]

<sup>53</sup> *Ibid* [BLA.001.0861] at 0862

<sup>54</sup> Dr Colvin – Day 2, pages 102–103; Dr Bathgate – Day 1, pages 31–32

<sup>55</sup> Dr Bathgate – Day 1, pages 31–32; Dr Colvin – Day 2, page 102

<sup>56</sup> Witness statement of Mrs Jean Black [PEN.001.0011] at 0012

<sup>57</sup> GRI Discharge Report following admission between 14 and 16 October 1987 [BLA.001.0859]; Dr Colvin – Day 2, page 104

<sup>58</sup> Dr Colvin's report [BLA.001.2281] at 2284

<sup>59</sup> Witness statement of Mrs Jean Black [PEN.001.0011] at 0012. As per statement by Counsel to the Inquiry (Day 2, page 70), Mrs Black confirmed that the word 'sclerosis' in paragraph 7 of her statement should be 'cirrhotic'.

were treated in a conventional way.<sup>60</sup> Injection sclerotherapy (injection of a hardening solution) was performed on the varices.<sup>61</sup>

**7.27** As noted in paragraph 17.23 above, the biochemical abnormalities found in December 1979 were typical of NANB Hepatitis/Hepatitis C infection. By 1987, Mr Black's condition had progressed: there were Grade 1 oesophageal varices, the liver and spleen were palpable and there was portal hypertension. Dr David Mutimer, Consultant Hepatologist, Queen Elizabeth Hospital, Birmingham, considered that it could be assumed that cirrhosis was present in 1987. Since Hepatitis C typically takes at least two decades to develop in a person infected when young, infection had probably been acquired by Mr Black in the 1960s.<sup>62</sup> Dr Mutimer's evidence is accepted.<sup>63</sup> Since his evidence was that it takes 'at least' two decades for the disease to develop, however, the beginning of the period within which transmission occurred remains uncertain.

### Source of infection

**7.28** No specific source of infection has been clearly demonstrated. In Dr Mutimer's experience, Mr Black's history was fairly typical of patients with haemophilia who acquired Hepatitis C at a fairly young age. After a long duration of infection, he developed severe liver damage with cirrhosis and portal hypertension.<sup>64</sup> Rates of progression to cirrhosis, decompensated cirrhosis, hepatocellular cancer and liver-related death are closely related to age at infection.<sup>65</sup>

**7.29** Since there were abnormal liver test results by 1979, and since cirrhosis was established by 1987, it is unlikely, but not impossible, that Mr Black was infected in the USA in 1970. He was then about 33 and at the lower end of the cohort of male patients at the highest risk of developing cirrhosis within 30 years.<sup>66</sup> Having regard to Dr Mutimer's evidence about the natural history of Hepatitis C, the period between 1970 and 1987 was probably too short to provide a reliable basis to infer that the infection was transmitted at this time. On the other hand, some 10% of patients do develop cirrhosis in 15 to 20 years and the possibility of infection in 1970 cannot be wholly excluded. Dr Mutimer's evidence more confidently excludes from responsibility for Mr Black's infection the use of Factor VIII concentrate in 1975 and 1978 and the use of cryoprecipitate in 1978 and later.

**7.30** There are three remaining possibilities: the use of blood and plasma up to the late 1950s, the single known infusion of AHG in 1965 and the cumulative use of cryoprecipitate up to the late 1960s. At the material time, AHG was prepared in Edinburgh from plasma pooled from small numbers of donors, limited by the processing capacity of the equipment available at the Royal Infirmary of Edinburgh (RIE). In 1965 the prevalence of Hepatitis C in the blood donor population is likely to have been relatively low and, statistically, the chances of an individual batch of AHG being infected were very low. In the absence of specific evidence it would be impossible to find positively that this procedure was the cause of Mr Black's infection. It might have transmitted infection, however: blood, plasma, AHG and cryoprecipitate were all capable of transmitting infection.

---

<sup>60</sup> Dr Colvin's report [BLA.001.2281] at 2284

<sup>61</sup> GRI Discharge Report following admission between 31 October 1987 and 16 November 1987 [BLA.001.0856] at 0857

<sup>62</sup> Dr Mutimer's report [BLA.001.2277] at 2277–2278

<sup>63</sup> See also Dr Mutimer, Day 1, pages 111–112; Professor Hayes, Day 78, pages 55–56 and Yee et al, 'The Natural History of HCV in a cohort of haemophilic patients infected between 1961 and 1985', *Gut*, 2000; 47:845–851 [LIT.001.4318] at 4323

<sup>64</sup> Dr Mutimer's report [BLA.001.2277] at 2277

<sup>65</sup> Chapter 13, *Knowledge of Viral Hepatitis Now*, paragraphs 13.68–13.69

<sup>66</sup> *Ibid* paragraph 13.71

**7.31** There was discussion of whether the continued use of cryoprecipitate in Mr Black's therapy in the period 1987–88 was appropriate.<sup>67</sup> Dr Colvin's evidence was that, at that time, to counter the risk of transmission of HIV, effective virus inactivation of factor concentrates had led to a change in recommended practice from the use of cryoprecipitate to the use of heat-treated concentrates. In 1986, when a test for HIV infection had become available, Mr Black had been tested and proved negative.<sup>68</sup> Dr Colvin's view was that, since Mr Black's liver function tests were already abnormal by the mid-1980s and Mr Black was HIV-negative, the use of cryoprecipitate after the introduction of virally inactivated large pool concentrates in the mid-1980s was clinically irrelevant to his case. That view is accepted.

**7.32** So far as is material, Dr Colvin thought that Mr Black had probably had enough single donor unit products to expose him to a high risk of having already contracted Hepatitis C before he was first treated with a large pool concentrate around 1975.<sup>69</sup>

**7.33** Dr Mutimer reviewed Mr Black's medical records. In his view, exposure to Hepatitis C was almost inevitable as a consequence of the treatment he received for haemophilia.<sup>70</sup> His view was similar to Dr Colvin's.<sup>71</sup> Mr Black had been treated with doses of single donor cryoprecipitate and with Factor VIII concentrate. The more bags or bottles of cryoprecipitate a patient received on a random basis, the greater the chance was that eventually the patient would receive a dose that was infected with Hepatitis C. Every time the patient was treated the risks were the same and, eventually, an infected unit would be transfused.

**7.34** In conclusion, Mr Black contracted Hepatitis C from infected blood products. For all practical purposes, infection with Hepatitis C was inevitable given the requirements of haemophilia therapy. Given the wide range of possible durations implicit in Dr Mutimer's evidence about the natural history of the disease, it is not now possible to be specific as to the source of infection. On balance, and on the evidence available to the Inquiry, the most likely source was therapeutic blood products administered in Scotland. It is highly likely that Mr Black was infected by NHS cryoprecipitate or concentrates, probably in the 1960s.<sup>72</sup>

### **Progress of infection**

**7.35** Mr Black was due to visit Kenya and Uganda in February 1986. He had a series of tests in advance and it was noted that his transaminases were markedly elevated at that time.<sup>73</sup> In November 1986 and August 1987 he had further dental treatment supported by cryoprecipitate.<sup>74</sup> On each occasion further treatment was required for post-extraction bleeding.

**7.36** At about this time Mr Black's health began to take a turn for the worse. As noted in paragraph 7.25 above, he was admitted to hospital in the USA on 30 September 1987. Beginning on 14 October 1987, after his return to Scotland, he had frequent and

---

<sup>67</sup> Dr Colvin's report [BLA.001.2281] at 2285; Day 2, pages 113–118

<sup>68</sup> GRI Blood Investigation Sheet (HIV -ve on 21 November 1986) [BLA.001.2232]

<sup>69</sup> Day 2, pages 111–112

<sup>70</sup> Report [BLA.001.2277]

<sup>71</sup> Dr Colvin's report [BLA.001.2281] at 2286

<sup>72</sup> Dr Colvin – Day 2, pages 111–112

<sup>73</sup> Letter from GRI to GP dated 16 December 1985 [BLA.001.0863]

<sup>74</sup> GRI Haemophilia Centre Treatment Sheet [BLA.001.2231]

substantial cryoprecipitate therapy for gastro-intestinal bleeding.<sup>75</sup> In March 1988, he was treated with SNBTS Factor VIII concentrate.<sup>76</sup> Home treatment with SNBTS Factor VIII was prescribed from January 1990 and amounted to 24,850 units in the course of the year.<sup>77</sup> Home treatment continued into 1991. By September 1991, the presumption of his clinicians was that Mr Black's varices were secondary to Hepatitis C as a consequence of the blood products he had received over the years for haemophilia.<sup>78</sup> On 14 October 1991, Mr Black was found to be positive for the antibody to Hepatitis C and that was confirmed by the RIBA-2 test.<sup>79</sup> In August 1992, Monoclate, a commercial Factor VIII product, was prescribed.<sup>80</sup> In 1993, he received further commercial concentrate, HP Factor VIII.<sup>81</sup> Mr Black was now being treated more frequently with factor concentrates.

**7.37** In March 1994 a referral was made for consideration of Interferon therapy for the treatment of Hepatitis C. There was extensive discussion and the consultant gastroenterologist, Dr J F MacKenzie, advised that therapy should be tried.<sup>82</sup> Dr Colvin thought it unlikely that treatment would have been effective, however.<sup>83</sup> Dr Mutimer agreed: Mr Black had already developed cirrhosis with evidence of decompensation. Interferon was the only therapy available and was unlikely to help under those circumstances. In retrospect, in all probability, had antiviral therapy been given, it 'would have caused significant morbidity and was unlikely to cure the infection'.<sup>84</sup> Therapy was not started, partly because Mr Black was reluctant to undergo treatment.<sup>85</sup> This was an early indication of Mr Black's attitude to therapy which he was to repeat in response to advice from time to time thereafter.

**7.38** In late spring 1994, Mr Black was again in the USA. While there, he developed gross ascites and pitting oedema (abnormal accumulations of fluid in body cavities), both due to salt and water retention and attributable to liver failure.<sup>86</sup> When back in Glasgow, he was told that he would not be well enough to travel to Italy two weeks' from then as he had intended.<sup>87</sup>

**7.39** On 6 April 1995, Dr MacKenzie reported to Professor Lowe that there had been a very slow deterioration in liver function and that Mr Black remained 'unkeen' on any medication. Dr MacKenzie suggested that a liver transplant might become an option within the next few years.<sup>88</sup> In May 1995, Dr MacKenzie raised the subject of transplant with Mr Black again. Following discussion, he referred the question whether early- or medium-term transplant would be appropriate, to Dr Alastair MacGilchrist at the Liver Transplant Unit (LTU), RIE, in a letter dated 22 May. Mr Black had indicated that he wanted to discuss the matter with Dr MacGilchrist.<sup>89</sup>

---

<sup>75</sup> Ibid [BLA.001.2231]

<sup>76</sup> GRI Haemophilia Centre Treatment Sheet [BLA.001.2230]

<sup>77</sup> GRI Haemophilia Centre Home Treatment Sheet [BLA.001.2228]

<sup>78</sup> Letter from Haemophilia Unit GRI to Department of Surgery GRI dated 24 September 1991 [BLA.001.0303]

<sup>79</sup> 'Recombinant Immunoblot Assay'; Regional Virus Laboratory Report dated 14 October 1991 [BLA.001.0533]

<sup>80</sup> GRI Haemophilia Centre Home Treatment Sheet [BLA.001.2226]

<sup>81</sup> GRI Haemophilia Centre Treatment Sheet [BLA.001.2225]

<sup>82</sup> Letter from GRI General Medicine to GRI Haemophilia Unit dated 13 April 1994 [BLA.001.0283]

<sup>83</sup> Dr Colvin – Day 2, page 109; Dr Colvin's report [BLA.001.2281] at 2285 (para 4.3) and 2286 (para 5.2)

<sup>84</sup> Dr Mutimer's report [BLA.001.2277] at 2278

<sup>85</sup> Witness statement of Mrs Jean Black [PEN.001.0011] at 0013; Letter from GRI General Medicine to GP dated 3 May 1994 [BLA.001.0281]

<sup>86</sup> Dr Mutimer – Day 2, page 125; Letter from GRI General Medicine to GP dated 13 June 1994 [BLA.001.0279]

<sup>87</sup> Letter from GRI General Medicine to GP dated 13 June 1994 [BLA.001.0279]

<sup>88</sup> Letter from GRI General Medicine to GRI Haemophilia Unit dated 6 April 1995 [BLA.001.0263]

<sup>89</sup> Letter from GRI General Medicine to LTU RIE dated 22 May 1995 [BLA.001.0260]

**7.40** Dr MacGilchrist saw Mr Black and reported to Dr MacKenzie on 3 July 1995. His assessment was:

Reverend Black is a good candidate for liver transplantation. Clearly, it will be a major undertaking for the blood transfusion service to supply sufficient quantities of Factor 8 to cover the procedure, but this should not be a major problem and ... transplantation has been undertaken successfully with patients with haemophilia elsewhere.<sup>90</sup>

**7.41** Mr Black returned to the LTU in September 1995 and was seen by a registrar. He had been researching his condition on his own initiative but was finding it difficult to obtain statistics regarding haemophilia patients who had been transplanted. He was reported to be 'anxious and giving rather mixed messages'. The registrar's view was that he was 'terrified' that his condition was going to deteriorate suddenly to the extent that it would preclude transplantation. She had tried to emphasise to him that that was not the natural course of events and proposed that he should come in for assessment.<sup>91</sup> He agreed and in October/November an assessment was carried out over four days.<sup>92</sup> After comprehensive review by a multidisciplinary team, it was decided that his current liver function and quality of life were such that he did not require liver transplantation at that stage.<sup>93</sup>

### **The transplant and progression of disease**

**7.42** In 1996, Mr Black's liver function had deteriorated to the point at which transplantation was considered appropriate.<sup>94</sup> Arrangements were made for him to be admitted for assessment on 18 March.<sup>95</sup> A liver transplant was performed on 21 April 1996<sup>96</sup> and Mr Black was in hospital from 20 April until 13 May. After the operation there was some fluid retention and he was prescribed antibiotics for spontaneous bacterial peritonitis but, by the time of discharge, he looked well with no symptomatic pallor, jaundice or leg swelling. He was to be reviewed in May.<sup>97</sup> The family was encouraged to be optimistic. Mrs Black told the Inquiry, 'The projections at this time were that his new liver would last his lifetime before the Hepatitis C had the chance to affect it.'<sup>98</sup>

**7.43** One potentially important finding was made at this time. Mr Black's own explanted liver was sent for detailed pathological examination following the transplantation procedure where it was discovered that his cirrhosis had been complicated by the development of primary hepatocellular cancer.<sup>99</sup> The extent to which that information influenced, or did not influence, his medical care over the following period became the subject of investigation at a later stage and is referred to in paragraph 7.55 onwards below.

**7.44** After surgery in April 1996, Mr Black continued to be monitored. When he was reviewed on 24 October 1996 there was a discussion of his long-term prospects. The report from a registrar in the LTU to his GP noted that Mr Black was obviously quite an anxious man. He had enquired about the long-term impact of Hepatitis C recurrence and

---

<sup>90</sup> Letter from LTU RIE to GRI General Medicine dated 3 July 1995 [BLA.001.1675] at 1676

<sup>91</sup> Letter from LTU RIE to GP dated 26 September 1995 [BLA.001.0253]

<sup>92</sup> LTU RIE Discharge Summary for GP dated 15 November 1995 [BLA.001.0249]

<sup>93</sup> Ibid [BLA.001.0249] at 0250

<sup>94</sup> Letter from LTU RIE to GP dated 7 March 1996 [BLA.001.1664]

<sup>95</sup> Letter from LTU to Mr Black dated 5 March 1996 [BLA.001.1665]

<sup>96</sup> LTU RIE Operation Record dated 21 April 1996 [BLA.001.1646]

<sup>97</sup> Discharge Letter from LTU RIE to GP dated 21 May 1996 [BLA.001.1422]

<sup>98</sup> Witness statement of Mrs Jean Black [PEN.001.0011] at 0014

<sup>99</sup> Pathology Result Enquiry Report dated 25 April 1996 [BLA.001.2289]; Dr Mutimer's report [BLA.001.2277]

the chances of developing cirrhosis. He was advised that the long-term prognosis was hard to predict, although it was reasonable to predict that his quality of life should be fairly good for the next 10 years.<sup>100</sup>

**7.45** Monitoring continued over the period from 1996 to 2002 and there were frequent discussions about the possibility of drug therapy for his ongoing Hepatitis C when Mr Black attended hospital. He remained uncertain, however. Dr MacGilchrist saw him on 11 December 1997. At that time he was keeping extremely well and working as hard as ever but his liver function tests were causing some concern. Those test results never returned completely to normal and, in particular, his ALT was quite significantly raised. Dr MacGilchrist thought that the results were most likely to represent recurrent hepatitis in his new liver. In order to avoid worrying him over the Christmas period, Mr Black was told only that his liver tests were slightly abnormal and that he should have a repeat test done by his GP in January 1998.<sup>101</sup>

**7.46** Mr Black was reviewed during 1998. In April, he was doing well and his liver function test results were slightly better.<sup>102</sup> In November 1998, however, his liver function test results were again causing concern.<sup>103</sup> When Mr Black was seen at the LTU in February 1999, matters had developed further. The report of the review to his GP stated:

He was informed that his liver biopsy showed recurrence of hepatitis C and that we would probably consider treating him for hepatitis C. He himself was not quite sure if that would be the best option for him at this present time as he felt that the side effects of Interferon would be too much for him. He agreed though to have an appointment with our hepatitis C team which will help discuss the options with him.<sup>104</sup>

**7.47** The review process continued in and after 1999. In June 1999 combination treatment with Interferon and Ribavirin was discussed with him but he remained rather reluctant to start it.<sup>105</sup> That continued to be his position for a period thereafter.

**7.48** In February 2001, Mr Black had a liver biopsy for further assessment of his Hepatitis C. Although he had earlier declined anti-viral therapy, consideration was again given to its commencement.<sup>106</sup>

**7.49** In April 2001, Dr Kenneth Simpson, LTU, had a long discussion with Mr Black about treatment. He commented in a letter to his GP that, with the introduction of combination Interferon and Ribavirin, treatment had improved and that Mr Black seemed much more receptive to the idea and had agreed to think about receiving treatment.<sup>107</sup> When he attended for review on 27 September 2001, Mr Black felt that he would be happier to wait before undertaking this therapy in view of the potential side-effects which he might find disruptive to his life. He was very busy at work.<sup>108</sup> Mr Black remained uncertain and Dr Mutimer thought that there was probably uncertainty on the side of the physicians as

---

<sup>100</sup> Letter from LTU RIE to GP dated 30 October 1996 [BLA.001.1453]

<sup>101</sup> Letter from LTU RIE to GP dated 18 December 1997 [BLA.001.1451]

<sup>102</sup> Letter from LTU RIE to GP dated 7 April 1998 [BLA.001.1442]

<sup>103</sup> Letter from LTU RIE to GP dated 12 November 1998 [BLA.001.1583] at 1584

<sup>104</sup> Letter from LTU RIE to GP dated 16 February 1999 [BLA.001.1416]

<sup>105</sup> Letter from LTU RIE to GP dated 2 June 1999 [BLA.001.1418]

<sup>106</sup> Letter from LTU RIE to GP dated 08 February 2001 [BLA.001.1428] at 1429

<sup>107</sup> Letter from LTU RIE to GP dated 20 April 2001 [BLA.001.0117]

<sup>108</sup> Letter from LTU RIE to GP dated 16 October 2001 [BLA.001.0111]



well: they were aware that the treatment was associated with significant side-effects and that the chances of success were fairly low. He thought that the decision Mr Black took to decline treatment was quite understandable.<sup>109</sup>

**7.50** In early 2002, Mr Black's liver function test results continued to show elevated ALT levels.<sup>110</sup> His work commitments were heavy, however, and a decision to start treatment was again deferred. In April 2002 Mr Black had an ultrasound scan with satisfactory results.<sup>111</sup> Liver biopsy revealed Hepatitis C virus fibrosis in the transplanted liver, short of cirrhosis but thought to be more advanced compared to the year before.<sup>112</sup>

**7.51** When seen in April 2002, Mr Black said that he might be more amenable to treatment as he was reducing his workload.<sup>113</sup> By that stage he had been told of dual therapy and the improved prospects of success it offered. He was seen by Dr Simpson on 8 August 2002. The diagnosis recorded in a letter to his GP and copied to other clinicians listed the transplant, previous haemophilia and recurrent Hepatitis C with significant fibrosis on liver biopsy.<sup>114</sup> On this occasion Mrs Black was at the review. The letter stated:

I had a long chat with Rev Black about the possibility of treatment, the conversation I had had with him previously. Certainly his liver biopsies have clearly demonstrated progressive fibrosis, and without attempting anti-viral treatment it is clear that he will develop recurrent cirrhosis. He again seemed quite keen in the clinic to start anti-viral treatment ....<sup>115</sup>

**7.52** In December 2002, Mr Black commenced treatment with pegylated Interferon and Ribavirin.<sup>116</sup> By then fibrosis was more advanced. The anti-viral treatment did not run smoothly.<sup>117</sup> He experienced anaemia severe enough to necessitate a transfusion.<sup>118</sup> The treatment was abandoned.<sup>119</sup>

**7.53** Dr Mutimer said:

The problem with the anaemia is due to the ribavirin component of his treatment, and the main problem is that the dose needs to be adjusted very carefully and frequently in patients if they have any degree of kidney dysfunction, which is quite common in the transplant patient. So I suspect the severe anaemia was because the level of the ribavirin was too high for the patient. But there are no useful published guidelines on picking the right dose.<sup>120</sup>

**7.54** In May 2003, Mr Black was admitted for ultrasound-guided liver biopsy. Scans had suggested a possible focal lesion. Two cores of tissue were taken and pathology confirmed hepatocellular carcinoma.<sup>121</sup> Dr Andrew Bathgate, by then a consultant physician at the LTU, told Mr Black that this had happened, and that it was clear from the imaging that

---

<sup>109</sup> Day 2, pages 134–135; Report [BLA.001.2277] at 2278

<sup>110</sup> Letter from LTU RIE to GP dated 27 February 2002 [BLA.001.0108]; Dr Mutimer – Day 2, pages 136–137

<sup>111</sup> Letter from LTU RIE to GP dated 30 April 2002 [BLA.001.0106]

<sup>112</sup> Letter from LTU RIE to GP dated 10 July 2002 [BLA.001.0102]

<sup>113</sup> Letter from LTU RIE to GP dated 30 April 2002 [BLA.001.1248]

<sup>114</sup> Letter from LTU RIE to GP dated 13 August 2002 [BLA.001.1244]

<sup>115</sup> Ibid [BLA.001.1244]

<sup>116</sup> Letter from LTU RIE to GP dated 16 December 2002 [BLA.001.1234]; Dr Mutimer – Day 2, page 138; Report [BLA.001.2277] at 2279

<sup>117</sup> Dr Mutimer – Day 2, page 138; Dr Mutimer's report [BLA.001.2277] at 2279

<sup>118</sup> Letter from LTU RIE to GP dated 27 January 2003 [BLA.001.0091]

<sup>119</sup> Letter from LTU RIE to GP dated 31 January 2003 [BLA.001.0090]; Dr Mutimer's report [BLA.001.2277] at 2279

<sup>120</sup> Day 2, page 138. (See Chapter 13, *Knowledge of Viral Hepatitis Now*, paragraphs 13.97–13.105, on current guidance on treatment for HCV infection.)

<sup>121</sup> Letter from LTU RIE to GP dated 4 June 2003 [BLA.001.0079]

the cancer was multifocal.<sup>122</sup> The cancer had spread, probably with multiple nodules throughout the liver.<sup>123</sup> It could not be treated.<sup>124</sup> Mr Black died on 31 October 2003.<sup>125</sup>

### **Hepatocellular cancer in the explanted liver: Mr Black's management as a patient**

**7.55** As noted in paragraph 7.43, Mr Black's pathology records revealed that the liver removed at the time of the transplant in 1996 was cancerous. Mrs Black said that it had come as a shock to the family to learn that Mr Black's own liver had been affected by cancer. She said that Mr Black was not aware of that fact and that the family was not aware either. Having regard to the evidence as a whole, including the retrospective investigations carried out by Dr MacGilchrist and comment by Dr Bathgate, it is clear that Mr Black was not told of the hepatocellular cancer in the explanted liver. The discharge letter sent to Mr Black's GP made no mention of any tumours.<sup>126</sup> Consequently, other than in relation to a communication dated 22 December 1998 (see paragraph 7.63 below) there is nothing to suggest that the GP knew of the finding.

**7.56** The full findings relating to the explanted liver were recorded in a pathology report dated 25 April 1996.<sup>127</sup> The external appearance was reported to be that of a macronodular cirrhotic liver showing a number of nodules of varying sizes. On section, the left lobe was found to contain a tumour mass of at least 4 x 3 x 3cm showing areas of necrosis as well as a large cystic necrotic cavity 2cm in diameter and a number of adjacent separate nodules, some of which showed necrosis. A separate nodule 2cm in diameter also displayed extensive necrosis. Throughout the right lobe there were several nodules that did not show significant necrosis but one, 2.5cm in diameter, showed extensive necrosis. In a summary of micro-examination it was noted that there were at least five separate nodules showing features of hepatocellular carcinoma on the left lobe and a further three tumours on the right lobe.

**7.57** Following his transplant surgery, Mr Black was transferred to the main ward of the LTU on 22 April 1996.<sup>128</sup> Apart from a weekend at home, he remained in hospital until 13 May.<sup>129</sup> During that time, his In-Patient Clinical Notes did not refer to cancer in the explanted liver. The letter sent to Mr Black's GP after review on 29 May 1996, noted as diagnosis: 'liver transplant for Hepatitis C related cirrhosis and Haemophilia A'.<sup>130</sup> On 17 June Mr Black returned to hospital when his notes recorded three diagnoses: Haemophilia A, Hepatitis C cirrhosis and that Mr Black was cytomegalovirus positive. In a side note it recorded: '(incidental HCC at op)' without further detail.<sup>131</sup>

**7.58** The detailed pathology report dated 25 April 1996 was not in the copy of the hospital records originally recovered by the Inquiry from the Crown Office. On 17 December 2010, the Central Legal Office wrote to the Inquiry with the information that an unnamed

---

<sup>122</sup> Letter from LTU RIE to GP dated 10 June 2003 [BLA.001.0078]; Dr Mutimer explained in evidence (Day 2, page 139) that a 'multifocal' tumour is one that has spread with multiple nodules.

<sup>123</sup> Dr Mutimer – Day 2, page 139

<sup>124</sup> Letter from LTU RIE to GP dated 10 June 2003 [BLA.001.0078]; Dr Mutimer – Day 2, page 140

<sup>125</sup> Death Certificate [BLA.001.2118]; Letter from Strathcarron Hospice to GP dated 4 November 2003 [BLA.001.1471]

<sup>126</sup> Letter from Surgical Registrar to GP dated 21 May 1996 [BLA.001.1422]

<sup>127</sup> Pathology Result Enquiry Report dated 25 April 1996 [BLA.001.2289]

<sup>128</sup> LTU RIE Clinical Notes [BLA.001.1760]

<sup>129</sup> Discharge letter from LTU RIE to GP dated 21 May 1996 [BLA.001.1422]; LTU RIE Clinical Notes dated 2 to 6 May 1996 [BLA.001.1764]

<sup>130</sup> Letter from LTU RIE to GP dated 5 June 1996 [BLA.001.1637]

<sup>131</sup> In-Patient Clinical Notes [BLA.001.1768] 'HCC' is a standard abbreviation for hepatocellular cancer.

haemophilia clinician had noted that a pathology report did not appear to be included in the records. With the letter were enclosed copies of a number of reports including a copy of the report dated 25 April 1996. The copy,<sup>132</sup> which appeared to be a print of an electronic record, was thereafter used during the Oral Hearings.

**7.59** Copies of the records of the LTU came to hand after the completion of the Oral Hearings. The original paper records had been scanned on 13 August 2012 and then destroyed. The LTU retains patients' records in electronic form in its TRAK record system and routinely destroys paper records. Electronic and hard copy prints of Mr Black's LTU records were sent to the Inquiry on 16 August 2013. They contained a further copy of the pathology report of 25 April which was initialled by Dr Bathgate, showing that the report had been received from pathology and entered the LTU records for Mr Black. The precise date when that occurred is not known but it was probably entered around the date it bears. Dr Bathgate explained in a letter dated 13 December 2013 that, at that time, written reports of explant pathology were routinely sent to the LTU doctors' room.<sup>133</sup> The transplant registrar was responsible for signing all laboratory reports before they were filed in the paper records of the LTU. The reports were reviewed at meetings of the consultant hepatologists and gastroenterology registrars held on Mondays at lunchtime. At the time it was not LTU practice to discuss explant pathology with patients while they were recovering from surgery. That remains the practice at present.

**7.60** It is clear from the evidence, and in particular from Dr Bathgate's letter, that the report of 25 April 1996 which he initialled as transplant registrar was at all material times contained in the paper and electronic records of the LTU relating to Mr Black and available to the clinical team looking after his interests from time to time. Dr Bathgate ceased to be transplant registrar at the end of April 1996. He was replaced by Dr Khalid Bzeizi.

**7.61** As already indicated, Mr Black was reviewed regularly at the LTU between May 1996 and July 1998. Letters to his GP reporting his progress frequently noted as his diagnosis as liver transplant for Hepatitis C, related cirrhosis and Haemophilia A. His history of hepatocellular carcinoma and the risk of recurrence were not mentioned.

**7.62** So far as the Inquiry has been able to discover, the next reference to the condition of the explanted liver after June 1996, was in December 1998. The clinical notes for 9 December said that Mr Black had been admitted for liver biopsy, noting abnormal LFTs and 'HCC recurrence'.<sup>134</sup> An explanatory note stated: 'Liver transplant for HCV cirrhosis 1996 Apr incidental HCC at operation', effectively repeating the note made on 17 June 1996. A subsequent note on the same day commented: 'note incidental HCC at OLT – (P) USS today + biopsy at that time ...'.<sup>135</sup> The reason for this procedure was Mr Black's continually raised liver function test scores.<sup>136</sup> On 10 December, it was reported that radiology and ultrasound scanning found no focal lesion.<sup>137</sup> Liver biopsy was performed and the provisional report showed changes compatible with recurrent Hepatitis C.<sup>138</sup>

---

<sup>132</sup> Copy of Report [BLA.001.2289]

<sup>133</sup> Dr Bathgate's letter to the CLO dated 13 December 2013 [PEN.019.1446]

<sup>134</sup> In Patient Clinical Notes (Surgical) [BLA.001.1773]

<sup>135</sup> In Patient Clinical Notes (Surgical) [BLA.001.1774]; 'OLT' and '(P) USS' are understood respectively to be abbreviations for 'Orthotopic Liver Transplant' and 'Planned Ultrasound Scan'.

<sup>136</sup> Letter dated 12 November 1998 from LTU RIE to GP [BLA.001.1583] at 1584

<sup>137</sup> In Patient Clinical Notes (Surgical) [BLA.001.1774]

<sup>138</sup> Letter from RIE to GP dated 22 December 1998 [BLA.001.1436]

**7.63** The discharge letter following these procedures, dated 22 December 1998 and sent to Mr Black's GP, listed under 'Diagnosis':

1. Liver transplant for hepatitis C cirrhosis – April 1996
2. Five small HCC in explanted liver (undiagnosed pre transplant)
3. Previous haemophilia
4. Abnormal liver function tests secondary to recurrent hepatitis C.<sup>139</sup>

**7.64** Although the second item in the list did not accurately reflect the information contained in the pathology report of 25 April 1996, it notified the GP that there had been cancer in the explanted liver.

**7.65** With the exception of the (inaccurate) 'Diagnosis' in the letter of 22 December 1998, hepatocellular cancer was not mentioned in the letters sent to Mr Black's GP, nor does it appear as an issue in the records up to that point, with the exception of the entries of 9 December 1998. There is nothing to suggest that the understanding reflected in the letter of 22 December was treated as significant.

**7.66** Mr Black showed an interest in his risk of cancer in general. For example, in November 1998, when he was seen at the LTU,<sup>140</sup> he was concerned about spots on his forehead and neck because he had previously had malignant spots removed from his back. He was referred to a dermatologist to exclude the possibility of malignancy; in the event, Mr Black required minor surgery for the removal of two basal cell carcinomas. The dermatologist's history noted previous Haemophilia A and Hepatitis C infection at liver transplant in 1996 only<sup>141</sup> and there is no evidence that the dermatologist was aware of the cancer in Mr Black's explanted liver: there was no reference to it in the records of the dermatologist's examination of Mr Black. If Mr Black had known of his previous hepatocellular cancer, he might have discussed it with the dermatologist examining the spots for malignancy. If that had been recorded, it would have been significant. It might not have been recorded even if Mr Black did mention it, however, and little turns on the absence of any record.

**7.67** Mr Black continued to be monitored. He was reviewed at the LTU in February 1999. The letter following this review, in common with other letters from the Unit up until this time (with the exception of the letter of 22 December 1998), set out the diagnosis as follows:

1. Liver transplant for hepatitis C cirrhosis – April 1996
2. Previous haemophilia
3. Abnormal liver function tests, recurrence of hepatitis C.

**7.68** There was again no reference to hepatocellular cancer in the explanted liver.<sup>142</sup>

**7.69** With one exception, the hospital reports continued in the same way until cancer was again diagnosed in the liver in 2003.<sup>143</sup> A record sheet dated 13 March 2002 of what appears to have been part of a research exercise, had commented: 'HCCs found in removed patient's liver' without further comment.<sup>144</sup> Other records from the same date contain no similar reference.

---

<sup>139</sup> Ibid [BLA.001.1436]

<sup>140</sup> Letter from Transplant Coordinator RIE to GP dated 12 November 1998 [BLA.001.1438]

<sup>141</sup> In Patient Clinical Note dated 8 December 1998 [BLA.001.1775]

<sup>142</sup> Letter from locum lecturer LTU RIE to GP dated 16 February 1999 [BLA.001.1416]

<sup>143</sup> Letter from specialist registrar to GP dated 4 June 2003 [BLA.001.0079]

<sup>144</sup> Record Sheet [BLA.001.1430]

**7.70** In 1996, routine pre-operative imaging for transplant assessment in Edinburgh involved ultrasound scanning of the liver.<sup>145</sup> Ultrasound examinations in 1994 and 1995 reported that there were no focal lesions or masses. Ultrasound examination on 2 November 1995 showed a 'very shrunken cirrhotic liver', but 'nil focal'.<sup>146</sup> The policy in 1996, where hepatocellular cancer was recognised prior to transplant or discovered in the explanted liver, was to continue ultrasound scans and measurement of serum alpha fetoprotein every six months after transplant.<sup>147</sup> The records show that serum alpha fetoprotein was regularly monitored in Mr Black's case. Ultrasound examinations of the liver graft were also recorded. It would not, however, be possible to infer that these steps were taken in pursuit of the protocol described or that they implied actual knowledge of the cancer in the explanted liver. Mr Black was seen much more frequently than the protocol required and this issue was not raised.

**7.71** The Inquiry asked Dr MacGilchrist to investigate the medical records in an attempt to explain the omission from them of a full record relating to the pathology in Mr Black's management. He did not discover an explanation. He reported on his review of the records on 1 March 2011.<sup>148</sup> Dr MacGilchrist speculated that the finding was somehow overlooked, which would explain why it was not discussed with Mr Black's family and, by implication, with Mr Black himself. In his report Dr MacGilchrist apologised to Mr Black's family for any distress caused by the disclosure of the existence of cancer in the explanted liver. It is clear from the report that he would have expected the discovery of such an extensive multifocal carcinoma as in Mr Black's case to have been discussed with the patient at the time. Dr Mutimer said that this was information that should have been shared with the patient.<sup>149</sup> That was not done.

**7.72** In answer to Mr Anderson, counsel representing NHS interests, Dr Mutimer dealt with the suggestion that there might have been no benefit in telling Mr Black, who was clearly an anxious man:

I think it is honesty really. It is providing the patient with information that will be of interest to him and it may actually determine his attitude to his illness and his recovery. So I think it's appropriate to discuss it with him. You are quite right that it may have unfortunate consequences in causing anxiety and the cancer may never recur, in which case in retrospect you might look back and say, "I wish we had never told him," but I don't think we are in a position to manage patients like that. This is important information that should have been shared with the patient ....

I think there are circumstances in medicine where it might be suggested that it is in everyone's interest, including the patient's, for information to be withheld, but I don't see that in this case.<sup>150</sup>

**7.73** The discharge letter of 21 May 1996 sent to Mr Black's GP should have included reference to the cancerous tumours. Mr Black's subsequent management ought to have

---

<sup>145</sup> Dr MacGilchrist's report [PEN.013.1091] at 1092

<sup>146</sup> Clinical Record [BLA.001.1737]. 'Nil focal' indicates that no tumour was identified.

<sup>147</sup> Dr MacGilchrist's report [PEN.013.1091] at 1092. Alpha fetoprotein is the major protein found in fetal serum (the blood of unborn children). Usually undetectable after birth, its detectable presence in adult blood is a sign of hepatocellular carcinoma.

<sup>148</sup> Dr MacGilchrist's report [PEN.013.1091]

<sup>149</sup> Day 2, page 147

<sup>150</sup> Ibid pages 153–154

been informed by the findings from the explant pathology report and steps should have been taken to ensure that Mr Black was aware of them. Notwithstanding Dr MacGilchrist's research and the Inquiry's investigations, no evidence has been uncovered that might explain the omission to discuss the report. It appears that the pathology report was overlooked throughout the relevant period, as Dr MacGilchrist and Dr Bathgate suggested. That would be consistent with the clinical notes and correspondence in the medical records.

**7.74** Mr Black was seen by consultants following the rota system in operation. That system has considerable advantages for patients, who are assured of regular attention from senior staff, which would be less easy and perhaps impossible to secure if the patient was under the exclusive attention of a single individual.

**7.75** So far as the Inquiry is aware, the omission to inform Mr Black of the cancer in his explanted liver was a unique lapse. With the exception of the group discussions, the records of the LTU were comprehensive. There was no lapse in record keeping. The failure related to the use of the records available. Responsibility for the RIE at the time lay with the Royal Infirmary of Edinburgh National Health Service Trust and now lies with the Lothian Health Board. Standard protocols for the preparation of records of team discussion appear to be management matters for the Board.

### **Treatment for Hepatitis C**

**7.76** The procedure of liver transplantation 'cured' Mr Black's haemophilia because the transplanted liver produced Factor VIII. Reinfection of the liver with Hepatitis C was inevitable, however.<sup>151</sup> The Hepatitis C virus would not have been cleared by the transplant procedure and the new liver was vulnerable to infection. Further, treatment was not without complications and there was a low level of success.

**7.77** Dr Mutimer said in his report:

According to the records, the possibility of antiviral therapy was discussed with the patient on a number of occasions during 1999, 2000, 2001 and 2002. At that time, there were few published data to encourage the use of antiviral therapy for Hepatitis C after transplantation. It was recognised that the results of Interferon treatment were poor with very few patients cured. In addition, it was recognised that Interferon was associated with significant side effects and that treatment could precipitate rejection of the transplanted liver.

[T]he year 1997 saw the first report of combination antiviral therapy for transplanted patients .... Compared with Interferon alone, it appeared that the combination therapy was more likely to be successful ....

Between 1997 and 2002, the peer-reviewed medical literature included approximately 10 small reports that described the results of combination antiviral therapy. The average cure rate in those reports was less than 20%. Therefore, the results of treatment were still disappointing and side effects were significant ....<sup>152</sup>

---

<sup>151</sup> Dr Colvin's report [BLA.001.2281] at 2285

<sup>152</sup> Dr Mutimer's report [BLA.001.2277] at 2278–2279

**7.78** Dr Mutimer thought that the decision Mr Black took to decline treatment up to December 2002 was quite understandable.<sup>153</sup>

**7.79** It must remain a matter for speculation how Mr Black might have responded to information about the cancer in his own liver. It might have influenced him, especially if he was informed about the risk of recurrence of cancer in the transplanted liver, and made him more receptive at an earlier stage to proposals that he should have treatment after his liver transplant in 1996. In general, it is clear from the evidence of Dr Mutimer in particular that Mr Black was entitled to have all information that might have had a bearing on his attitude to treatment.<sup>154</sup> It is not possible to form a view on whether a different course of management would have been adopted, but that might have happened if Mr Black had been fully informed.

### **Consequences of not detecting cancer pre-transplant**

**7.80** As events turned out, the fact that cancer was not detected in Mr Black's own liver before the transplant in 1996 was not altogether to his disadvantage. Dr Mutimer summarised the position disclosed in the pathology reports from 1996.<sup>155</sup> The explanted liver showed extensive primary liver cancer, as already narrated.

**7.81** In view of the size of the largest tumour, 4 x 3 x 3cm, it might have been expected that it would have been seen on imaging before the transplant operation. That did not happen. The chance of discovery depended on the procedures followed and on the equipment available at the time. Ultrasound examination of the liver was routine in pre-transplant imaging assessment in Edinburgh in 1996 but that technology might have failed to detect even the extensive and numerous tumours found in the explant. Subsequently, more advanced imaging techniques became available and, had they been available in 1996, the lesions may well have been detected.<sup>156</sup>

**7.82** Had Mr Black's cancer been discovered pre-transplant, and follow-up investigations carried out which disclosed tumours of the number and size involved in both the left and right lobes of the liver, it is likely that Mr Black would have been considered unsuitable for transplant. Dr MacGilchrist concurred with Dr Mutimer's view that the risk of tumour recurrence was proportional to the size and number of tumours in the liver and commented that only patients with a limited size and number of tumour nodules were considered suitable for transplant.<sup>157</sup>

**7.83** The transplant was carried out, however, and that prolonged Mr Black's life. It also created the context for later developments, and for the question that now arises.

### **Recurrent or new tumour?**

**7.84** If, as was to happen, Mr Black did have a transplant and cancer developed in the new graft, there would be two possibilities: either this would be a recurrence of the original tumour or development of new tumour in the transplanted liver. That issue arose for discussion among senior clinicians when cancer in Mr Black's liver was next diagnosed in 2003. It was seven years after transplant and an unusual development. Dr MacGilchrist

---

<sup>153</sup> See paragraph 7.41; Dr Mutimer – Day 2, page 135; Report [BLA.001.2277] at 2278

<sup>154</sup> Day 2, pages 142–148, 152–154; Supplementary Report [BLA.001.2287] at 2288

<sup>155</sup> Supplementary Report [BLA.001.2287] at 2288

<sup>156</sup> Mr MacGilchrist's report [PEN.013.1091] at 1092

<sup>157</sup> Ibid [PEN.013.1091] at 1092

agreed with the conclusion reached at the time: that it was most likely to be a new tumour rather than a recurrence.<sup>158</sup>

**7.85** Dr Mutimer thought, as did Dr MacGilchrist, that having regard to the number and the size of the tumours in the explanted liver, there had been a significant risk of recurrence in Mr Black's case. On the other hand, seven years was an unusually long period before recurrence: it was usually found within two years. He had hardly ever encountered a period as long as five years. The length of the period did not completely resolve the question whether this was a recurrence or a new cancer, however. Dr Mutimer was reminded during his oral testimony that the annual ultrasound examination in 2002 showed no evidence of cancer.<sup>159</sup> He said that indicated that any cancer, if present, was extremely small, probably less than one centimetre in size but that possibly the cancer had not yet developed.<sup>160</sup> In his view, post mortem findings did not indicate whether the cancer represented recurrent cancer or a new cancer in the graft.<sup>161</sup>

**7.86** Dr Mutimer said:

I think that when transplantation is undertaken in the presence of cancer, we know that there is a proportion of cases where the cancer will recur following transplantation and there are no established strategies which will prevent that and, once recurrence does occur, if it is recurrence, then there are no proven therapies to prolong life ....

[T]he other possibility [is] that this is a new tumour. We know that when there is cirrhosis, there is a risk for cancer, and cirrhosis had developed in the graft, so it is possible that the cancer arose merely in the graft rather than representing cancer which had been lurking for seven years and then recurred as a form of recurrent cancer.<sup>162</sup>

**7.87** Dr Mutimer thought that forensic pathologists might have or be able to develop techniques for differentiating the possibilities.<sup>163</sup> The known techniques involved ascertaining the gender of the tumour and comparing it with the sex of the recipient. In this case, if the tumour was female, then the tumour would definitely be of donor origin. If the donor had been male, however, that avenue of investigation would not be open. In this case the donor was male.<sup>164</sup> It seemed that further exploration of developing technology would not have assisted the Inquiry in resolving the issues raised by the Terms of Reference and that the researches that he suggested as possibilities would not have been a worthwhile exercise in this case.

**7.88** If the fatal cancer was a recurrence, Dr MacGilchrist's view was substantially the same as Dr Mutimer's: if the patient is unlucky enough to develop a recurrent tumour, it is almost invariably incurable.<sup>165</sup> If Mr Black's tumour was a recurrence of the cancer in the explanted liver, nothing could have been done to prevent that and there would have been no reasonable possibility of successful treatment of that tumour.

---

<sup>158</sup> Ibid [PEN.013.1091] at 1093

<sup>159</sup> Day 2, pages 137 and 148-149; Letter from RIE to GP dated 30 April 2002 [BLA.001.0106]; Dr Mutimer's supplementary report [BLA.001.2287] at 2288

<sup>160</sup> Day 2, page 151

<sup>161</sup> Supplementary report [BLA.001.2287]

<sup>162</sup> Day 2, pages 147-148

<sup>163</sup> Dr Mutimer's supplementary report [BLA.001.2287]; Day 2, pages 149-150.

<sup>164</sup> Dr MacGilchrist's report [PEN.013.1091]

<sup>165</sup> Ibid [PEN.013.1091] at 1092



**7.89** The alternative hypothesis which, on balance, appears to be more likely on the expert evidence as a whole, is that this was a new tumour. That was the view of Dr MacGilchrist<sup>166</sup> and his colleagues, and it is consistent with Dr Mutimer's observations on the likelihood of recurrence of the original tumour.<sup>167</sup> In that event, it was Dr Mutimer's view that:

Antiviral therapy if given successfully during the early years after transplantation may have prevented the development of graft cirrhosis. If his hepatocellular carcinoma represented *de novo* cancer in the graft, then the prevention of cirrhosis by antiviral therapy may have prevented the development of cancer.<sup>168</sup>

**7.90** As set out above, the possibility of antiviral treatment was discussed with Mr Black after his transplant when he attended hospital. He eventually began treatment in December 2002, by which time cirrhosis was established in the graft: it was, by that stage, too late.

**7.91** However, on the hypothesis that it was a new tumour, Mr Black's prospects might have been improved by treatment with antiviral therapy commenced soon after transplant and before cirrhosis developed. If he had been made aware of the cancer in his explanted liver then, faced with advice about the benefits of antiviral treatment in avoiding or arresting the progression to cirrhosis, either from the outset, or at least when successful dual antiviral therapy became available, it is possible that Mr Black would have been inclined to take the advice tendered that he should undergo treatment after transplant sooner rather than later and that he should persist with it. It was Dr Mutimer's view that, if it was a new tumour, prevention of the progression to cirrhosis with successful antiviral therapy would probably have prevented a new tumour from developing. However, his opinion was that successful antiviral treatment, or cure, occurred in less than 20% of patients after transplant.<sup>169</sup> It is impossible to say that there was any actual disadvantage from failure to inform Mr Black: by late 2002, when dual treatment started, he tolerated it very badly and he may not have tolerated treatment at any stage. Further, it is possible that by the time dual treatment was available he had developed cirrhosis again. At most there was a possible, if remote, chance of improvement of his prospects.

**7.92** As noted above (paragraph 7.81), it was the policy in 1996, where incidental hepatocellular cancer was discovered in an explanted liver, for continuing ultrasound scans to be performed and for monitoring of serum alpha fetoprotein to continue on a prescribed basis. These procedures were aimed at identifying possible tumour recurrence post transplant. Although not conforming to the protocol at the time, Mr Black did have these tests carried out and, as late as 2002, ultrasound showed no tumour. In the circumstances, he was not prejudiced by missing the chance of regular screening and, with it, possible detection of a tumour, by standard protocol monitoring.

**7.93** Leaving aside these possibilities, there was no criticism of Mr Black's management as a patient. Mr Black was one of the first patients with haemophilia to receive a transplant in the UK. The procedure was a remarkable success in giving him a prolonged life. He survived for seven years from liver transplant and had more than five years of good quality life.

---

<sup>166</sup> Ibid [PEN.013.1091] at 1093

<sup>167</sup> Dr Mutimer's supplementary report [BLA.001.2287] at 2288

<sup>168</sup> Dr Mutimer's report [BLA.001.2277] at 2279

<sup>169</sup> Ibid [BLA.001.2277] at 2278

**7.94** Dr Mutimer did not think that alternative management strategies following transplant could have changed the eventual outcome.<sup>170</sup> His conclusions were that:

- Detection of the extent of the tumour in the explanted liver in 1996 would not have altered management of Mr Black's disease in 1996 immediately after the transplantation.
- In the interval between 1996 and 2003, knowledge that there was cancer in the explanted liver would not have made any difference in his management following transplantation.<sup>171</sup>

**7.95** It was Dr Mutimer's opinion that the failure to inform did not impact on Mr Black's medical treatment which was at all times appropriate and that his treatment was beneficial. His opinion has a material bearing on the assessment of the chance that Mr Black might have had a better outcome had he been informed of his previous cancer and elected to receive treatment earlier.

**7.96** With the exception of the failure to provide information, Dr Mutimer had no concerns at all about the treatment given to Mr Black. From the time that Mr Black developed complications of liver disease, his medical management in Glasgow and Edinburgh seemed to him to be entirely appropriate.<sup>172</sup> Dr Colvin found no evidence of unreasonable or inappropriate treatment in this case.<sup>173</sup> These views are accepted, subject to the qualifications that necessarily arise from the failure to disclose the finding of cancer in the explanted liver.

### **Cause of death**

**7.97** The death certificate listed four conditions as contributing to Mr Black's death. In reverse order these charted the course of events chronologically: Mr Black suffered from haemophilia, which led to the transfusion of blood products, which caused Hepatitis C, which caused hepatocellular carcinoma in his transplanted liver.<sup>174</sup>

**7.98** As matters transpired, there was no doubt about the cause of death in Mr Black's case. The final development of hepatocellular carcinoma was a direct result of cirrhosis caused by Hepatitis C infection, whether the cancer was a recurrence of the original tumour or was a new tumour in the transplanted liver. Mr Black had mild to moderate Haemophilia A which was appropriately treated with cryoprecipitate and Factor VIII concentrates, prior to the development of virus inactivation for Factor VIII concentrates in the mid-1980s. Infection with Hepatitis C in Mr Black's case was not avoidable and, before the introduction of pegylated Interferon and Ribavirin, specific antiviral therapy for Hepatitis C was generally ineffective. It was not surprising that the transplanted liver became infected and cirrhotic or that a hepatocellular carcinoma developed. It is a matter of agreement on the part of Mrs Black and other 'patient interest' Core Participants that there were no reasonable precautions whereby death might have been avoided and that is clearly the case.<sup>175</sup>

---

<sup>170</sup> Day 2, pages 147–148

<sup>171</sup> Ibid pages 150

<sup>172</sup> Report [BLA.001.2277] at 2279

<sup>173</sup> Report [BLA.001.2281] at 2286

<sup>174</sup> Death Certificate [BLA.001.2118]

<sup>175</sup> Patient Interest Core Participant closing submissions [PEN.019.0773]

## Conclusions

**7.99** Factors contributing to the death of Mr Black were:

(i) Mr Black's death on 31 October 2003 was due to Hepatitis C infection in the transplanted liver, originally transmitted by blood products, together with hepatocellular carcinoma.

**7.100** Infection with Hepatitis C:

(ii) Infection was inevitable given Mr Black's requirements for factor replacement therapy.

(iii) On the balance of probabilities Mr Black acquired Hepatitis C infection before the end of the 1960s in the course of haemophilia therapy in Scotland.

**7.101** Progression of disease following transplant:

(iv) With the development of hepatocellular carcinoma in the transplanted liver, there were no reasonable precautions that might have avoided death.

(v) It is impossible to form a firm conclusion on whether the fatal tumour was a new tumour rather than recurrence of the tumour in his explanted liver but, on balance, having regard to the expert evidence as a whole, the cancer which developed in Mr Black's liver graft was likely to have been a new tumour.

(vi) Antiviral therapy, if successful, during the early years after transplant might possibly have prevented or postponed the development of graft cirrhosis.

(vii) Prevention or postponement of progression to cirrhosis through antiviral therapy might possibly have prevented or significantly postponed development of a new tumour.

(viii) It is not possible to form a view whether earlier antiviral treatment would have been successful. It is no more than a possibility – estimated generally by Dr Mutimer to be less than 20%. Mr Black's lack of tolerance of treatment from December 2002 lengthened the odds against his ability to tolerate the necessary full course of antiviral treatment whenever attempted.

**7.102** Mr Black's management as a patient:

(ix) Mr Black was not told that there had been cancer in his explanted liver. Appropriate steps should have been taken to ensure that he was aware of the relevant explant findings in the pathology report. Failure to inform him was a lapse from acceptable standards of patient management.

(x) This lapse was not evidence of systemic failure. On the evidence available it was a unique occurrence.

(xi) Mr Black was entitled to have information on all relevant factors in considering whether to undergo antiviral treatment of his recurrent Hepatitis C infection. The history of hepatocellular carcinoma in the explanted liver may have influenced his decisions from 1996 and more particularly from December 1998, had he been aware of it.

(xii) Failure to inform Mr Black of the cancer in the explanted liver deprived him of the chance, however remote, of a longer life that might have followed successful earlier antiviral treatment and eradication of Hepatitis C.

(xiii) With that one exception Mr Black's management as a patient was at all times appropriate and of a high standard and reasonably related to his needs.

## Eileen O'Hara

**7.103** Mrs O'Hara was born on 9 October 1930. She was employed as an orderly at Stobhill Hospital from about 1980 to 1990 when she retired at age 60.<sup>176</sup> She died on 7 May 2003. The certified causes of death were:

- I (a) Hepatic Failure
- I (b) Septic Shock
- II Mitral Valve Disease.<sup>177</sup>

## Mrs O'Hara's medical history to July 1995

**7.104** Mrs O'Hara had a complicated medical history, starting in about 1963, involving cardiac, obstetric and gynaecological problems.<sup>178</sup> It is highly likely that the significant events that may have exposed her to transmission of the Hepatitis C virus happened before November 1990.

**7.105** On 11 January 1963, Mrs O'Hara had surgery for mitral stenosis (narrowing of the mitral valve of the heart).<sup>179</sup> The background to that condition was rheumatic heart disease: Mrs O'Hara had rheumatic fever as a child, probably in the late 1930s or early 1940s.<sup>180</sup> It was a common disorder in Scotland up to the late 1940s. With its origin in streptococcal infection, until penicillin became widely available, after about 1945, there was no effective treatment for the infection. Additionally, without the benefit of antibiotic treatment in childhood, the patient often presented later with the heart manifestations of rheumatic fever which specifically affected the heart valves, often leading to stenosis.<sup>181</sup>

**7.106** In early 1963, bypass procedure during surgery had not been introduced.<sup>182</sup> Treatment for mitral stenosis involved adjustment of the valve by manual valvotomy.<sup>183</sup> In this procedure, the chest was opened, usually under the left breast. A vent was inserted and the surgeon used his fingers to enter the left atrium of the heart and widen the mitral valve.<sup>184</sup> It was a skilful, but quite brief, operation and frequently it did not require transfusion. The available records did not resolve the question of whether Mrs O'Hara had received a transfusion in 1963 but left it open as a possibility. However, in November 1971 Mrs O'Hara was seen at the obstetrics department of Stobhill Hospital.<sup>185</sup> Her mitral valve disease was noted and it was recorded at that time that she had previously had a blood transfusion. While the source of that information was not disclosed, it suggests that it is highly likely that Mrs O'Hara did have a blood transfusion at the time of her surgery in January 1963.

**7.107** In March 1972, Mrs O'Hara received a blood transfusion on the birth of her son by Caesarean section.<sup>186</sup> Two bottles of whole blood were issued, of which one, numbered 5209, was transfused.<sup>187</sup> Subsequent research by the SNBTS has shown that the blood was

---

<sup>176</sup> Witness Statement of Mrs Kennedy (Mrs O'Hara's daughter) [WIT.003.0420]

<sup>177</sup> Death certificate [OHA.001.2641]

<sup>178</sup> Dr Mutimer's report [BLA.001.2298]; Letter to GP dated 4 February 1963 [OHA.001.2627]

<sup>179</sup> Letter to GP dated 4 February 1963 [OHA.001.2627]

<sup>180</sup> Letter to GP from Cardiology clinic [OHA.001.2608]; Mrs Kennedy – Day 3, page 3; Dr Dunn – Day 3, page 109

<sup>181</sup> Dr Dunn – Day 3, pages 109–110; Rheumatic fever could also lead to aortic 'incompetence' or leaking.

<sup>182</sup> Dr Dunn – Day 3, page 114

<sup>183</sup> Ibid page 114

<sup>184</sup> Ibid pages 114–115

<sup>185</sup> Request for out-patient consultation form dated 1 November 1971 [OHA.001.0899]

<sup>186</sup> Haematology Department report dated 30 March 1972 [OHA.001.0881]; see Mrs Kennedy – Day 3, page 22

<sup>187</sup> Glasgow Northern Hospitals (Stobhill) Anaesthetic chart dated 31 March 1972 [OHA.001.0430]; Stobhill Haematology Department report dated 30 March 1972 [OHA.001.0881]; Dr Mutimer's report [BLA.001.2298]

donated at Lockerbie on 5 March 1972.<sup>188</sup> There was no test for non-A, non-B Hepatitis/Hepatitis C in existence at that time.<sup>189</sup> There is no record of the donor having been subsequently tested for Hepatitis C.<sup>190</sup>

**7.108** On 28 November 1979, Mrs O'Hara had a hysterectomy at Stobhill. She received one unit of whole blood and one unit of packed cells in the course of the procedure.<sup>191</sup> Subsequent SNBTS research again traced the donations, to Coatbridge and East Kilbride, in November 1979. There was no record of either donor having been tested for Hepatitis C at any time.<sup>192</sup>

**7.109** In February 1984, Mrs O'Hara was seen in the medical out-patient clinic at Stobhill by Dr Francis Dunn, Consultant Cardiologist.<sup>193</sup> The main focus was heart disease. It was noted that liver function tests (LFTs) were abnormal and it was suggested that this might be a consequence of her mitral valve disease: patients with mitral valve disease likely to require surgery were also likely to have mild abnormalities of liver function.<sup>194</sup> At that stage, before successful replacement of her mitral valve, Mrs O'Hara had significant heart failure; pressure on the right side of her heart was significantly elevated in 1985 and that would have given rise to back pressure on the liver, leading to abnormal LFTs.<sup>195</sup> That was a reasonable view at the time according to Dr David Mutimer, Consultant Hepatologist at the Queen Elizabeth Hospital, Birmingham, who provided expert evidence to the Inquiry.<sup>196</sup> It could not have been concluded by her doctors before that date that she had acquired a chronic liver disease.

**7.110** In June 1985, Mrs O'Hara had cardiac surgery at the Glasgow Royal Infirmary (GRI). On that occasion a Wessex porcine bioprosthetic valve was inserted.<sup>197</sup> On 5 June, five packs of concentrated red cells were issued prior to surgery on 7 June.<sup>198</sup> All five were used.<sup>199</sup> Plasma was also administered.<sup>200</sup> The SNBTS was not able to trace the donors.<sup>201</sup>

**7.111** In early 1990, Mrs O'Hara was found to have diabetes mellitus.<sup>202</sup> Although her diabetes was initially controlled by diet, on 7 March 1990 her GP referred her to Stobhill Ophthalmology after an optician reported having found some signs of diabetic retinopathy (damage to the retina caused by diabetes).<sup>203</sup> Ocular examination at Stobhill was unremarkable, however, and she was discharged in to the care of her GP.<sup>204</sup>

**7.112** Later in 1990 Mrs O'Hara became unwell. Her GP arranged liver function tests, which were found to be mildly deranged. The GP told her that there were problems with the results and referred Mrs O'Hara to the GRI for tests on 29 May 1990.<sup>205</sup> In her referral letter, the GP wrote that Mrs O'Hara did not take any alcohol and wondered whether

---

<sup>188</sup> SNBTS Response to the Inquiry – January 2011 [PEN.001.0032]

<sup>189</sup> The Hepatitis C virus was discovered in 1988 and testing was introduced in the UK in 1991.

<sup>190</sup> SNBTS Response to the Inquiry – January 2011 [PEN.001.0032]

<sup>191</sup> Day 3, page 25; Recovery room chart [OHA.001.0076]; Haematology Department Form [OHA.001.0738]

<sup>192</sup> SNBTS Response to the Inquiry – January 2011 [PEN.001.0032]

<sup>193</sup> Letter from Stobhill to GP dated 21 February 1984 [OHA.001.2565]

<sup>194</sup> Dr Dunn – Day 3, page 116

<sup>195</sup> Ibid page 117

<sup>196</sup> Dr Mutimer's report [BLA.001.2298] at 2299

<sup>197</sup> Explanation by Counsel to the Inquiry – Day 3, page 22; GRI Report form dated 1 July 1985 [OHA.001.2554]; GRI operation report dated 7 June 1985 [OHA.001.2555];

<sup>198</sup> Explanation by Counsel to Inquiry – Day 3, page 20; Blood bank form [OHA.001.1303]

<sup>199</sup> Blood loss/replacement chart [OHA.001.1425]

<sup>200</sup> I.V. Therapy Prescription sheet [OHA.001.1428]

<sup>201</sup> SNBTS Response to the Inquiry [PEN.001.0032] at 0033. See paragraph 7.211.

<sup>202</sup> Letter from Stobhill to GP dated 10 May 1990 [OHA.001.2539]; Mrs O'Hara was later treated with insulin for Type II diabetes.

<sup>203</sup> Referral letter [OHA.001.2543]

<sup>204</sup> Letter to GP dated 10 May 1990 [OHA.001.2539]

<sup>205</sup> Letter [OHA.001.1178]

drug therapy was the cause of her abnormal LFTs.<sup>206</sup> Mrs O'Hara continued going to the GP 'for several months'.<sup>207</sup> It seems to be in the context of those visits that consumption of alcohol was raised, presumably because she had persistently abnormal liver blood tests. Mrs O'Hara's daughter, Mrs Roseleen Kennedy, said that her mother had commented that the GP kept asking her whether she was drinking. In fact, she drank very little and became upset that she appeared to be being dealt with as an alcoholic.<sup>208</sup> Given her liver function test results, however, questions about alcohol consumption were routine. As reported in the letter to the GRI, the GP accepted that Mrs O'Hara did not drink alcohol.<sup>209</sup>

**7.113** The GRI's report to her GP on 1 June 1990 stated that Mrs O'Hara's cardiac position was good. No hepatic enlargement was identified on examination in hospital. The GP was, however, encouraged to continue with liver function tests and to seek ultrasound tests or a gastroenterologist's report if her liver function tests continued to show mild derangement.<sup>210</sup>

**7.114** In September 1990, the GP referred Mrs O'Hara to the GRI Gastroenterology Department commenting that she had mild persistent derangement of her LFTs and frequent loose bowel motions. The GP noted that Mrs O'Hara had only ever taken a moderate amount of alcohol and that her liver function tests were still deranged on abstinence.<sup>211</sup> In a full report dated 5 November 1990, the gastroenterology registrar, Dr J Morris, set out the clinical findings on examination that day.<sup>212</sup> Significantly, the tip of the spleen was palpable. Overall, it was thought that she had mild congestive cardiac failure. Dr Morris did not feel that this explained her abnormal blood tests, however.

**7.115** In her history so far Mrs O'Hara had experienced a significant exposure to blood transfusion. Dr Morris did not have that information available when examining her. In his letter to the GP on 5 November 1990, he wrote:

Although I was unsure whether she received blood transfusions with her various operations in the past ... I suppose this remains a possibility and I have therefore checked hepatitis screens including hepatitis C, further I have rechecked liver function tests, urea and electrolytes, chest x-ray, ECG, echocardiogram auto antibodies and an abdominal ultrasound. I think it is important that we check on the function of her valve replacement to [see] whether there is any regurgitation contributing to heart failure. Secondly we have persistent abnormal LFTs and hopefully the above investigations will give some idea of how we should proceed with further investigations. This may well be on the basis of a liver biopsy should the other investigations fail to turn up a clue to the problems.<sup>213</sup>

**7.116** Blood was taken for hepatitis tests on 5 November 1990. Dr Morris wrote to Mrs O'Hara's GP on 4 December, observing that the recent investigations had shown a fair degree of valve dysfunction that would need to be looked at further.<sup>214</sup> By then the results of some tests had been reported by the GRI Microbiology Department. HBsAg tests (for

---

<sup>206</sup> Ibid [OHA.001.1178]; Witness Statement of Mrs Kennedy [WIT.003.0420] at 0421

<sup>207</sup> Witness Statement of Mrs Kennedy [WIT.003.0420] at 0421

<sup>208</sup> Ibid

<sup>209</sup> Letter to the GRI [OHA.001.1178]

<sup>210</sup> Letter to GP [OHA.001.2538]

<sup>211</sup> Letter dated 6 September 1990 [OHA.001.2536]

<sup>212</sup> Letter to GP [OHA.001.2535]

<sup>213</sup> Ibid [OHA.001.2535]

<sup>214</sup> Letter to GP [OHA.001.1172]

Hepatitis B) were negative;<sup>215</sup> the IgM anti-HAV (for Hepatitis A) test was negative;<sup>216</sup> Epstein-Barr virus and Cytomegalovirus had not been detected.<sup>217</sup> The test for Hepatitis C antibody was not reported until 18 December 1990: it too was negative.<sup>218</sup> Dr Morris said he would write to Mrs O'Hara with a view to bringing her back to the clinic to discuss the results.

**7.117** Dr Morris duly wrote to Mrs O'Hara on 4 December 1990, enclosing a clinic appointment for two weeks later.<sup>219</sup> He saw her on 17 December. According to a file note prepared in January 1991, Mrs O'Hara remembered a series of tests, including an ECG, being carried out at the 17 December appointment. She was told that she would be referred to Cardiology and that she would receive an appointment in the near future.<sup>220</sup> She was referred to Dr AR Lorimer, a cardiologist at the GRI, by Dr Morris on behalf of Dr JF MacKenzie, the Senior Consultant, on 17 December.<sup>221</sup> In his letter to Dr Lorimer, Dr Morris referred to her raised LFT results and said:

The most striking abnormality, however, on examination was evidence of both mitral and tricuspid regurgitation .... An Ultrasound of the abdomen shows the liver and spleen to be enlarged with splenic vein dilatations. Overall, these are the appearances we would expect with congestion secondary to primary cardiac abnormality. Certainly we feel that this is the most likely cause of her abnormal liver function tests.

**7.118** Mr El Fiky from Cardiothoracic Surgery at the GRI saw Mrs O'Hara on 18 January 1991. His clinical findings supported Dr Morris. An echocardiogram had shown that her heart valves and consequent heart failure were more severe than had been expected and he recommended that she should have an early appointment at Dr Lorimer's clinic with a view to mitral valve replacement as soon as possible.<sup>222</sup> Dr Lorimer saw her and reported to her GP on 7 February.<sup>223</sup> He found signs of a degree of incompetence and stenosis of the valve. He reported that the liver was not unduly enlarged that day. He suspected a further myocardial factor and arranged for her admission for further, more detailed evaluation.

**7.119** She was duly admitted to the GRI on 25 February 1991. She was seen by Mr Dimitri of the department of Cardiac Surgery, where cardiac catheterisation and transoesophageal echocardiogram investigations were carried out to investigate her mitral valve.<sup>224</sup> The discharge notes recorded that Mrs O'Hara had 3cms hepatomegaly (enlargement of the liver) which was slightly tender. LFT results were reported to be normal apart from slightly raised Gamma-glutamyltransferase (GGT, an enzyme found in many body tissues but especially the liver. Elevated GGT can be a marker of liver disease).<sup>225</sup> This minor abnormality was not considered to be significant.

---

<sup>215</sup> Test results [OHA.001.1276]; [OHA.001.1273]

<sup>216</sup> Test results [OHA.001.1275]; [OHA.001.1273]

<sup>217</sup> Test results [OHA.001.1274]

<sup>218</sup> Test results [OHA.001.1272]

<sup>219</sup> Letter to Mrs O'Hara [OHA.001.1171]

<sup>220</sup> File note dated 17 January 1991 [OHA.001.1162]: Mrs O'Hara's recollection was that she attended the Urology Clinic, but in fact she was seen by Dr Morris.

<sup>221</sup> Referral letter [OHA.001.1168]

<sup>222</sup> Letter to Dr Lorimer dated 18 January 1991 [OHA.001.1167]

<sup>223</sup> Letter to GP [OHA.001.1160]

<sup>224</sup> GRI discharge report dated 3 April 1991 [OHA.001.1155]

<sup>225</sup> Ibid [OHA.001.1155] at 1156

**7.120** Mr Dimitri reported to Dr Lorimer on 7 March. Clinically, Mrs O'Hara had signs of prosthetic malfunction and was in atrial fibrillation (deviation from the normal rhythm of the heart) and there was stenosis (narrowing) of the valve. It was noted on examination that her increased hepatomegaly suggested a progressive enlargement of the liver.<sup>226</sup> Mr Dimitri commented that replacement of her mitral prosthesis was required but suggested to Dr Lorimer that an angiogram might be appropriate to delineate her coronary anatomy.

**7.121** Meanwhile, a further appointment had been arranged for Mrs O'Hara to attend the Gastroenterology Clinic at the GRI on 11 March 1991. She did not attend, however. The consultant gastroenterologist, Dr MacKenzie, thought this might be explained by the fact that she had just returned home from her hospital admission (she had been discharged on 1 March) and wrote to her GP that she would be sent another appointment for a month later.<sup>227</sup> Investigations have not shown whether or not Mrs O'Hara or her GP asked for or received a further appointment. There is no evidence in the medical records that she attended Gastroenterology about this time.

**7.122** On 8 April 1991, Professor Lorimer, as he had become, reported to Mrs O'Hara's GP, copied to Mr Dimitri, with the GRI's clinical summary commenting that she was a candidate for mitral valve replacement and confirming that she was on his waiting list for the further investigation proposed by Mr Dimitri.<sup>228</sup> The GP had written to Professor Lorimer on 17 May questioning the need for further coronary angiography<sup>229</sup> but the procedure was carried out in July 1991. Her coronary arteries were normal. It was decided that Mrs O'Hara would go forward to mitral valve replacement and that otherwise her management should continue on current lines.<sup>230</sup> Mr Dimitri confirmed in a letter to Professor Lorimer on 30 July that she would be admitted for replacement of her mitral prosthesis.<sup>231</sup>

**7.123** The mitral valve replacement surgery was delayed for family reasons. Mrs O'Hara was admitted on 15 October 1991. She had a valve replacement with a St Jude bileaflet mechanical valve on 18 October 1991.<sup>232</sup> The procedure was successful.

**7.124** Mrs O'Hara was monitored at the GRI. She was seen at Mr Dimitri's clinic on 17 December 1991 when it was noted that her recovery had been quick and smooth, that she was doing well and had no complaints.<sup>233</sup> She was reviewed in February 1993.<sup>234</sup> There were no symptoms of heart failure and her prosthetic valve was functioning normally. Her next annual review, in February 1994, was unremarkable.<sup>235</sup>

**7.125** Mrs O'Hara was referred to the Diabetic Day Unit at Stobhill in August 1994. On examination there, she was found to have hepatosplenomegaly (enlarged liver and spleen). The consultant physician, Dr McLaren, who was surprised at the finding, thought that it might be secondary to her mitral valve replacement and proposed writing to the cardiac unit at the GRI. If hepatosplenomegaly had been noted before it was unlikely to be

---

<sup>226</sup> Letter [OHA.001.1146]

<sup>227</sup> Letter dated 11 March 1991 [OHA.001.2529]

<sup>228</sup> Letter to GP [OHA.001.1153]; GRI discharge report dated 3 April 1991 [OHA.001.2527]

<sup>229</sup> Letter to the GRI [OHA.001.1152]

<sup>230</sup> Discharge letter from the GRI to GP dated 5 August 1991 [OHA.001.1151]

<sup>231</sup> Letter [OHA.001.1154]. At this stage it was known that the operation would be delayed until after a family wedding at the beginning of October.

<sup>232</sup> GRI discharge report [OHA.001.2520]

<sup>233</sup> Letter from GRI to GP dated 17 December 1991 [OHA.001.1138]

<sup>234</sup> Letter from GRI to GP dated 16 February 1993 [OHA.001.1137]

<sup>235</sup> Letter from GRI to GP dated 27 February 1994 [OHA.001.1136]



significant. If it was new, however, he thought that an ultrasound examination, at least, would be required.<sup>236</sup> He wrote to that effect on 5 August 1994.<sup>237</sup> He was to find the reply from the cardiothoracic surgeon less than illuminating:

In the absence of gross failure it would be appropriate to investigate the hepatosplenomegaly. I suspect that we will not find anything but nevertheless there is justification for doing so.<sup>238</sup>

**7.126** On 16 August 1994, Dr McLaren wrote to Mrs O'Hara's GP.<sup>239</sup> He said he had received a 'rather delphic communication from the cardiothoracic surgeons, the burden of which ... is that they have not noted hepatosplenomegaly before'. Further investigations were put in hand. Dr McLaren arranged for an ultrasound of her abdomen. On 9 September, Dr McLaren wrote again, confirming that Mrs O'Hara had very marked splenomegaly (enlarged spleen) and mild hepatomegaly. A biochemical screen on her last visit had been normal but he had done a full blood screen and arranged ultrasound examination.<sup>240</sup> On 22 September, Dr McLaren intimated the results of tests.<sup>241</sup> Ultrasound tests had confirmed the presence of splenomegaly and suggested a degree of portal hypertension (high blood pressure in the portal vein system at the liver). He suggested, correctly, as events were to prove, that the findings might all be secondary to cirrhosis.

**7.127** Dr McLaren saw Mrs O'Hara again on 19 October 1994. Mrs O'Hara told him that she had previously been told there was 'something wrong with her liver' due to her heart disease. Dr McLaren's report to the GP reflected some annoyance. Hepatosplenomegaly had been noted in 1990 and he asked for correspondence from the GP's records which might relate to the topic. Further ultrasound examination had confirmed the presence of hepatomegaly and there was further indication of cirrhosis.<sup>242</sup> The GP responded on 4 November 1994, enclosing the GRI report of 3 April 1991 and confirming that Mrs O'Hara had deranged LFTs in January 1994.<sup>243</sup>

**7.128** Following discussions between Dr McLaren and Dr Dunn, Mrs O'Hara was seen in the department of cardiology, Stobhill, on 21 December 1994 by Dr Dunn and Dr Tait, the registrar in cardiology. The registrar subsequently reported to Dr McLaren and to the GP.<sup>244</sup> The letter noted that Dr McLaren had detected hepatosplenomegaly and that possible fat infiltration of the liver had been detected with prominence of the portal vein and marked splenomegaly. Dr Mutimer thought, in retrospect, that any fat infiltration was probably related to Mrs O'Hara's diabetes.<sup>245</sup> The letter also acknowledged that abnormalities in liver function tests had been detected in 1990, with hepatomegaly and with the tip of the spleen possibly being palpable. It was noted that the slight enlargement of the liver and spleen found in 1990 were attributed to right heart failure consequent to mitral re-stenosis with a degree of pulmonary hypertension. The liver abnormalities did not appear to have been re-checked following her mitral valve replacement in 1991.<sup>246</sup> Her condition

---

<sup>236</sup> Letter from Stobhill to GP dated 5 August 1994 [OHA.001.2502]

<sup>237</sup> Letter from Stobhill to GRI [OHA.001.1135]

<sup>238</sup> Letter from GRI to Stobhill dated 11 August 1994 [OHA.001.1134]

<sup>239</sup> Letter [OHA.001.2501]

<sup>240</sup> Letter to GP [OHA.001.2496]

<sup>241</sup> Letter to GP [OHA.001.2500]

<sup>242</sup> Letter to GP dated 26 October 1994 [OHA.001.2494]

<sup>243</sup> Letter [OHA.001.2493]; GRI discharge report dated 3 April 1991 [OHA.001.1155]

<sup>244</sup> Letter from Stobhill dated 5 January 1995 [OHA.001.2486]

<sup>245</sup> Dr Mutimer – Day 3, page 42

<sup>246</sup> The implication of the comment appears to be that if right heart failure had been the cause of the enlarged liver and spleen in 1990, the abnormalities would have disappeared following the successful operation.

on clinical examination was reported. The conclusion reached was that an alternative cause for her hepatosplenomegaly appeared to be indicated and required investigation.<sup>247</sup> Dr Dunn explained that, because of the success of the mitral valve procedure and her satisfactory cardiac status at the time, it was unlikely that the condition of her liver and spleen was related solely to her heart disease.<sup>248</sup>

**7.129** Investigation of Mrs O'Hara's liver was initiated by Dr Tait.<sup>249</sup> Dr Dunn explained that, at that time, doctors in his department were often 'gatekeepers,' doing initial investigations before referring on for other specialist consideration.<sup>250</sup> Hepatitis testing was carried out and reported in February 1995. It was confirmed that Mrs O'Hara was positive for Hepatitis C antibody.<sup>251</sup> Dr Mutimer explained that this test confirmed that she had been exposed to Hepatitis C at some stage but not whether the virus was still present.<sup>252</sup> Later tests confirmed that it was.<sup>253</sup>

**7.130** Mrs O'Hara was reviewed at Stobhill cardiology clinic on 27 February 1995.<sup>254</sup> She had developed herpes zoster (shingles) affecting her leg and abdominal wall. Typically, the condition causes pain and, in Mrs O'Hara's case, irritation of the nerves continuing after her rash had resolved. She had been admitted to hospital as an emergency as a result of this complication, known as post-herpetic neuralgia.<sup>255</sup> Further investigation of her hepatosplenomegaly was delayed until she was feeling better.<sup>256</sup> However, investigation continued and Dr Dunn reported to her GP on 29 March 1995.<sup>257</sup> Mrs O'Hara's case had been discussed with gastroenterology colleagues and it was agreed that liver biopsy was indicated. Advice was given on her continuing cardiac issues. Dr McLaren wrote to the GP on 3 April.<sup>258</sup> He reported on her herpes zoster infection. In addition he commented on the possibility that the antibodies against Hepatitis C (indicating Hepatitis C infection) that had been identified were attributable to blood transfusions and suggested that would explain why she might have developed cirrhosis, the presumed diagnosis. Fuller, subsequent, evaluation was to prove that he was probably right.<sup>259</sup>

**7.131** On 12 May 1995 Dr Dunn reported to the GP on the results of CT scanning of Mrs O'Hara's abdomen.<sup>260</sup> There was significant hepatosplenomegaly and, in particular, splenomegaly. It was suggested that the condition of her lymph nodes might have a malignant source, for example lymphoma.<sup>261</sup> This was to prove a false trail.

**7.132** Bone marrow and liver biopsy investigations were carried out in June and July 1995.<sup>262</sup> The tests were related to the risk of a malignant source of her lymph node condition.<sup>263</sup> There was no evidence of lymphoma or of malignancy.<sup>264</sup> There was no

---

<sup>247</sup> Letter from Stobhill dated 5 January 1995 [OHA.001.2486]

<sup>248</sup> Dr Dunn – Day 3, pages 117–118

<sup>249</sup> Dr Mutimer – Day 3, pages 42–43

<sup>250</sup> Dr Dunn – Day 3, page 118

<sup>251</sup> Regional Virus Laboratory test results dated 8 February 1995 [OHA.001.0834]

<sup>252</sup> Dr Mutimer – Day 3, page 44

<sup>253</sup> Regional Virus Laboratory PCR test results dated 3 April 2003 [OHA.001.2710]

<sup>254</sup> Letter from Stobhill to GP dated 9 March 1995 [OHA.001.2476]

<sup>255</sup> Dr Mutimer – Day 3, page 45; letter from Stobhill to GP dated 9 March 1995 [OHA.001.2476]

<sup>256</sup> Dr Mutimer – Day 3, page 46

<sup>257</sup> Letter from Stobhill to GP [OHA.001.2475]

<sup>258</sup> Letter [OHA.001.2474]

<sup>259</sup> Dr Mutimer – Day 3, page 47

<sup>260</sup> Letter [OHA.001.2473]

<sup>261</sup> Dr Dunn – Day 3, pages 119–120

<sup>262</sup> Letter from Stobhill to GP dated 02 August 1995 [OHA.001.2469]

<sup>263</sup> Dr Mutimer – Day 3, pages 51–52

<sup>264</sup> Letter from Stobhill to GP dated 02 August 1995 [OHA.001.2469]

evidence of malignant infiltration of the bone marrow. The strong likelihood was that the 'enlarged lymph nodes' that had prompted discussion of lymphoma were in reality enlarged blood vessels in the abdomen resulting from portal hypertension (as had been suggested in September 1994). Liver biopsy showed cirrhosis with lymphocytic infiltrate, appearances that were typical of Hepatitis C.<sup>265</sup> The lymphocytic infiltrate was an indication of the body's immune cells reacting to the presence of the virus in the liver.<sup>266</sup> Mrs O'Hara was told that she had cirrhosis.<sup>267</sup>

### **Mrs O'Hara's medical history after July 1995**

**7.133** Until about mid-1995, Mrs O'Hara's liver disease was relatively asymptomatic. She appeared to her daughter to have been well until June of that year. She looked after her granddaughter, born in 1992, from the point when Mrs Kennedy returned to work, until June 1995. At that point, Mrs O'Hara began to appear unwell and complained of fluid retention in her legs and of a swollen abdomen. She looked pale and tired, felt nauseated and started to lose her appetite.<sup>268</sup> Mrs Kennedy said that her mother slowly deteriorated from 1995.<sup>269</sup> The family account of Mrs O'Hara's general health was a reasonable fit with her medical history. In the period 1991–94, as noted later, she frequently attended her GP for relatively minor ailments. Late 1995 was the time when Mrs O'Hara began undergoing extensive and continuing investigations.

**7.134** After July 1995, when the diagnosis of cirrhosis was finally arrived at and intimated to Mrs O'Hara, matters did not progress swiftly for a time. Mrs O'Hara continued to attend her GP with relatively minor complaints.<sup>270</sup> She was examined following spontaneous haemorrhage in her left eye on 29 July. On 3 August, she reported pain in her left shoulder. Co-codamol was prescribed but did not help. Pain in the back of her neck was extending to her hand. Her shoulders were stiff and she had chest pain. She also reported vomiting and sweating.<sup>271</sup> After review of the findings in September 1995, Dr Prasad, a Stobhill cardiologist, indicated to the GP that Mrs O'Hara should be reviewed by Dr Forrest, consultant gastroenterologist at Stobhill.<sup>272</sup> A letter of referral was sent to Dr Forrest on 12 September 1995.<sup>273</sup> Enclosed with the letter was a copy of Mrs O'Hara's 'recent clinic letter', which appears to have been Dr Prasad's letter to the GP. It stated:

This lady who was sent to our clinic with possible congestive cardiac failure was found to have hepatosplenomegaly and subsequently has been investigated by the haematologists and ourselves. The liver biopsy showed cirrhosis with lymphatic infiltrate. The appearances were non-specific but in keeping with Hepatitis C .... In view of these findings I think in the first instance we should ask our Gastroenterology colleagues to review her and further assess the need for additional treatments such as Interferon .... I will arrange to see her again in four months time but we will wait until Dr Forrest's review.<sup>274</sup>

---

<sup>265</sup> Letter from Stobhill to GP dated 12 September 1995 [OHA.001.2468]; Dr Mutimer – Day 3, page 52

<sup>266</sup> Dr Mutimer – Day 3, page 52

<sup>267</sup> Letter from Stobhill to GP dated 02 August 1995 [OHA.001.2469]

<sup>268</sup> Witness Statement of Mrs Kennedy [WIT.003.0420] at 0421 and 0422

<sup>269</sup> Ibid [WIT.003.0420] at 0424

<sup>270</sup> GP's clinical notes [OHA.001.2287] at 2287-89

<sup>271</sup> Ibid [OHA.001.2287] at 2288

<sup>272</sup> Letter from Stobhill to GP dated 12 September 1995 [OHA.001.2468]

<sup>273</sup> Letter from Dr Prasad to Dr Forrest both Stobhill dated 12 September 1995 [OHA.001.1011]. (This letter was dictated 11 September but typed and presumably sent on 12 September 1995 rather than on 12 May 1995 which appears to be a typographical error).

<sup>274</sup> Letter from Stobhill to GP dated 12 September 1995 [OHA.001.2468]

**7.135** In 1995 Stobhill Hospital was managed, and its consultants were employed, by Stobhill National Health Service Trust. Responsibility for the hospital and its staff now lies with Greater Glasgow Health Board.

**7.136** Dr Forrest replied on 3 November 1995, without seeing Mrs O'Hara. Since this represented a significant stage in her care it is appropriate to quote from his letter:

I note that she was found to have hepatosplenomegaly around 1990 and that a recent liver biopsy shows an established cirrhosis. This could be idiopathic [of unknown origin] but could be related to Hepatitis C, but there is no obvious continuing Hepatitis from the biopsy report.

If her cirrhosis is due to Hepatitis C (and of course it could be cryptogenic [another term indicating unknown origin]) then she must have contracted her Hepatitis C very many years ago as cirrhosis develops very slowly following infection with Hepatitis C.

Interferon has been used for Hepatitis C but the results in terms of clearing the virus from the patient's serum are disappointing. Perhaps only around 25% of patients will respond on a long term basis and all the evidence suggests that patients who are cirrhotic have a much lower response rate than this. The other factor is that Greater Glasgow Health Board has instructed the General Practitioners not to prescribe Interferon for chronic Hepatitis C and the Trust will also not prescribe it. The Health Board have apparently given £200,000 for a trial to be started at the Royal and the Western. At the present time I have not seen the protocol to see which sort of patients would be suitable for treatment, but I doubt if this lady would be a candidate. Having said that I will arrange to review her liver biopsy to see if there is any ongoing evidence of Hepatitis and will write to you further after that.<sup>275</sup>

**7.137** On 30 November 1995, Mrs O'Hara was seen at Dr Dunn's clinic.<sup>276</sup> The cardiac findings, in context, suggested that her cardiac status overall was stable.<sup>277</sup> Dr Dunn explained that his department remained reasonably happy with Mrs O'Hara's heart condition at this time and this remained the case up to about 1998.<sup>278</sup>

**7.138** Dr Bong (Senior House Officer, Department of Cardiology, Stobhill) renewed the request to Dr Forrest for advice in March 1996.<sup>279</sup> Dr McLaren reminded Dr Forrest of the request in May.<sup>280</sup> By letter from a senior registrar in Cardiology, which was dictated on 28 June and typed on 12 July, Mrs O'Hara's GP was told that Dr Forrest planned to review her case on the day of dictation and that the GP would hear directly from Dr Forrest.<sup>281</sup>

**7.139** Dr Forrest reviewed Mrs O'Hara's liver biopsy but did not see her in person. He wrote to Dr McLaren on 10 July 1996 apologising for his delay in responding. He confirmed that her liver biopsy in 1995 showed established cirrhosis and that he had reviewed the biopsy recently.<sup>282</sup> He thought that she did not need a repeat liver biopsy. He doubted very much whether she was a candidate for Interferon treatment. Dr McLaren wrote directly to Mrs

---

<sup>275</sup> Letter to Dr Dunn [OHA.001.1003]

<sup>276</sup> Letter from Stobhill to GP dated 16 January 1996 [OHA.001.2464]

<sup>277</sup> Dr Dunn – Day 3, pages 120–123

<sup>278</sup> Ibid pages 122–123

<sup>279</sup> Letter from Stobhill Cardiology to Dr Forrest dated 11 March 1996 [OHA.001.1008]

<sup>280</sup> Letter from Stobhill General Medicine to Dr Forrest dated 09 May 1996 [OHA.001.1012]

<sup>281</sup> Letter from Stobhill Cardiology to GP dated 12 July 1996 [OHA.001.1013]

<sup>282</sup> Letter from Dr Forrest to Dr McLaren, both Stobhill [OHA.001.1017]

O'Hara and to the GP passing on the information from Dr Forrest that repeat liver biopsy was not necessary.<sup>283</sup> These matters are discussed more fully in paragraphs 7.202–7.211 below.

**7.140** Mrs O'Hara was seen at Stobhill Department of Haematology on 21 April 1997.<sup>284</sup> She had been referred because of her neutropenia and thrombocytopenia (reductions in white cell and platelet counts in the blood respectively), both of which are observed in patients with cirrhosis.<sup>285</sup> She had hepatosplenomegaly and was anaemic.<sup>286</sup> The haematologist found that Mrs O'Hara was developing early iron deficiency. He arranged for further endoscopic examination to see whether she was bleeding from her upper gastrointestinal tract as a consequence of her cirrhosis. Subsequent endoscopic examination on 14 July 1997 showed that there were varices proximal to the gastro-oesophageal junction.<sup>287</sup> There was evidence of portal hypertension with the varices but it was thought that this was extremely unlikely to be the cause of her iron deficiency anaemia. There were no stigmata (signs) of recent bleeding. A report was sent to Mrs O'Hara's GP on 28 July.<sup>288</sup>

**7.141** Dr Mutimer interpreted the report:

They would be looking for a cause of blood loss ... [T]he haematologist thinks that the patient is iron-deficient, which means there is likely to be some chronic blood loss. That can be due to the portal hypertension, it can be due to the cirrhosis. It is appropriate that she has an endoscopy for two reasons. One is to see whether the varices are present and if they are small or large, and at the same time the endoscopist can look around the stomach to make sure that there is no additional cause of blood loss, like a stomach ulcer or a stomach cancer.<sup>289</sup>

**7.142** Mrs O'Hara was admitted to Stobhill as an emergency patient between 21 and 27 May 1999 for 'stabilisation of really quite severe cardiac failure'.<sup>290</sup> Dr Dunn explained that valve prostheses last a variable period of time. It appeared that some elevation of pressure was starting on the right side of the heart, leading to swelling of the ankles. Sometimes this could be reactive: it did not necessarily mean that the valve was the source of the trouble as patients often had a degree of elevation of the pressure on the right side of the heart at the time of the operation. This can be relieved but can subsequently return and the tricuspid valve (located on the right side of the heart) can start to dilate creating back pressure causing failure, predominantly of the right side of the heart. Ankle swelling may also occur as a consequence of cirrhosis and portal hypertension. From Dr Dunn's recollection, her problems were with the right side rather than the left side of the heart.<sup>291</sup>

**7.143** In September 2001, Mrs O'Hara was again reviewed.<sup>292</sup> Her shortness of breath was stable but she reported chest pain on exertion. It was thought that the pain was likely to be ischaemic in nature (caused by inadequate flow of blood to the heart). In Mrs O'Hara's case this was probably caused by her atrial fibrillation, a heart rhythm disorder.<sup>293</sup>

---

<sup>283</sup> Letter from Dr McLaren to Mrs O'Hara dated 24 July 1996 [OHA.001.1020]; Letter from Dr McLaren to Dr Forrest, copied to GP, dated 24 July 1996 [OHA.001.1019]

<sup>284</sup> Letter from Stobhill to GP dated 23 April 1997 [OHA.001.2439/40]

<sup>285</sup> Dr Mutimer – Day 3, pages 63–64

<sup>286</sup> *Ibid* page 64

<sup>287</sup> Stobhill surgeon's notes [OHA.001.1045]

<sup>288</sup> Letter from Stobhill Haematology to GP [OHA.001.1049]

<sup>289</sup> Dr Mutimer – Day 3, pages 64–65

<sup>290</sup> Letter from Stobhill to GP dated 14 June 1999 [OHA.001.1083]

<sup>291</sup> Dr Dunn – Day 3, pages 123–124

<sup>292</sup> Letter from Stobhill to GP dated 18 October 2001 [OHA.001.2184]

<sup>293</sup> Dr Dunn – Day 3, pages 125–126

**7.144** In March 2002, Mrs O'Hara reported that medication had reduced her chest pain and, on examination, she appeared well.<sup>294</sup> Her medication remained as before. However, to achieve stability of her heart complaint, she required a significant dose of Frusemide, a diuretic.<sup>295</sup> By this time her diabetes had already become severe enough to require regular insulin treatment.<sup>296</sup>

**7.145** Mrs O'Hara became very unwell in March 2003. She had abdominal pain and was vomiting.<sup>297</sup> Her GP at Springburn Health Centre thought she had pancreatitis. He referred Mrs O'Hara to Stobhill on 24 March 2003.<sup>298</sup> She had developed right hypochondrial (under the ribs) pain. The GP suggested urgent abdominal ultrasound examination. Her liver function tests were mildly abnormal but within her usual range.<sup>299</sup> A Hepatitis C PCR<sup>300</sup> test in April 2003 was positive, showing that the Hepatitis C virus was still present at that time.<sup>301</sup> A CT scan on 31 March showed pronounced hepatosplenomegaly. In addition, there were extensive varices, some of which were entwined round the pancreas explaining the previous belief, arising from the earlier ultrasound examination, that there might have been a pancreatic mass. There was no such mass. There was moderate ascites (accumulated fluid in the abdomen).<sup>302</sup> She had an enlarged heart. There were gallstones. The cause of her pain was severe pancreatitis.<sup>303</sup> The investigations did not disclose another cause of her pain.<sup>304</sup> In a patient of Mrs O'Hara's age, the most common cause of pancreatitis is probably gallstones and, in severe cases, it is frequent practice to try to clear stones away from the bile duct.<sup>305</sup>

**7.146** Mr Robertson took up Mrs O'Hara's care at Stobhill. His initial likely diagnosis was gallstone acute pancreatitis.<sup>306</sup> Her amylase count was many times over the reference level applied at Stobhill to confirm a diagnosis of acute pancreatitis in association with her other symptoms and, in particular, gallstones.<sup>307</sup> She had raised INR (International Normalised Ratio: an indication of how easily the blood clots, normally measured for patients treated with warfarin).<sup>308</sup> After a period of conservative management that appeared to stabilise her condition, CT examination of her abdomen showed marked changes of acute pancreatitis but no obvious necrosis (death of cells or tissue) or local complication. Of the alternative approaches to open surgery, laparoscopic cholecystectomy (removal of gall bladder) was excluded by anaesthetic considerations, including the difficulty in restoring natural respiration after surgery under artificial ventilation.<sup>309</sup> It was therefore decided to proceed to ERCP and endoscopic sphincterotomy, procedures that could be performed under sedation.<sup>310</sup>

---

<sup>294</sup> Letter from Stobhill to GP dated 09 May 2002 (dictated on 13 March 2002) [OHA.001.1112]

<sup>295</sup> Dr Dunn – Day 3, pages 126–127

<sup>296</sup> Letter from Stobhill to GP dated 09 May 2002 (dictated on 13 March 2002) [OHA.001.1112]. The medication listed included 'Humulin'.

<sup>297</sup> Witness Statement of Mrs Kennedy [WIT.003.0420] at 0424

<sup>298</sup> Letter from GP to Stobhill dated 24 March 2003 (see handwritten note dated 26 March 2003 on page 2) [OHA.001.2156]

<sup>299</sup> Ibid [OHA.001.2156]

<sup>300</sup> Polymerase Chain Reaction test (see Glossary).

<sup>301</sup> Dr Mutimer – Day 3, page 45; Test result [OHA.001.2710]

<sup>302</sup> Stobhill Diagnostic Imaging Report dated 31 March 2003 [OHA.001.0844]

<sup>303</sup> Dr Mutimer- Day 3, page 68; Dr Mutimer's Report [BLA.001.2298] at 2300

<sup>304</sup> Dr Mutimer – Day 3, pages 66–67

<sup>305</sup> Ibid pages 68–69

<sup>306</sup> Letter from Stobhill to GP dated 15 May 2003 [OHA.001.1451]

<sup>307</sup> Dr Robertson – Day 3, page 93

<sup>308</sup> Ibid

<sup>309</sup> Letter from Stobhill to GP dated 15 May 2003 [OHA.001.1451]

<sup>310</sup> Dr Robertson – Day 3, page 94: 'ERCP' is Endoscopic Retrograde Cholangiopancreatography (see Glossary).

**7.147** The surgical procedure, as described in evidence by Mr Robertson, to deal with Mrs O'Hara's gallstones was protracted and difficult.<sup>311</sup> The target area was very small and the surrounding mucosa (mucous membrane) swollen.<sup>312</sup> An initial procedure failed.<sup>313</sup> A second procedure was partly successful in that the sphincter muscle, the ampulla of Vater, was cut. Difficulties had been anticipated on account of Mrs O'Hara's other health problems and there was a risk of bleeding. The cut caused bleeding that had to be dealt with and the procedure was suspended with only partial success having been achieved.<sup>314</sup> A third attempt on 18 April completed the operation.<sup>315</sup> The bile duct was cleared of the obstructions (stones) that had gathered at its junction with the pancreas.<sup>316</sup>

**7.148** Mr Robertson asked for cardiological and gastroenterological input to help her overall management. It was known that Mrs O'Hara had underlying liver pathology: she had cirrhosis. It was also known that she had cardiac disease and impaired heart function as a result. The control of these conditions by medication was impaired and the symptoms that they might cause were more manifest.<sup>317</sup> Furthermore she had insulin-dependent diabetes.

**7.149** Her pancreatitis seemed to be resolving. However, she developed a tense abdomen with marked ascites, probably reflecting a combination of decompensated<sup>318</sup> hepatic and cardiac failure, along with a degree of hypoalbumina (shortage of white blood cells), and cellulitis (bacterial infection of the skin) affecting mainly the lower limbs. The medication that had controlled her liver and heart disease lost effectiveness. With gastroenterological and cardiac help, she seemed to improve but there was marked oedema below the knees.<sup>319</sup> Mr Robertson thought that bacterial endocarditis (inflammation of the lining of the heart cavity) could have developed, but accepted the view of Dr Petrie that that was unlikely.<sup>320</sup>

**7.150** On 3 May, Mrs O'Hara deteriorated further, with increasing confusion and shortness of breath. She was clearly moving in the direction of 'multi-organ failure', a condition that is associated with very high mortality. Consideration had been given to ventilation in the Intensive Therapy Unit but it was felt that she could not be removed from artificial ventilation once it had been commenced. Hence she was moved from the surgical unit and admitted to the coronary care unit for intensive cardiac monitoring and support.<sup>321</sup>

### **Mrs O'Hara's final admission and death**

**7.151** Mrs O'Hara died on 7 May 2003. Her final admission was very difficult and complicated. She had pancreatitis. Gallstones were probably the most common cause of pancreatitis in a patient of her age and it was common practice to try to clear some of these away from the bile duct. She developed cellulitis. In the course of this illness Mrs O'Hara had a lot of problems with fluid retention and that would be manifest in a couple of ways. One would be that she would develop ascites, which was seen on the

---

<sup>311</sup> Day 3, pages 96–98

<sup>312</sup> Dr Robertson – Day 3, page 98

<sup>313</sup> Stobhill surgeon's notes dated 07 April 2003 [OHA.001.1455]

<sup>314</sup> Dr Robertson – Day 3, page 99; Stobhill surgeon's notes dated 10 April 2003 [OHA.001.1454]

<sup>315</sup> Dr Robertson – Day 3, page 100

<sup>316</sup> Stobhill surgeon's notes dated 18 April 2003 [OHA.001.1453]

<sup>317</sup> Dr Robertson – Day 3, pages 100–101

<sup>318</sup> 'Decompensation' is a failing condition of an organ, such as the liver.

<sup>319</sup> Letter from Stobhill to GP dated 15 May 2003 [OHA.001.1451]

<sup>320</sup> Dr Robertson – Day 3, page 103; Dr Robertson's report [PEN.010.0170] at 1071; Dr Petrie's letter to CLO dated 23 February 2011 [PEN.010.0182]

<sup>321</sup> Dr Robertson's report [PEN.010.0170] at 0172; Dr Robertson – Day 3, page 106

CT scan, but, in addition to that, the fluid retention was likely to be more generalised and particularly to affect her lower limbs and buttocks. In those circumstances there was a susceptibility to infection because of swelling of the tissue with fluid. In the event, she developed very serious infection in those tissues.<sup>322</sup>

**7.152** As noted in paragraph 7.103, the causes of death registered on her death certificate were hepatic failure, septic shock and mitral valve disease.<sup>323</sup> Mrs Kennedy had commented on the absence of reference to Hepatitis C.<sup>324</sup> When asked if he would have expected Hepatitis C to have been mentioned, Dr Mutimer said:<sup>325</sup>

Yes, it is a cause of the liver disease, so if the liver failed, then it would be appropriate that Hepatitis C is listed on the death certificate.

**7.153** He was asked if, by 'appropriate' he meant that it should have been listed and he confirmed that he did.<sup>326</sup> In relation to pancreatitis, he added:

I think that pancreatitis seems to be missing as well ... her final illness was due to severe pancreatitis. At the end of that illness ... the cause of death was infection. That would be very typical of severe pancreatitis. The ability to cope with an illness of this severity would be affected by the fact that the patient has cirrhosis, and the cause of the cirrhosis is Hepatitis C. So the liver was not the cause of the final illness but it probably affected her potential to survive this illness, but I can't say to what extent because patients with normal livers die of severe pancreatitis in this sort of setting.<sup>327</sup>

**7.154** Dr Mutimer explained his view that Hepatitis C infection was unlikely to have made a major contribution to shortening Mrs O'Hara's life. He said:

[I]t was certainly my view after going through all of the records ... I can only have an impression. I never saw the patient, of course, but it was my impression that her health was not very good at that stage [between 1999 and 2003] and that there was diabetes, there was possibly additional cardiac problems, possibly angina. So it is difficult in that setting to say what her prognosis would be if she did not have cirrhosis of the liver.

On balance, I think that her life expectancy was not long because of those issues. The Hepatitis C and the cirrhosis may have shortened her life.<sup>328</sup>

**7.155** Asked to explain what he meant by 'may have shortened her life', he said:

I think "may" means a better than 50 per cent chance that it contributed but ... severe pancreatitis in a patient aged 72 is associated with ... severe morbidity and with mortality, and that can be observed regardless of the presence or absence of cirrhosis. I think that the cirrhosis may have contributed to the fact that this patient did not survive the illness.<sup>329</sup>

---

<sup>322</sup> Dr Mutimer – Day 3, pages 68–69

<sup>323</sup> Death certificate [OHA.001.2641] – the death certificate was signed by Dr Petrie; Email from Dr Petrie dated 24 February 2011 [PEN.010.0157]

<sup>324</sup> Witness statement of Mrs Kennedy [WIT.003.0420] at 0425

<sup>325</sup> Day 3, page 79

<sup>326</sup> Ibid page 79

<sup>327</sup> Ibid pages 79–80

<sup>328</sup> Ibid pages 83–84

<sup>329</sup> Ibid page 80



**7.156** In the days leading to her death, many tests were carried out. Dr Mutimer commented on some of the results relating to her liver.<sup>330</sup> Having looked at the records of her prothrombin time (a measure of coagulation activity) measured by INR, Dr Mutimer confirmed his view that Mrs O'Hara's liver managed remarkably well in the early phases of this final admission, despite her severe pancreatitis.<sup>331</sup> In a patient with cirrhosis of the liver who developed a serious problem elsewhere, like pancreatitis or any other serious non-liver illness, then probably the best way to see whether the liver had sufficient strength to cope with the stress was to look at the patient's serum bilirubin<sup>332</sup> level and also the INR. It was really only at the very end of Mrs O'Hara's life that the bilirubin started to go up. Her INR was affected by warfarin. The doctors had to stop the warfarin but, when they did that, Mrs O'Hara's prothrombin time returned almost to normal values. The liver is responsible for the synthesis of several proteins required for normal blood clotting. If the function of the liver is impaired, that is reflected in prolonged INR. Normal INR implies that the liver is functioning well. Mrs O'Hara's liver was coping remarkably well during the first weeks of this really very serious illness after withdrawal of warfarin therapy. This indicated to Dr Mutimer that if she had not developed serious illness, the liver would still have had 'significant mileage' left in it.<sup>333</sup>

**7.157** Dr Mutimer noted that, in the last few days of her illness, her C-reactive protein was very high, as was her white cell count. These were markers of very severe infection.<sup>334</sup> Her albumin count was indicative of severe pancreatitis.<sup>335</sup> She had renal failure and worsening hepatic failure in the context of overwhelming sepsis (infection).

**7.158** Dr Mutimer's view of the cause of death was sepsis, due to pancreatitis, with contributory causes including cirrhosis due to Hepatitis C and diabetes.<sup>336</sup> Mr Robertson thought one could not express a view on her prospects if cirrhosis and Hepatitis C were removed from the equation: her morbidities were all interrelated.<sup>337</sup>

**7.159** In his report for the Inquiry, Dr Petrie expressed the view that Mrs O'Hara had 'overwhelming sepsis, felt likely secondary to pancreatic collection. She tolerated this poorly due to her longstanding liver and heart disease and developed new acute renal failure'.<sup>338</sup> Dr Dunn commented:

Yes, I think that's fairly accurate. Often in these situations – I mean, acute pancreatitis is in itself a very severe illness and when the patient is afflicted with that and already has significant multi-organ difficulties, and in her case I think her diabetes and her extensive past cardiac conditions were put under the kind of stress with the pancreatitis, that while she was managing not too badly, the pancreatitis just led to a failure of these other organs. I think it is just an effect almost like a domino effect. If one system goes, then the next system goes under pressure and so on and so forth. So I would think that certainly the sepsis was the – the result of the pancreatitis was what caused this. So I would agree with

---

<sup>330</sup> Ibid pages 70–74

<sup>331</sup> Ibid Pages 75–76

<sup>332</sup> Bilirubin is a product of the red blood cells of the body, formed from broken-down haemoglobin. See Chapter 13, *Knowledge of Viral Hepatitis Now*, paragraphs 13.55–13.56

<sup>333</sup> Day 3, pages 74–75

<sup>334</sup> Ibid pages 70 and 73

<sup>335</sup> Ibid page 72

<sup>336</sup> Ibid page 85

<sup>337</sup> Dr Robertson – Day 3, pages 104–105

<sup>338</sup> Report [PEN.010.0182]

that. I get the impression that on reflection, Dr Petrie felt that Hepatitis C should have been mentioned in the death certificate and I would agree with that.<sup>339</sup>

**7.160** Dr Dunn, having re-considered Mrs O'Hara's history of diabetes, her cardiac status and Hepatitis C, said:<sup>340</sup>

I have looked at this again, just reflecting on it, and I think there is no doubt these factors, each of them would contribute a substantial increase, perhaps doubling. If we say that mortality from the pancreatitis was, say, 7 to 10 per cent, I think each of these factors would add another 10 per cent, perhaps not the diabetes but her cardiac status and her Hepatitis would each, in my view, contribute another 10 per cent to decreasing her likelihood of survival.

So whereas it would have been say 10 per cent, it might have gone to 20 per cent because of the presence of Hepatitis C and because of her cardiac failure, but that's not an exact science. I have discussed this with experts on pancreatitis and that was their kind of sense from hearing the situation, that that would be the kind of impact of these additional conditions on her survival.

**7.161** However, he was not wholly comfortable with arithmetical or mathematical expressions in this context: it was more a multi-system failure and the accumulation of problems significantly increased the mortality risk. It was, he thought, more a matter of sense rather than modelling.<sup>341</sup> In a patient over 70 years of age, severe acute pancreatitis, quite apart from the patient's other diseases, carries a high mortality.

**7.162** Dr Dunn discussed the possible connection between Mrs O'Hara's cardiac condition and the development of cirrhosis in view of the known connection in certain circumstances.<sup>342</sup> Cardiac cirrhosis rarely causes the classic cirrhotic pattern seen in primary liver disease. Mrs O'Hara's history was not consistent with such a connection. Dr Dunn's view was that her cardiac condition did not pre-dispose her in any significant way to the development of cirrhosis, though he did not exclude it entirely.<sup>343</sup>

## Cause and date of Hepatitis C infection

### *The Hepatitis C antibody test of 5 November 1990*

**7.163** As noted in paragraph 7.116, tests for antibody to Hepatitis C were carried out on blood samples taken on 5 November 1990. The samples were reported to be negative after microbiological testing. If that was a true reflection of Mrs O'Hara's condition – a truly negative test – it is highly unlikely that she acquired Hepatitis C virus infection prior to November 1990.

**7.164** In retrospect, however, having regard to the progression of Mrs O'Hara's Hepatitis C-related liver disease, it is now clear that the negative test result was a false negative. In Dr Mutimer's view that was almost certainly the case: Hepatitis C infection was established and had already caused cirrhosis at this stage.<sup>344</sup> As a matter of probability there is no reason to doubt that the result was a false negative.

---

<sup>339</sup> Day 3, pages 129–130

<sup>340</sup> Ibid pages 132–133

<sup>341</sup> Dr Dunn – Day 3, page 134

<sup>342</sup> Ibid page 131

<sup>343</sup> Ibid pages 131–132

<sup>344</sup> Ibid pages 32 and 81; Dr Mutimer's report [BLA.001.2298] at 2301

**7.165** The reliability of the test was explored with Dr Sheila Cameron of the West of Scotland Specialist Virology Centre, one of those who carried out the test (and signed the report of the results on 18 December 1990).<sup>345</sup> In her written statement, she commented that the test would have been carried out using the Ortho first-generation ELISA:

This was the first HCV antibody test. It was introduced in 1989 and was of limited sensitivity and specificity, ie there were false positives and false negatives. No confirmation test was available in our laboratory at that time. I would not exclude HCV infection on the basis of this result. There is a wealth of published data which supports this view.<sup>346</sup>

**7.166** The weight of evidence before the Inquiry indicated that there were problems with the sensitivity of this test. The test results were frequently wrong in Scotland: early work carried out in Glasgow on anti-Hepatitis C virus testing by Dr Dow and others showed a significant proportion of false negative results. A likely explanation is that the tests were developed and validated using North American blood and that the predominant strain (genotype) of the Hepatitis C virus in North America was different from the predominant genotypes in Scotland.<sup>347</sup> So far as appears from the information available to the Inquiry, Mrs O'Hara's Hepatitis C was never genotyped.<sup>348</sup> It is possible, but highly speculative, that this explains the negative result in November 1990. Whatever the explanation, however, it is appropriate to dismiss the test result as a factor bearing on the date of infection.

#### *The cause of Mrs O'Hara's Hepatitis C infection*

**7.167** Having regard to the finding that the November 1990 result was a false negative, and bearing in mind Dr Mutimer's view that on clinical grounds Hepatitis C infection was already established by then, Mrs O'Hara was clearly infected with Hepatitis C some time before November 1990 and the cause of her infection has to be found before that date.

**7.168** Specific blood tests for the presence of Hepatitis C infection were not available anywhere in June 1985, the date of her last transfusion prior to November 1990, and reliable screening tests would not become available in Scotland for some time thereafter. This was because the virus itself was not identified until 1988. Screening for Hepatitis C of blood intended for transfusion commenced in the UK in September 1991. Mrs O'Hara had therefore probably been exposed to unscreened blood on transfusion on four occasions by the date of the false negative test in November 1990.

**7.169** There were two possibilities: blood transfusion or a nosocomial (hospital acquired) source not directly related to transfusion. Dr Mutimer explained:

[I]nfections can be acquired in hospital, it is not just from blood transfusion, and that includes Hepatitis C. So we see people who have acquired Hepatitis C without ever having received a transfusion but who have had complex and difficult medical problems over a long period of time. With them it is likely that they somehow come into contact with it in the hospital setting. So 'nosocomial' refers to that.

---

<sup>345</sup> Test results [OHA.001.1272]

<sup>346</sup> Enzyme-linked Immunosorbent assay; letter from Dr Cameron dated 03 December 2010 [PEN.001.0025]

<sup>347</sup> A brief explanation is given by Dr Dow – Day 4 pages 58–59. The topic is discussed in detail in his report [PEN.001.0016] and in the report of Mr Laing's death. See also: Chapter 16, *Knowledge of Viral Hepatitis 3 – 1986 Onwards*, paragraphs 16.31 and 16.47.

<sup>348</sup> Explained by Counsel to the Inquiry Day 3, page 33.

So the blood may have been the source of Hepatitis C infection, we can't be certain. It is most likely but, with so many and such complex past illnesses, the hospital setting, including the blood transfusion, is likely to have been the source of her infection.<sup>349</sup>

**7.170** So far as nosocomial infection is concerned, Mrs O'Hara had been an orderly in Stobhill Hospital<sup>350</sup> and could have been infected in the course of her work there. She had also been exposed to a large number of procedures in hospital and Dr Mutimer thought that blood transfusion was a more likely cause of infection than some other mechanism. Of Mrs O'Hara's various transfusions, Dr Mutimer said:

[W]e don't know if she had a transfusion in 1963, and in 1963 the frequency of Hepatitis C in the blood donor pool was probably incredibly low, so I don't think it would have been 1963. We know that in [1985] she already had abnormal liver function tests and I suspect it was Hepatitis C. So perhaps the transfusions in 1985 and 1991 are unlikely, in that Hepatitis C was probably already present. Which means 72 and 79, and perhaps the risk then was proportional to the magnitude of the transfusion. So there was one unit in 1972 and two units in 1979. So perhaps Sherlock Holmes might decide on 1979.<sup>351</sup>

**7.171** He thought that it was never going to be possible to know. Dr Dunn thought that the transfusions in 1972, 1979 and 1985 were possibilities<sup>352</sup> but Dr Mutimer's analysis was, on balance, more persuasive.

**7.172** There is no acceptable evidence to suggest that she might have acquired the infection in any other way: nosocomial transmission remains as a possibility but is unsupported by any relevant facts. The probability is that Mrs O'Hara was infected by blood transfusion. Having regard to the volume of transfused blood, the transfusion in 1979 was the more likely of the two earlier events to have infected her.

### **Mrs O'Hara's management as a patient in 1990–91**

#### *The role of Gastroenterology*

**7.173** The final submissions on behalf of the patient interest core participants, including Mrs Kennedy, relative to Mrs O'Hara's management as a patient,<sup>353</sup> raise two questions that relate to this period:

- Whether, following the negative Hepatitis C result in 1990, and against the background of findings of abnormal LFTs, Mrs O'Hara's liver condition should have continued to be monitored by Gastroenterology.
- More specifically, whether consideration should have been given to further investigation once the second generation of HCV tests had become available in September 1991.

**7.174** Expressed in this way, the questions are not very helpful. Together, they imply that Gastroenterology did not continue to monitor Mrs O'Hara after November 1990. As a specific issue, the second has no time reference and no reference to any context defined by Mrs O'Hara's medical treatment.

---

<sup>349</sup> Day 3, page 81

<sup>350</sup> Mrs Kennedy – Day 3, page 3

<sup>351</sup> Day 3, pages 82–83

<sup>352</sup> Ibid page 113

<sup>353</sup> Closing submissions of patient interest core participants (para 5) [PEN.019.0779] at 0781

**7.175** As the narrative at paragraphs 7.114–7.116 above shows, Dr Morris of the Gastroenterology Department at the GRI did continue to deal with Mrs O'Hara's management after November 1990. It appears to be clear that Dr Morris considered that Mrs O'Hara should be seen after that date. In November 1990 he arranged for tests to be carried out, with a view to bringing her back to the clinic to discuss the results. She attended his clinic on 17 December. An arrangement was made at or after that date for an appointment at the gastroenterology clinic on 11 March 1991. Mrs O'Hara did not attend. Mrs O'Hara's failure to attend the clinic is, as Dr MacKenzie suggested,<sup>354</sup> understandable given the intensive care she had been receiving and was continuing to receive at the GRI for her cardiac problems at the time. There is no criticism of Mrs O'Hara. From the medical records it is not possible to form a view of what happened after 11 March 1991 so far as further Gastroenterology clinic appointments are concerned. It is clear, however, that, notwithstanding the referral to the GRI Cardiology Department, the 1990 test results (including the Hepatitis C result reported on 18 December 1990) did not end the GRI Gastroenterology department's interest in Mrs O'Hara as a patient.

**7.176** There is no basis in the written records for a view that the Hepatitis C test result was treated as definitive or that it was the sole or main basis on which diagnosis was reached by Dr Morris and Dr MacKenzie resulting in the referral to the GRI Cardiology. Dr Morris' view, in his report dated 5 November 1990, was that mild congestive cardiac failure did not explain Mrs O'Hara's splenomegaly and abnormal blood tests.<sup>355</sup> He instructed further tests against that background. The particular test finding that Mrs O'Hara was negative for Hepatitis C antibody had not been reported by 17 December 1990, the date of Dr Morris' referral letter to Dr Lorimer, in which he set out the reasons for considering that cardiac investigations were appropriate (particularly the echocardiogram which suggested worsening heart valve problems).<sup>356</sup>

**7.177** Dr Mutimer agreed with Dr Morris' view that chronic mild congestive heart failure might not explain Mrs O'Hara's abnormal liver function tests. He gave additional explanations of his view. Her abnormal LFTs had been causing concern for several months, reflected in questioning about alcohol consumption. In addition, some of the clinical findings suggested significant liver damage: the tip of the spleen was palpable, a potentially significant abnormality which often implies the presence of cirrhosis.<sup>357</sup>

**7.178** Having reviewed the records as a whole, Dr Mutimer's view was that, with the exception of the November 1990 blood test result, everything pointed to Hepatitis C infection.<sup>358</sup> However, he contrasted the state of knowledge of Hepatitis C in the early 1990s with current knowledge. At that time, most GPs and hospital clinicians would have had very little knowledge of Hepatitis C. He said:

I think people's familiarity with Hepatitis C in the early 90s was really quite poor. Remember, the virus was only discovered in 89. The first tests available in clinics in 1990. So a lot of our knowledge about Hepatitis C at that stage was fairly superficial .... Perhaps it is that first test in 1990 which has really thrown them off track, I think, and that was unfortunate because, you know,

---

<sup>354</sup> See paragraph 7.110

<sup>355</sup> Letter to GP [OHA.001.1173]

<sup>356</sup> Dr Morris' referral letter [OHA.001.1168]

<sup>357</sup> Day 3, pages 30–31

<sup>358</sup> Ibid pages 32–33; Report [BLA.001.2298] at 2301

it was a very clever thing for the doctor to do in 1990, to say there has been transfusion. There is liver disease, is it Hepatitis C? And then unfortunately an erroneous result has thrown him off track, I think.<sup>359</sup>

**7.179** It is possible that Dr MacKenzie and Dr Morris were thrown off the track, to some extent, by the negative test result. It is, however, reasonably clear that it was not the test result that interrupted their management of Mrs O'Hara's case. Dr Morris did not express a view that the result was reliable. There were unanswered questions, so far as he was concerned, in his approach to Mrs O'Hara's signs and symptoms. It cannot be said that he treated the result as definitive, given the investigations he instructed into the other signs and symptoms Mrs O'Hara had at the time.

**7.180** In Dr Morris' letter to Dr Lorimer dated 17 December 1990, written on behalf of Dr MacKenzie, he referred to the echocardiogram showing 'moderate to severe mitral regurgitation and mild to moderate tricuspid regurgitation'.<sup>360</sup> It appears that the echocardiogram findings were a significant factor in the gastroenterologists' thinking at the time. Together with enlargement of the liver and spleen, and splenic vein dilatation, these appearances suggested to them that congestion secondary to primary cardiac abnormality was the most likely cause of Mrs O'Hara's abnormal liver function tests. That appears to have been a clinical judgement on the basis of the findings set out in his letter.

**7.181** Mrs O'Hara was to turn out to have severe cardiac problems requiring attention. The decision to refer her to Dr Lorimer was clearly correct. Throughout most of 1991, Mrs O'Hara was treated intensively for her cardiac problems. Replacement of her mitral prosthesis was necessary. Preliminary investigations of her coronary arteries were required. The surgical procedure in October 1991 was successful.

**7.182** The question can be posed whether reliance on the test results of November 1990 had a significant and adverse effect on Mrs O'Hara's management. There is no evidence that management decisions were taken on the basis of the test results. It is of course clear that, had a positive and accurate result been reported, it is likely that a management plan would have been developed that took account of that finding. Not least, it would have had an influence on surgical procedures in 1991, given the potential risk of accidental transmission from patient to staff. It would have been a positive indication that, following her cardiac care, Mrs O'Hara would have required active care by gastroenterologists. On the basis of his earlier comments, Dr Morris would have wished a biopsy, for example. It does not follow that the negative finding prevented further gastroenterological input: it did not, in fact, as the narrative of follow-up arrangements into early 1991 shows.

**7.183** Dr Mutimer was asked about the absence of gastroenterological involvement in the period between 1990 and 1995.<sup>361</sup> Whilst he initially observed that Mrs O'Hara should have 'remained in their domain', he was not critical, in all the circumstances, of the fact that this did not happen. That view is accepted. Mrs O'Hara was in the care of the cardiac department and was regularly monitored in hospital.

---

<sup>359</sup> Ibid pages 48–49

<sup>360</sup> Dr Morris' letter to Dr Lorimer [OHA.001.1168]

<sup>361</sup> Day 3, pages 34 and 51

### ***Further investigation following introduction of second-generation anti-Hepatitis C tests***

**7.184** Against this background, it is appropriate to return to the core participants' second question: whether consideration should have been given to further investigation once the second generation of anti-Hepatitis C tests had become available in September 1991.

**7.185** As discussed in Chapter 31, *The Introduction of Screening of Donated Blood for HCV*, in the period between the first anti-Hepatitis C test released for evaluation in November 1989 and September 1991, there were significant developments in technology relating to anti-Hepatitis C testing.<sup>362</sup> A pharmaceutical company, Ortho, intimated to Professor Cash, SNBTS, and Dr Gunson, NBTs, in November 1989, that their ELISA<sup>363</sup> had received an export permit from the US Food and Drug Administration that would allow the use of the test for diagnostic use. By December 1989, the West of Scotland BTS had arranged to receive Abbott Laboratories' test kits for evaluation. The lack of a confirmatory test at that time was a factor that contributed to delay in introducing the tests routinely. Ortho's first generation RIBA<sup>364</sup> confirmatory test was sent to the United Kingdom for evaluation in February 1990. The recipients included Dr Follett at Ruchill Hospital in Glasgow. Ortho's second generation ELISA, with improved sensitivity, was anticipated in a marketing announcement in October 1990 and at a scientific symposium in November 1990. The availability of second generation Ortho kits for evaluation was intimated to the Advisory Committee on the Virological Safety of Blood on 21 November 1990. By then Abbott had further developments in hand. Their test was launched on 6 December 1990. In Scotland, anti-Hepatitis C screening of blood donations was introduced generally on 1 September 1991.

**7.186** The type of Hepatitis C test used in Mrs O'Hara's case is not identified in the hospital laboratory reports.<sup>365</sup> It was carried out at the GRI Microbiology Department on the instructions of Dr Morris and reported on 18 December 1990. Having regard to the chronology above, it appears highly likely that it used one or other of the less developed test systems then available. That was Dr Cameron's evidence: she informed the Inquiry in her letter that the test would have been the first generation Ortho test.<sup>366</sup> Lack of sensitivity and specificity had been material factors in delaying the introduction of the test systems for general use. Locally, Dr Dow and others had reported in December 1989 that the Ortho Hepatitis C ELISA kit then commercially available had an acceptable specificity but an apparent reduced sensitivity compared with the development model they had previously tested.<sup>367</sup>

**7.187** Improvements in technology in the course of 1991, leading to the general adoption of anti-Hepatitis C screening of blood donations in September, might have been expected to persuade gastroenterologists, if confronted by a patient's continuing pattern of deranged LFTs, to have submitted blood for further virus serology testing.

**7.188** However, Mrs O'Hara was not in the care of the gastroenterologists at the material time and there was nothing to trigger a reference by the cardiac surgeons back to gastroenterology when her cardiac treatment was completed. It is recorded that, on

---

<sup>362</sup> Details of the developing picture are given in the Preliminary Report at paragraphs 9.163, 9.167, 9.186, 9.235 and 236, 9.245 and 9.284, and are discussed in this report in Chapter 31, *The Introduction of Screening of Donated Blood for Hepatitis C*.

<sup>363</sup> Enzyme-linked immunosorbent Assay.

<sup>364</sup> Recombinant Immunoblot Assay.

<sup>365</sup> Test result [OHA.001.1272]

<sup>366</sup> Letter from Dr Cameron dated 03 December 2010 [PEN.001.0025]

<sup>367</sup> Dow et al, 'SNBTS Evaluation of the Ortho HCV Antibody ELISA Test System', 13 December 1989 [SNF.001.1180] at 1209

her discharge from hospital in October 1991, following her heart valve replacement, her LFTs were normal. Consideration could only have been given to further investigations following the availability of second-generation anti-Hepatitis C tests if there had been in place mechanisms (which were never defined in the evidence) to secure the continuing involvement of relevant specialists in her care and management. There is no basis in the evidence before the Inquiry for a need, separate from arrangements for Mrs O'Hara's management while in gastroenterology care, to give consideration to further investigation related to the particular development of second-generation tests.

**7.189** So far as the evidence discloses, there was no mechanism by which a former patient could be identified by a hospital following on a scientific development that might have a bearing on the patient's care or treatment and, on the initiative of the hospital, brought in for further investigation. Having regard to the obvious impracticability of implementing such an arrangement, it would not be appropriate for the Inquiry to make any recommendation that such a mechanism should be introduced.

### **Mrs O'Hara's management to late 1995**

**7.190** When admitted to the GRI on 25 February 1991, Mrs O'Hara had cardiac issues and she also had increased hepatomegaly, suggesting progressive enlargement of the liver, and her liver was slightly tender. In Dr Mutimer's view, these findings were not of themselves necessarily indicative of developing liver disease. At that stage, her cardiac problem could have caused congestion of the liver and could have contributed to her enlarged tender liver or the enlargement of her liver could have represented intrinsic liver disease, now known to be due to the inflammation of Hepatitis C.<sup>368</sup>

**7.191** Mrs O'Hara required cardiac care in the first half of 1991. As noted above, there is no basis for criticism of the decision to refer her to the cardiac clinic at that time. If there is a problem, it arises from the fact that there was no engagement of the gastroenterologists in her management after March 1991. The substantive issue focused in the first question<sup>369</sup> is whether, in light of what was known at the time, and what developed during and after cardiac care, it was appropriate for her management to proceed without further advice from gastroenterologists after 1990 and, specifically, whether it was for gastroenterology to take the initiative and call her for review.

**7.192** This issue has to be considered against the background of what was generally a good standard of management at the time. Dr Mutimer was asked whether, having regard to the medical records, there was 'someone missing from the team' from 1990, such as a gastroenterologist or a liver specialist.<sup>370</sup> The underlying concern was whether Mrs O'Hara's care might have been inadequate up to May 1995. He said:

She has got a good diabetic specialist and a good cardiologist, I think. They are probably very well trained physicians in the early 90s. They probably have very good background training in general medicine, including gastroenterology. So I don't have any reason to criticise any of the doctors who have been involved with her care so far ... It has taken a long time to get to the right diagnosis and to say what the stage of the disease is.

---

<sup>368</sup> Day 3, page 37

<sup>369</sup> Whether, following the negative Hepatitis C result in 1990, and against the background of findings of abnormal LFTs, Mrs O'Hara's liver condition should have continued to be monitored by Gastroenterology: paragraph 7.173

<sup>370</sup> Day 3 pages 49–50



[T]here have been a number of doctors at a number of hospitals who have been involved and eventually they have got there ....<sup>371</sup>

**7.193** He commented further:

[I] think again, if there had been no background cardiac problems, this probably would have come to a correct diagnosis much more quickly but this lady has been distracted by the need for, really quite major cardiac surgery, and it has also muddied the thinking about the cause of her abnormal liver function tests. So I can understand the delays that we see in establishing the correct diagnosis. It could have been diagnosed more quickly but I can understand why it took as long as it did.<sup>372</sup>

**7.194** Until 1994 Mrs O'Hara reported no problems relevant to possible liver disease at annual review. It was in August 1994 that the condition of her liver again came to the fore.

**7.195** As noted above, Mrs O'Hara frequently attended her GP in 1991, 1992, 1993 and 1994. On 17 June 1994 a diabetic assessment was noted as required and a blood test was taken.<sup>373</sup> The first LFTs noted in the GP records were reported on 9 February 1995 and were then normal.<sup>374</sup> No entry in the GP records raised an issue about Mrs O'Hara's liver or suggested a need for referral to gastroenterology.

**7.196** Given Dr Mutimer's opinion of the position at 25 February 1991, it cannot be said that the views expressed in Dr Morris' letter of 5 November 1990 were untenable.<sup>375</sup> Dr Mutimer's evidence was careful and balanced and it was not contradicted or qualified by any other evidence. Mrs O'Hara was a difficult case, given her history and the range of symptoms and signs presented. In retrospect, and in the light of Dr Mutimer's evidence, it is unfortunate that Mrs O' Hara was not monitored by gastroenterologists between early 1991 and July 1995. Had such monitoring occurred the progression in her liver disease might have been identified.

**7.197** Leaving aside the possibility that a different course of management might have been followed, there is a question whether Mrs O'Hara's Hepatitis C might have been diagnosed earlier in the course of her cardiac care. In Dr Mutimer's view, she was a patient with abnormal liver function and a patient who probably had significant liver disease.<sup>376</sup> As stated in his letter of 5 November 1990, Dr Morris thought that her cardiac problems did not entirely explain her liver problems. Liver disease was not investigated further, however, until she was referred back to the diabetic day unit at Stobhill in August 1994.

**7.198** By that time, there had been a number of specialists involved in her care, and the focus since 1991 had been on her cardiac problems. Dr Mutimer thought that the hepatosplenomegaly noted in August 1994 was not, as the consultant physician at the time thought, possibly secondary to her mitral valve replacement. It was, he considered, much more likely that this showed liver damage.<sup>377</sup> He thought that there had possibly been some crossing of wires and that perhaps investigations that had been performed

---

<sup>371</sup> Ibid pages 48–49

<sup>372</sup> Ibid page 51

<sup>373</sup> GP Records [OHA.001.2291]; Test report [OHA.001.2329]

<sup>374</sup> [OHA.001.2088] at 2289. The exception relating to Gamma GT is insignificant for this purpose.

<sup>375</sup> Letter from Dr Morris to GP dated 05 November 1990 [OHA.001.2535]; discussed at paragraph 7.104

<sup>376</sup> Day 3, page 34

<sup>377</sup> Ibid pages 38–39

previously had gone out of focus.<sup>378</sup> Once Mrs O'Hara's heart was in good condition, however, people began to pay more attention to the enlargement of the liver and spleen. Matters began to develop thereafter.

**7.199** In the circumstances that developed in 1994 and 1995, it is likely that the cardiologists would be looking for a cause of the enlargement of the liver and spleen other than her cardiac surgery. Dr Mutimer said:

I think in 1994 it is two or three years after she had a successful valve replacement? So I would be surprised if the cardiologist would accept responsibility for the enlargement of the liver and spleen. And I think it is much more likely that this is showing disease of the liver and then the enlargement of the spleen is almost certainly due to that. So it all points to the likely presence of cirrhosis at this stage, with portal hypertension, in other words pressure building up behind the liver, and that includes enlargement of the spleen.<sup>379</sup>

**7.200** It appears that particular interest in Mrs O'Hara's problem among members of the GRI's cardiac team may have been generated by Dr McLaren's letter of 5 August 1994.<sup>380</sup>

**7.201** Dr Mutimer thought that the management plan developed after review at Stobhill cardiology clinic in March 1995 was entirely acceptable at that stage.<sup>381</sup> However, the investigation did not run smoothly. As noted above in paragraph 7.126, significant hepatosplenomegaly and, in particular, splenomegaly were found but, in his letter dated 12 May 1995, Dr Dunn suggested that the condition of her lymph nodes might have a malignant source, for example lymphoma. Dr Mutimer thought that this reflected lack of knowledge of underlying clinical details: this was simply a case of cirrhosis due to Hepatitis C. Lymphoma was a possibility, but not likely<sup>382</sup> and it proved to be a false trail.

#### Dr Forrest

**7.202** A new phase in Mrs O'Hara's treatment began with her referral to Dr Forrest. His response to the referral is set out at paragraph 7.136. Dr Forrest's report of 3 November 1995, based on her care records, noted hepatosplenomegaly from 1990 and biopsy evidence of established cirrhosis.<sup>383</sup> It commented on possible alternative aetiologies and it commented on the possibilities of treatment at the Royal and the Western Infirmarys, Glasgow, if the cirrhosis was due to Hepatitis C. He was not committed to a view that Mrs O'Hara's cirrhosis was due to Hepatitis C and doubted whether she was a candidate for Interferon treatment. He said he would arrange to review her liver biopsy. He was asked for further advice in March 1996 and reminded of that request in May 1996. On 10 July 1996, he reported his view that Mrs O'Hara probably had cirrhosis and a very mild continuing hepatitis.<sup>384</sup> He estimated the prospects of success with Interferon at 20–25% after prolonged treatment. He indicated that he was prepared to refer Mrs O'Hara to gastroenterologists at the Glasgow Western Infirmary for consideration of the then-new treatment with Interferon, which he described in his letter as having been funded on a 'limited basis'. He had still not seen Mrs O'Hara.

---

<sup>378</sup> Ibid page 39

<sup>379</sup> Ibid pages 38–39

<sup>380</sup> Letter from Dr McLaren, Stobhill to GRI dated 05 August 1994 [OHA.001.1135]; discussed at paragraph 7.114 above.

<sup>381</sup> Day 3, page 46

<sup>382</sup> Ibid pages 47–48

<sup>383</sup> Dr Forrest's letter [OHA.001.1003]

<sup>384</sup> Letter from Dr Forrest to Dr McLaren [OHA.001.1017]

**7.203** Dr Mutimer commented:

There is an elephant in the room, isn't there? So I would have thought it is all due to Hepatitis C, really. I'm not sure why he is suggesting that Hepatitis C is present but not responsible for the damage. That's not likely.<sup>385</sup>

**7.204** Dr Mutimer's criticism of Dr Forrest's observations is accepted. Dr Mutimer considered that the link between Mrs O'Hara's symptoms and her Hepatitis C infection ought to have been obvious. The other possible explanations canvassed were not.

**7.205** Dr Mutimer was broadly supportive of the line taken by Dr Forrest at this time relative to treatment, however.<sup>386</sup> He thought that Dr Forrest's estimates of possible success with Interferon, an estimated success rate of 25% overall, were optimistic, both generally and in the context of the treatment of patients with advanced liver disease. He did not think that data would have existed in 1995 for Dr Forrest to have made a more accurate estimate.<sup>387</sup> Mrs O'Hara had low prospects of a good outcome from treatment. She would not have been treated by Dr Forrest, however. Concentration of Interferon treatment in particular centres was common at the time and that was not surprising.<sup>388</sup> The drugs were expensive and there was a policy of restricting their use to a limited number of centres.<sup>389</sup> Mrs O'Hara would have been referred to Dr Morris, who had by then been appointed as a consultant and was running the treatment service.<sup>390</sup> In retrospect, Dr Mutimer thought that Mrs O'Hara was probably lucky that she did not have Interferon treatment: he suspected that she would have had a lot of side-effects and no success from the treatment.<sup>391</sup> Cardiac disease was probably also a counter-indication to Interferon treatment.<sup>392</sup> Review of the biopsy was an appropriate step, to satisfy the gastroenterologist that he agreed with the pathologist's views.<sup>393</sup>

**7.206** Mrs O'Hara's daughter, Ms Annette McDonald, was a nurse at Stobhill. She asked for further information for Mrs O'Hara, probably during or shortly after her admission for liver biopsy in June or July 1995.<sup>394</sup> A doctor saw Mrs O'Hara with Ms McDonald and they were told that Mrs O'Hara had Hepatitis C as well as cirrhosis.<sup>395</sup> The family knew that when cirrhosis was established it was possibly too late to do anything.<sup>396</sup>

**7.207** Dr Forrest had an opportunity to see Mrs O'Hara at this time; he did not do so. Another opportunity arose in July 1996 when he again reviewed her case; again he did not do so. Dr Mutimer was critical of Dr Forrest for carrying out only a 'desk-top' review of Mrs O'Hara's case in July 1996. The planned management that was developed was appropriate but Dr Mutimer thought that what might be missing was the chance to actually see the patient and to discuss her illness and the reasons why treatment was not suitable.<sup>397</sup>

---

<sup>385</sup> Day 3, page 55; Dr Mutimer's report [BLA.001.2298] at 2299–2301

<sup>386</sup> Dr Mutimer's report [BLA.001.2298] at 2300; Day 3, page 57

<sup>387</sup> Day 3, pages 56–57

<sup>388</sup> Dr Mutimer – Day 3, page 57

<sup>389</sup> *Ibid* page 57

<sup>390</sup> Letter from Dr Forrest to Dr McLaren dated 10 July 1996 [OHA.001.1017] at 1018

<sup>391</sup> Day 3, page 60

<sup>392</sup> Dr Mutimer – Day 3, page 61

<sup>393</sup> *Ibid* pages 58–59

<sup>394</sup> Witness Statement of Mrs Kennedy [WIT.003.0420] at 0422; Letter from Dr Forrest's SHO to Stobhill Urology dated 15 November 1994 [OHA.001.0978], although concerning another matter, includes the comment: 'Mrs O'Hara's daughter is a staff nurse ... at Stobhill & obviously very anxious'.

<sup>395</sup> Mrs Kennedy – Day 3, page 5; The doctor cannot be identified. This was probably an informal meeting and was not recorded at the time, so far as Stobhill's records show.

<sup>396</sup> Mrs Kennedy – Day 3, page 15

<sup>397</sup> Day 3, pages 61–62

**7.208** It also deprived Dr Forrest of the advantages that might reasonably have been expected to accrue from direct contact with the patient to discuss her history.

**7.209** Dr Mutimer's opinion that it would have been good practice for Dr Forrest to have seen Mrs O'Hara was clearly correct. Any patient would have benefited from an explanation of his or her condition and of why the forms of treatment that were available at the time were not suitable or were unlikely to be effective in his or her case. Given Mrs O'Hara's interest in obtaining explanations and information, this was not a case in which it might have been thought that there would be a disinclination to have the true position spelled out. She was, as were her daughters, 'mining' for more information about the implications for Mrs O'Hara of her infection.<sup>398</sup>

**7.210** Dr Forrest's reports do not appear to have been copied to Mrs O'Hara's GP. He did not, therefore, make provision for informed discussions between Mrs O'Hara and her GP. However, at this time patients would have been dependent on specialist knowledge of Hepatitis C: it was not a subject that most GPs would have known about.<sup>399</sup>

**7.211** Dr Forrest died on 26 June 2010, and it was not possible to have his observations on this chapter of evidence.

### **Counselling and information**

**7.212** A further issue raised by Mrs O'Hara's case relates to the failure to provide appropriate counselling and support for her Hepatitis C and its consequences after the diagnosis had been made in the summer of 1995. A particular complaint is that Mrs O'Hara was not told about the danger of secondary infection and appropriate precautions.<sup>400</sup>

**7.213** In the context of the look-back exercise begun in April 1995, a document entitled *Transfusion-transmitted Hepatitis C: Guidelines for Counselling Patients* was widely available to those engaged in tracing recipients of blood or blood components from donors known to be carriers of the Hepatitis C virus.<sup>401</sup> The purpose of look-back, discussed in more detail in Chapter 35, *An Investigation into the Steps Taken to Identify the Individuals Who Were Infected (Look-Back)* was to trace NHS patients who had received blood, blood components or blood products derived from donations by donors who tested positive for Hepatitis C antibodies after 1 September 1991, when screening was introduced, and who had previously donated blood which was found by retrospective testing also to have been infective. The document provided background information on transfusion-transmitted Hepatitis C infection, the discovery of the virus and the development of tests for it. Among the modes of transmission highlighted were: sharing needles during intravenous drug misuse; transfusion; tattooing and other skin-piercing procedures; and, to a limited degree, sexual transmission. Hepatitis C positive individuals were advised that they should not donate blood. They should not share toothbrushes or razors and they should inform dentists and doctors of their HCV status. Information was given about Alpha Interferon, the only licensed therapy for chronic Hepatitis C at the time. The document was not intended for patient use but it provided one measure of what might reasonably have been expected in counselling an infected individual at the time Mrs O'Hara was told that she had Hepatitis C and cirrhosis in the summer of 1995. She was never counselled along the lines of the document.<sup>402</sup>

---

<sup>398</sup> Dr Mutimer – Day 3, page 62; Mrs Kennedy – Day 3, pages 5 and 7; Witness Statement of Mrs Kennedy [WIT.003.0420] at 0422

<sup>399</sup> Dr Mutimer Day 3, page 78

<sup>400</sup> Closing submissions of patient interest core participants (para 6.1) [PEN.019.0779] at 0781

<sup>401</sup> Transfusion-transmitted Hepatitis C Guidelines [LAI.001.0020]

<sup>402</sup> Mrs Kennedy – Day 3, pages 9–12

**7.214** Mrs O'Hara was a person with clearly expressed concerns about her health and an anxious wish to have any treatment that was available. She found having Hepatitis C very difficult. Some of her concerns were created unnecessarily by inadequate and inaccurate information.

**7.215** Mrs Kennedy said they were all shocked when a doctor at Stobhill said that blood had been taken from American prisoners and that this might be a source of Hepatitis C.<sup>403</sup> This was a misapprehension on the part of the person who gave the information. The Inquiry has seen evidence that some commercial large-pool Factor VIII blood products imported into the UK in the 1970s and 1980s were manufactured from plasma that included donations from prisoners. No whole blood used for transfusion in Scotland was collected outwith Scotland, however. The infected blood in Mrs O'Hara's case was donated in Scotland.

**7.216** Other misapprehensions are less easy to deal with. Mrs Kennedy said that her mother hated having 'Hep C risk' stamped on the front of her medical notes and was embarrassed. She knew that Hepatitis C was an infection usually associated with drug addicts. She was well known in Stobhill, having worked there, and was worried that people might find out. She felt that the comment should have been concealed inside her notes.<sup>404</sup> However, none of the Stobhill records the Inquiry has recovered are so stamped and the two volumes of GP records both have the 'Special Hazards' section on the front page left blank. Certain sheets within the GP records are headed 'Hep C Risk'. The basis for apprehension that people in Stobhill might find out about her infection cannot be verified, although it was clearly real for Mrs O'Hara.

**7.217** Mrs O'Hara's other daughter, Ms Annette McDonald, asked for further information for her mother, probably in June or July 1995. The doctor who saw Mrs O'Hara with Ms McDonald said that Hepatitis C had possibly caused cirrhosis of the liver and that she had probably contracted Hepatitis C from a blood transfusion. Their impression at the time was that the doctor played down the significance of Hepatitis C and implied that it was a common infection: cirrhosis was a lot more serious.<sup>405</sup> No advice was given about avoiding transmission or about her blood.<sup>406</sup> There was no offer of counselling or further information.<sup>407</sup> Mrs O'Hara asked about possible treatment for Hepatitis C. She was told there was no treatment as she already had cirrhosis.<sup>408</sup> Mrs Kennedy said:

[I] think when you have been attending hospitals, you do ask about treatments because it has been your experience that usually something can be done, you know, when you have had heart problems. So we just wondered, and I know my mum wondered, if just anything could be done because she was very used to following doctor's instructions and she was very faithful to doctor's instructions, and I think she just thought if there was something she could do things might get a wee bit better.<sup>409</sup>

---

<sup>403</sup> Ibid page 7

<sup>404</sup> Witness Statement of Mrs Kennedy, para 12 [WIT.003.0420] at 0423

<sup>405</sup> Mrs Kennedy – Day 3, pages 5–6

<sup>406</sup> Witness Statement of Mrs Kennedy [WIT.003.0420] at 0422

<sup>407</sup> Ibid [WIT.003.0420] at 0422

<sup>408</sup> Ibid [WIT.003.0420] at 0423

<sup>409</sup> Day 3, page 7

**7.218** In April 1998, Mrs O'Hara again asked about Interferon treatment, based on her reading of media reports.<sup>410</sup> The haematologist who saw her on 20 April left it to her GP to decide whether to re-refer her to the gastroenterologists. There is no record of her having been re-referred for gastroenterological opinion at this time.<sup>411</sup> The issues raised by her care down to mid-1997 were not resolved.

**7.219** Except in relation to counselling relating to Mrs O'Hara's cirrhosis and the treatments that might have been available for it in her case, the complaints of Mrs O'Hara's family do not lend themselves to easy categorisation. The casual mis-information provided by an unidentified doctor about the source of blood would clearly have upset the family – but it had, and could have had, nothing to do with Mrs O'Hara's treatment. Her concern about entries in her Stobhill records referring to 'Hep C risk' would again be completely understandable given her long association with the hospital but the apprehension was not well founded in fact: the hospital records were not so marked.

**7.220** Once Mrs O'Hara's cirrhosis was diagnosed, the appropriate source of accurate information about her condition, its prognosis, and counselling in relation to any particular treatment was Dr Forrest, the Consultant Gastroenterologist to whom her case was referred in September 1998. He had the opportunity to provide both information and counselling, either directly to Mrs O'Hara or by copying his inter-departmental letters to the GP for the benefit of Mrs O'Hara. Generally, there was the model of the look-back guidance as a source of what was required for the benefit of the patient.

**7.221** It has been submitted that the treatment of Mrs O'Hara raises a systemic issue about the provision of counselling and support of patients with Hepatitis C. That there were deficiencies in her case is clear but there is no basis in the evidence as a whole for a view that these were due to any systemic failure. There were lapses attributable to an individual, Dr Forrest, but it cannot be found on that basis that there was a fundamental defect in the hospital's general procedures. Mrs O'Hara's case, while of great importance to her family, is not evidence of a universal or general failure on the part of the hospitals involved, nor on the part of the NHS as a whole.

## Other issues

**7.222** The SNBTS was not able to trace the donors whose blood was transfused during Mrs O'Hara's surgery in June 1985.<sup>412</sup> The GRI Blood Bank utilised an Apple computerised system from 1981–86. It has been explained that the Apple system could not accept the SNBTS donation number configuration. The GRI laboratory allocated an identifier that was entered into the Apple system and those records contained no cross-references to the SNBTS pack numbers. A paper record was kept of the respective numbers but the paper records for 1985–86 were destroyed in error during a laboratory move in 1995.<sup>413</sup> There are no extant records that would link the units used in Mrs O'Hara's case with the SNBTS unit numbers.<sup>414</sup>

---

<sup>410</sup> Letter from Stobhill to GP dated 23 April 1998 [OHA.001.2249]

<sup>411</sup> Dr Mutimer – Day 3, pages 65–66

<sup>412</sup> Explanation by Inquiry Counsel – Day 1, pages 143–150; Letter from Inquiry to Susan Murray, Central Legal Office dated 10 December 2010 [PEN.010.0074]; SNBTS response – January 2011 [PEN.001.0032] at 0033; Email from Inquiry to CLO dated 03 February 2011 [PEN.002.0762]; SNBTS Supplementary response – February 2011 [PEN.002.0760]

<sup>413</sup> Letter from Dr Rachel Green, NHS Greater Glasgow and Clyde Acute Services Division to CLO dated 25 August 2011 [PEN.017.2153]

<sup>414</sup> Letter from Dr Tait, GRI Haematology to Dr Rachel Green dated 25 November 2008 [PEN.010.0106]

**7.223** The destruction of the paper record does not, of itself, raise any systemic issue for the Inquiry. Accidents occur in any system and may or may not indicate structural deficiency. Dependence on a paper record as a necessary link in the recording may be a different matter.

**7.224** While it is understandable that the limitations of a particular computer system might prevent it from accommodating, or reading automatically, an electronic number configuration generated by a different system, it is less understandable that the text of a GRI laboratory record should not contain, by such means as the computer software allowed, the link number to the SNBTS source material.<sup>415</sup> If that was not possible at that time, reliance on a paper record inevitably meant those records were vulnerable to accidental or erroneous destruction.

**7.225** The circumstances of the 'unfortunate' error have not been explained other than that it related to a laboratory move in 1995. Carefully specified protocols for the retention and destruction of records relating to patient care are a fundamental pre-requisite of sound administration of the NHS. Whether such protocols were in place and whether they were applied remain unanswered questions. Allowing two separate numbering systems in the principal records of interdependent NHS organisations, with linkage depending on paper records, questionable in itself, gives added weight to the requirement for controls.

### **Reasonable precautions whereby Mrs O'Hara's death might have been avoided**

**7.226** It was not suggested in the closing written submissions by the patient interest core participants that there were any reasonable precautions that might have been taken by which Mrs O'Hara's death might have been avoided.<sup>416</sup> There were none.

### **Cause of death**

**7.227** The cause of Mrs O'Hara's death was acute pancreatitis complicated by sepsis and multi-organ failure. Possible contributory causes were:

- Hepatitis C virus cirrhosis consequent on blood transfusion prior to 1985.
- Chronic heart failure with prosthetic mitral valve consequent upon rheumatic fever in childhood.
- Type II diabetes.

**7.228** The failure to record Hepatitis C as a cause of death was an error but, in the overall complex circumstances of her death, not an important error. It has been submitted that this reflects a systemic defect in procedure. While there are indications elsewhere of disinclination on the part of some doctors, and some families, to have Hepatitis C recorded (as occurred also in the case of HIV/AIDS) there is no evidence that the failure in this case was attributable to any policy or widespread practice.

---

<sup>415</sup> Typically a free text box.

<sup>416</sup> Closing submissions of patient interest core participants (para 3) [PEN.019.0779]

## Conclusions

### 7.229 Infection with Hepatitis C and progression of disease:

- (i) While nosocomial transmission of the Hepatitis C virus cannot be excluded absolutely, it is highly likely that Mrs O'Hara was infected by blood transfusion.
- (ii) The most likely date of infection was 28 November 1979 when Mrs O'Hara received a transfusion in the course of a hysterectomy.
- (iii) Mrs O'Hara was tested for Hepatitis C infection by first-generation Ortho ELISA on 5 November 1990, with negative result.
- (iv) The test result was a false negative.
- (v) Mrs O'Hara developed cirrhosis due to infection with the Hepatitis C virus.
- (vi) Insofar as Hepatitis C contributed to her death (and the extent of that contribution cannot be resolved with any confidence) her infection with the virus in 1979 could not have been prevented.
- (vii) The failure to record Hepatitis C as a cause of death was an error but, within the context of the complex circumstances of Mrs O'Hara's death, not an important error. It was not found to be a systemic defect in procedure.

### 7.230 Mrs O'Hara's management as a patient:

- (viii) It is impossible to form a view on the evidence as a whole that there was reliance on the test results relating to the blood samples taken in November 1990 which had or may have had a significant and adverse effect on Mrs O'Hara's management in 1990–91.
- (ix) Mrs O'Hara had a complex medical history and, in particular, in 1990–91 had serious heart disease that warranted surgery.
- (x) The gastroenterologists in charge of Mrs O'Hara's care at the end of 1990 referred her to the GRI Cardiology.
- (xi) That decision was well founded, given their findings on examination and investigation. The diagnosis of congestive cardiac failure was sustainable.
- (xii) The actions of the gastroenterologists, and in particular Dr Morris, including arranging a follow-up appointment for early 1991, suggest that the test results were not treated as definitive at the end of 1990 and in early 1991.
- (xiii) Continuing gastroenterological supervision of Mrs O'Hara's case was interrupted in March 1991 when contact broke down.
- (xiv) It is not possible to conclude, on the evidence as a whole, whether, if Mrs O'Hara had attended the appointment with gastroenterology on 11 March 1991, further examination by gastroenterologists would have changed the course of her management: that would be speculative.
- (xv) Mrs O'Hara was receiving comprehensive cardiology care at the time and non-attendance was considered to be understandable. The records do not disclose follow-up at gastroenterology.
- (xvi) When discharged from hospital in October 1991, Mrs O'Hara's liver function tests were normal.



(xvii) Having not attended gastroenterology in March 1991, Mrs O'Hara's liver condition was not monitored systematically between 1991 and 1994.

(xviii) Mrs O'Hara remained asymptomatic of anything to suggest chronic liver disease until August 1994 and her liver function tests were at least sometimes within her normal range. There was nothing to stimulate interest in her liver condition until Dr McLaren raised the issue in August 1994.

(xix) Since Mrs O'Hara was not receiving care related to liver disease between September 1991 and August 1994, and had not reported signs and symptoms giving rise to concern about her liver, there were no grounds for referring her for testing with second-generation anti-Hepatitis C tests when they became available.

### **7.231** Counselling and information

(xx) There was a significant lapse in Mrs O'Hara's management as a patient after she was referred to Dr Forrest on 11 September 1995.

(xxi) Dr Forrest's initial review letter dated 3 November 1995 is not criticised as unduly delayed but he carried out a review of records without seeing Mrs O'Hara.

(xxii) A request for further review was sent to Dr Forrest in March 1996. He responded on 10 July 1996, again without seeing Mrs O'Hara.

(xxiii) Taken together, these periods amounted to unacceptable delay on the part of Dr Forrest in responding to the referral and a failure in management attributable to his repeated 'desk-top' disposal of issues relating to Mrs O'Hara.

(xxiv) Mrs O'Hara should have had an opportunity to meet Dr Forrest and discuss her condition and the reasons for his opinion that Interferon treatment was not considered suitable in her case.

(xxv) Mrs O'Hara should have been given advice and counselling about her Hepatitis C status along the lines of the April 1995 document: *Transfusion-transmitted Hepatitis C: Guidelines for Counselling Patients*.

(xxvi) She did not receive any such counselling and advice. Dr Forrest was in a position to tender counselling and advice and should have seen Mrs O'Hara for that purpose. These deficiencies in Mrs O'Hara's management as a patient were attributable to Dr Forrest, stemming from his failure to see Mrs O'Hara in person, and did not evidence a universal or general failure on the part of the hospitals involved, nor on the part of the NHS as a whole.

## **Alexander Black Laing**

### **Introduction**

**7.232** Mr Laing was born on 7 December 1923. He died on 4 September 2003. The certified cause of death was 'Hepatitis C Related Liver Disease'.<sup>417</sup>

**7.233** Mr and Mrs Laing were married in 1951. Mr Laing was, prior to retirement, a linesman with the North of Scotland Hydro Electric Board and its successors. He retired in 1985.<sup>418</sup> As with all of the deaths remitted for inquiry in Term of Reference 6, it is important to provide information that may help Mrs Laing and her family understand the

---

<sup>417</sup> Death Certificate [LAI.001.1068]

<sup>418</sup> Witness Statement of Mrs Annie Laing [WIT.003.0417]

background to Mr Laing's infection and ultimate death. On a more general level, however, his experience illustrates the natural history of Hepatitis C infection in a man who, at the time of infection, was older than others investigated. It is also an illustration of exemplary care.<sup>419</sup>

## Mr Laing's medical history

### *Surgery in 1990*

**7.234** Mr Laing had surgery at the Aberdeen Royal Infirmary (ARI) on 7 August 1990. He was 66 at the time. The diagnosis was Duke's C carcinoma, indicating that the cancer had infiltrated through the bowel.<sup>420</sup> The tumour had moved beyond the local territory of the bowel and penetrated one of the seven lymph glands which were sampled at operation and examined microscopically. The fact that the cancer had penetrated one only of those lymph glands offered a slightly better prognosis than had it penetrated more than one. It was, nevertheless, a cancer with a poor prognosis in the longer term and a high chance of recurrence.<sup>421</sup> In the event, Mr Laing made a good recovery.<sup>422</sup>

**7.235** In the course of surgery Mr Laing received blood transfusions. He received two units of whole blood and other blood components and products.<sup>423</sup> The transfusion of whole blood is relevant for the purposes of this Report as it was capable of transmitting Hepatitis C infection. At the end of a course of out-patient care following surgery, lasting some five years, Mr Laing was told that the cancer was clear but that he had contracted Hepatitis C infection from the blood transfusion.<sup>424</sup> Mr Laing had been identified as being at risk by the UK-wide look-back exercise into transfusion-related Hepatitis C virus (HCV) infection which was in progress in 1995.

### *Hepatitis C look-back*

**7.236** The purpose of look-back was to trace NHS patients who had received blood, blood components or blood products derived from donations by donors who tested positive for Hepatitis C antibodies after 1 September 1991, when screening was introduced, and who had previously donated blood which was found by retrospective testing also to have been infective. Formal written intimation that Mr Laing had been so identified was given in a letter from the Scottish National Blood Transfusion Service (SNBTS) to his GP dated 26 April 1995. Enclosed with the letter was a form for the assessment of Mr Laing's suitability for counselling. The form was completed by the GP on 28 April.<sup>425</sup> Procedures for managing the exercise had been developed on a national, UK-wide basis by a steering group of which Dr Graeme Alexander, Consultant Hepatologist, Addenbrookes NHS Trust, Cambridge, was chairman.<sup>426</sup>

---

<sup>419</sup> Dr Alexander – Day 4, page 42

<sup>420</sup> Letter from ARI to GP dated 20 August 1990 [LAI.001.0127]

<sup>421</sup> Dr Alexander – Day 4, page 8

<sup>422</sup> Witness Statement of Mrs Annie Laing [WIT.003.0417]

<sup>423</sup> ARI Record sheet dated 7 August 1990 [LAI.001.0829]; Letter from Aberdeen and North East Scotland BTS (SNBTS) to GP dated 26 April 1995 [LAI.001.0105]; Dr Alexander – Day 4, pages 8–9

<sup>424</sup> Mr Laing was so told by his surgeon at ARI, according to witness statement of Mrs Annie Laing [WIT.003.0417] and/or by his GP according to letter from the GP to him dated 6 June 1995 [LAI.001.0102]

<sup>425</sup> Letter from Aberdeen and North East Scotland BTS (SNBTS) to GP dated 26 April 1995 [LAI.001.0105]; Assessment form [LAI.001.0103]

<sup>426</sup> Dr Alexander – Day 4, pages 9–10

**7.237** The look-back exercise will be discussed in greater detail in Chapter 35, *An Investigation into the Steps Taken to Identify the Individuals Who Were Infected (Look-Back)*. At this stage, it is sufficient to note parts of the wider context. In the South East of Scotland Blood Transfusion Service, a local exercise had demonstrated that look-back was feasible. Scottish Health Ministers were persuaded by December 1994 that there should be a look-back exercise for Scotland as a whole. In England and Wales, proposals for a look-back study began to be considered almost as soon as Hepatitis C testing showed that some blood donors tested positive. Dr Alexander's group had started working in 1992–93.<sup>427</sup> However, until December 1994 the proposal was controversial. Objections were overcome by the end of the year and look-back was commenced throughout the UK in 1995.

**7.238** Dr Alexander said that the majority of Hepatitis C positive blood was donated by individuals who had, at some time in the past, used illegal drugs.<sup>428</sup> Over a long period, people with a history of intravenous drug use were asked not to give blood. Standard procedure at donation sessions before September 1991 included inspection of prospective donors for physical evidence of their having injected drugs. Drug use resulting in donor infection might have occurred many years earlier and been forgotten, however, or, in the absence of signs and symptoms of disease, may have been dismissed as irrelevant by the donor. Apart from physical inspection, investigation of the history of the prospective donor was inconsistent and seldom involved questioning in depth.<sup>429</sup> Practice improved in and after 1982 in response to the threat of AIDS but, as Dr Alexander's findings indicate, individuals with a history of intravenous drug use still made up the majority of those testing positive for Hepatitis C after September 1991.

**7.239** Another cohort of infected donors acquired Hepatitis C infection from blood transfusion, again in some cases many years earlier. In 1991–92, when Hepatitis C screening of donated blood began, Dr Alexander and his colleagues were surprised at how many blood donors coming to sessions tested positive: they had not anticipated that quite as many people might have acquired Hepatitis C from transfusion.<sup>430</sup> The majority of individuals with Hepatitis C infection, whether acquired by injecting drugs or by transfusion, did not become ill at the time of infection with the virus. Whether knowingly or not, some people potentially infective with Hepatitis C continued to give blood.

**7.240** At follow-up as part of the look-back exercise, it was ascertained that the donor in Mr Laing's case had received a blood transfusion around 20 years previously.<sup>431</sup> This was the only risk factor attributable to that particular donor. In his evidence, Professor Marc Turner, Medical Director of the SNBTS, outlined the approach to this risk factor. Deferral<sup>432</sup> of donors who had themselves received blood transfusion was not introduced in the UK until 2004. At that time, the SNBTS initiated deferral of donors who had received a blood donation since 1980. The measure was related to the risk of transmission of variant Creutzfeldt-Jakob disease (vCJD). The only other country of which Professor Turner was aware which defers donors permanently because they have themselves had a blood transfusion is France, where such a measure was introduced in 1997.<sup>433</sup>

---

<sup>427</sup> Ibid page 45

<sup>428</sup> Ibid page 44

<sup>429</sup> See Chapter 18, *Collection of Blood – General* and Chapter 26, *Donor Selection – Higher Risk Donors* for more detail.

<sup>430</sup> Dr Alexander – Day 4, pages 44–45

<sup>431</sup> Dr Dow's report [PEN.012.0344] at 0345

<sup>432</sup> It was explained by Professor Turner that, in blood donation circles, the expression 'deferral' is used rather than 'rejection' – Day 7, page 16

<sup>433</sup> Professor Turner – Day 7, pages 16–20; Witness Statement of Professor Turner [PEN.002.0452] at 0454

### *Counselling and forward planning*

**7.241** After the UK national look-back programme was initiated, the focus was on previous blood donors returning to make donations. If found to be Hepatitis C positive on return, it was assumed that the donor might also have been positive at the time of donations made before screening had started.<sup>434</sup> Recipients of any earlier donations could then be identified and approached with a view to counselling and testing to determine their Hepatitis C status. In Scotland, if the patient's GP was willing to undertake that role, the SNBTS would provide details of the blood samples needed and where these should be sent, and also offer any further support or advice required. If, on the other hand, the GP wished the Blood Transfusion Service to notify and counsel the patient, the SNBTS was happy to do that. It was recognised that it might not be advisable to tell some patients and provision was made for that situation.<sup>435</sup>

**7.242** Mr Laing's GP, Dr Lynch, elected to undertake his care in this regard and sought advice from the SNBTS.<sup>436</sup> On 31 May 1995, he was sent copies of the nationally agreed counselling guidelines and a form to report the outcome of the process.<sup>437</sup> Dr Lynch wrote to Mr Laing on 6 June 1995 inviting him to make an appointment.<sup>438</sup> On 27 June he again asked Mr Laing to call as the results of the blood tests had been received.<sup>439</sup> Dr Lynch saw Mr Laing and told him the outcome. He then wrote to Dr Yates, consultant at the North East Scotland Blood Transfusion Centre at the ARI, noting that the Hepatitis C antibody and confirmatory tests were positive, providing current liver function test results, which were abnormal, and noting:

I have told him that he seems to have contracted Hepatitis C from his transfusion 5 years ago and that it may or may not damage his liver and that he will be seeing a Specialist to advise about the possibility of Interferon or not. He accepts all this with equanimity.<sup>440</sup>

**7.243** Dr Alexander considered that a fair forward plan had been established.<sup>441</sup> Mr Laing was referred for hospital care at the gastrointestinal clinic.<sup>442</sup> His general health was reported to be perfect and he was said not to have hepatomegaly (enlargement of the liver). He was seen quite promptly in July 1995 and examinations were carried out on 15 August and reported to his GP. At that stage, Mr Laing was thought to have an asymptomatic infection with Hepatitis C attributed to the blood transfusion in 1990. He was not jaundiced and had no other stigmata (signs) of liver disease. Liver function tests were repeated and a PCR (polymerase chain reaction) test performed to confirm that he was still harbouring the virus. The history of Duke's C carcinoma was thought to be a problem and further tests were instructed<sup>443</sup> as it appears to have been thought that cancer might have recurred.<sup>444</sup> It was thought that Interferon therapy might be of no use to him.<sup>445</sup> In retrospect, Dr Alexander thought that the reasoning about cancer was

---

<sup>434</sup> Dr Alexander – Day 4, page 10

<sup>435</sup> Ibid pages 9–14

<sup>436</sup> Ibid pages 11–12

<sup>437</sup> Letter from Aberdeen and North East Scotland BTS (SNBTS) to GP dated 31 May 1995 [LAI.001.0019]; Counselling Guidelines [LAI.001.0020]; Form to document outcome of counselling (complete version) [PEN.017.2267-69]

<sup>438</sup> Letter from GP to Mr Laing [LAI.001.0102]

<sup>439</sup> Letter from GP to Mr Laing [LAI.001.0101]

<sup>440</sup> Letter from GP to Dr Yates dated 30 June 1995 [LAI.001.0100]

<sup>441</sup> Dr Alexander – Day 4, page 13

<sup>442</sup> Ibid page 14; GP Request for hospital care form dated 12 July 1995 [LAI.001.0098]

<sup>443</sup> Letter from ARI to GP dated 24 August 1995 [LAI.001.0095]

<sup>444</sup> Dr Alexander – Day 4, page 16

<sup>445</sup> Letter from ARI to GP dated 24 August 1995 [LAI.001.0095]

suspect but that the right decision had nonetheless been reached about treatment.<sup>446</sup> In 1995 clinicians did not have good insight into the natural history of Hepatitis C, particularly in the older age group of patients. The evidence at that time suggested that there was a 10–20 year lag before cirrhosis would be established.<sup>447</sup>

### *Hepatitis C infection in older patients*

**7.244** Dr Alexander explained that the contemporaneous assumption about progression to cirrhosis was now known to be wrong in the case of older patients.<sup>448</sup> The common assumption in 1995 was reflected in the report by Dr Sinclair, Consultant Gastroenterologist, sent to Dr Lynch on 17 November 1995:

We now know that the long term outlook with hepatitis C is probably, in someone of this age group, fairly benign as it would probably be a significant amount of time before he produced enough chronic liver damage to creat [*sic*] ill health and my guess is that he will die of something other than liver disease. He is completely unphased [*sic*] by the whole thing but I do think we are due him a clearcut opinion as to the state of his liver and the only way to do this is with liver biopsy.<sup>449</sup>

**7.245** Dr Alexander thought that recurrence of cancer in the longer term was more likely than not, with a related risk of mortality.<sup>450</sup> At the time, however, there was no evidence of metastasis from the Duke's C carcinoma.<sup>451</sup> A liver biopsy was carried out on 25 January 1996 which showed chronic active hepatitis and gave rise to a suspicion of cirrhosis.<sup>452</sup> The tissue sample extracted on biopsy was fragmented, which may happen when the liver has significant scarring. In such cases only softer tissue comes out with the needle; scar tissue is not withdrawn with the core. The findings were therefore not absolutely reliable. Dr Alexander interpreted the pathologist's comments as reflecting suspicion that there was cirrhosis, masked by the state of the core sample withdrawn.<sup>453</sup> That impression was strengthened by the degree of liver inflammation noted. Dr Alexander thought that Mr Laing probably had cirrhosis in 1996.<sup>454</sup>

### *Clinical management*

**7.246** Mr Laing's management was discussed on 2 May 1996 at a clinico-pathological conference attended, as was typical, by the clinicians involved in the patient's care and the hospital pathologists.<sup>455</sup> That was good practice. There might be one or two or maybe up to a dozen people at such a conference. Dr Alexander speculated that there would have been a discussion suggesting that the pathologist's views were guesswork, that Mr Laing was very well, that he did not have any signs of liver disease and that there was nothing clinical to suggest cirrhosis.<sup>456</sup> It cannot be concluded that this did happen but the outcome was consistent with the hypothesis.

---

<sup>446</sup> Dr Alexander – Day 4, page 17

<sup>447</sup> *Ibid* pages 17–18

<sup>448</sup> *Ibid* page 17

<sup>449</sup> Letter from ARI to GP dated 17 November 1995 [LAI.001.0092]

<sup>450</sup> Day 4, page 17

<sup>451</sup> Letter from ARI to GP dated 17 November 1995 [LAI.001.0092]

<sup>452</sup> ARI Histopathology report dated 30 January 1996 [LAI.001.1009]; Dr Alexander's report [LAI.001.1125] at 1126

<sup>453</sup> Day 4, pages 19–21

<sup>454</sup> *Ibid* page 22

<sup>455</sup> ARI handwritten note dated 2 May 1996 [LAI.001.0625]; Letter from ARI to GP dated 15 May 1996 [LAI.001.0087]; Dr Sinclair's report [PEN.010.0174]

<sup>456</sup> Day 4, pages 39–40

**7.247** The overall conclusion was that the patient did not have cirrhosis. The consensus that emerged was that the biopsy showed mild inflammation affecting the liver with some early fibrosis which was a different conclusion from that of the pathologist.<sup>457</sup> Dr Alexander thought that this slightly underestimated the condition.<sup>458</sup> He questioned the approach: he had always worked on the assumption that one took the worst possible news when making clinical decisions rather than the best possible news. If the pathologist was suspicious that it was cirrhosis, it was reasonable to follow his view. Others, however, worked in different ways.<sup>459</sup> Dr Alexander thought that the pathologist's report was quite clear that there were features of cirrhosis but that it would have made no difference at all to Mr Laing's clinical management had the pathologist's view prevailed.<sup>460</sup>

**7.248** Among clinicians at this time there was no enthusiasm for therapy, given Mr Laing's age, the absence of symptoms of Hepatitis C and his mildly abnormal liver function test results.<sup>461</sup> Later, in September 1996, it was thought that there might be a case for Interferon treatment and that was discussed with Mr Laing. Mr Laing's preference was to 'take his chances' and not to have treatment. Dr Lynch was asked to keep an eye on his liver function tests.<sup>462</sup> As at September 1996, Dr Alexander's data over a 10 year period showed a success rate with Interferon of less than nine per cent across the board. When the position was reviewed in about 2000–01, it was found that people over 60 did not respond at all. In addition to questions about its effectiveness, the treatment was unpleasant to administer. Dr Alexander thought that Mr Laing and his doctors had taken the right decision: on balance, Mr Laing had little to gain and a lot to lose by being treated.<sup>463</sup>

**7.249** Monitoring continued and regular blood tests were taken. Mr Laing was told that there was little that could be done for the infection and that such treatment as there was might make him worse. In Mrs Laing's words, he 'just got on with his life' but he was careful to protect his family. If he had a cut, he would warn family members to keep clear of the blood.<sup>464</sup>

**7.250** There was an unfortunate incident in September 2000 when Mr Laing needed some dental treatment and his own dentist refused to treat him because he was Hepatitis C positive.<sup>465</sup> Dr Alexander said that incidents of this kind happened all too often.<sup>466</sup> Some dentists were apprehensive that liver disease pre-disposed the patient to bleeding but there was no reference to clotting problems in the record and Dr Alexander could not assume that the dentist had made his decision on concerns about bleeding rather than a more general fear of infection transmission.<sup>467</sup>

### *The return to ill health*

**7.251** In about 2000, Mr Laing began to become tired. His appetite was poor and he developed a tremor in both hands. He slept a lot and gave up bowling.<sup>468</sup>

---

<sup>457</sup> Letter from ARI to GP dated 15 May 1996 [LAI.001.0087]

<sup>458</sup> Day 4, page 40; Report [LAI.001.1125] at 1127

<sup>459</sup> Ibid page 21

<sup>460</sup> Ibid page 40; Report [LAI.001.1125] at 1128

<sup>461</sup> Letter from ARI to GP dated 11 April 1996 [LAI.001.0088]

<sup>462</sup> Letter from ARI to GP dated 7 October 1996 [LAI.001.0083]

<sup>463</sup> Day 4, pages 23 and 40; Report [LAI.001.1125] at 1127

<sup>464</sup> Witness Statement of Mrs Annie Laing [WIT.003.0417] at 0418

<sup>465</sup> GP request for appointment form dated 4 September 2000 [LAI.001.0067]

<sup>466</sup> Day 4, page 24

<sup>467</sup> Ibid page 25

<sup>468</sup> Witness Statement of Mrs Annie Laing [WIT.003.0417] at 0418

**7.252** In December 2001, he attended the ARI complaining of anorexia, lower abdominal and back pain, insomnia, dark urine and light stools over a period of two to three weeks. He was admitted to hospital between 8 and 11 December. Mr Laing's liver function test results were deranged. An abdominal ultrasound scan failed to reveal any relevant abnormalities, in particular in the liver. It was decided that he had had gallstones that had passed.<sup>469</sup> Nevertheless, on 31 December he was referred to the surgical out-patient department for surgical assessment on the view that gallstone disease was the underlying problem.<sup>470</sup> Dr Alexander thought that the blood tests and ultrasound results were not consistent with that diagnosis. In reaching the decision that the underlying problem was an early manifestation of liver failure, he was not influenced by the fact that no gallstones were noted in the gall bladder as they could have been missed. Rather, there was nothing to suggest that gallstones were the cause of the symptoms or the likely cause of Mr Laing's problems. The symptoms were more likely to be an early manifestation of liver failure due to Hepatitis C.<sup>471</sup>

**7.253** In addition to gallstones, the reference letter to the ARI of 31 December 2001 referred to Mr Laing's chronic active Hepatitis C.<sup>472</sup> In January 2002, Mr Laing began vomiting again.<sup>473</sup> He was seen at hospital on several occasions in January, February and March.<sup>474</sup> Vomiting persisted. The department of Biochemistry and Haematology reported on 24 April 2002 that his biochemical metrics were consistent with hepatic impairment, repeating a report of 5 December 2001.<sup>475</sup>

**7.254** On 19 November 2002, Mr Laing was referred to the breast clinic at the ARI for investigation of a swelling beneath his right nipple.<sup>476</sup> The GP was unsure of its significance. Right gynaecomastia (enlarged breast) was diagnosed. In a letter dated 18 February 2003, the consultant reported:

He does not appear to have any particular predisposing factors to gynaecomastia.

**7.255** She noted that he had reported weight loss, loss of appetite and vomiting and suggested that he might be referred back to gastroenterology.<sup>477</sup>

**7.256** Mr Laing was seen at the ARI Gastroenterology Clinic on 4 March 2003. The consultant's report of the examination to the GP stated:

He feels well with no nausea or vomiting. His breast pain has decreased. I note that he had a liver biopsy back in 1996, which suggested fibrosis and it is conceivable that he has now progressed to cirrhosis. It may be that the Gynaecomastia is associated with the cirrhosis. He has no abdominal or ankle swelling and feels well and therefore there is no indication for any further intervention at present.

**7.257** He was to be reviewed in six months.<sup>478</sup>

---

<sup>469</sup> Letter from ARI to GP dated 21 December 2001 [LAI.001.0057] at 0058

<sup>470</sup> Ibid [LAI.001.0057] at 0058; GP request for appointment dated 31 December 2001 [LAI.001.0055]

<sup>471</sup> Day 4, page 26

<sup>472</sup> Letter from GP to Mr Laing dated 31 December 2001 [LAI.001.0056] and Request by GP for outpatient appointment [LAI.001.0055]

<sup>473</sup> Witness Statement of Mrs Annie Laing [WIT.003.0417] at 0418

<sup>474</sup> Medical records dated 14 and 15 January 2002 [LAI.001.0183]; 28 January and 1 March 2002 [LAI.001.0182]

<sup>475</sup> Reports [LAI.001.0202] and [LAI.001.0210]

<sup>476</sup> Referral letter [LAI.001.0044] and [LAI.001.0045]

<sup>477</sup> Letter from ARI to GP [LAI.001.0043]

<sup>478</sup> Letter from ARI to GP [LAI.001.0041]

### ***Advanced liver disease***

**7.258** Early in June 2003, Mr Laing was so unwell he could not get out of bed to go to the toilet. He was vomiting, his abdomen was distended, his speech was slurred and he was dribbling from the mouth. Mr Laing was not a man to call the doctor but Mrs Laing did call for help.<sup>479</sup> The GP visited on 6 June and prescribed medication to settle his stomach and assist sleep. Mrs Laing contacted the GP again on 16 June.<sup>480</sup> Following examination, the GP referred him to gastroenterology at Woolmanhill Hospital, Aberdeen,<sup>481</sup> and it was arranged that he would be admitted there.<sup>482</sup> The referral letter on this occasion set out fully the GP's findings and Mr Laing's recent history; Mr Laing had gynaecomastia, thought to be due to his cirrhosis, weight loss, loss of appetite, nausea and vomiting. On examination the GP had found him to be jaundiced. He had tremor on both hands and his abdomen was distended. He had slight epigastric (abdominal) tenderness and was unsteady on his feet, among other signs and symptoms. There was a concern that his neurological symptoms of unsteadiness, including positive Romberg's sign and tremor, indicated some cerebellar dysfunction.<sup>483</sup> In the event, he was seen at the gastroenterology and liver service department at the ARI. It was reported by the clinic that he had no problems in relation to Hepatitis C and did not want to be treated.<sup>484</sup> His bloods were checked and it was noted that arrangements had been made for him to be seen at the clinic in six months.

**7.259** Dr Alexander explained that the gynaecomastia was a sign of advanced liver disease caused by excess oestrogen changing the balance of hormones in circulation. In advanced liver disease more oestrogen circulates freely and more female characteristics develop.<sup>485</sup> In his view the picture was of advanced liver failure with hepatic encephalopathy (brain disorder caused by liver dysfunction) which characteristically comes with unsteadiness of gait and tremor.<sup>486</sup> Dr Alexander considered that many of the symptoms at that time would have been readily attributable to evolving liver disease.<sup>487</sup>

**7.260** Mr Laing was seen at Woolmanhill Hospital on 2 July 2003 before being admitted to the ARI from 7 to 28 July 2003.<sup>488</sup> A Computerised Tomography (CT) scan was performed on 24 July.<sup>489</sup> Dr Alexander highlighted the significant findings from the scan. The liver was small. With most liver disorders the liver initially becomes enlarged and then, as the process evolves over years or even decades, the liver shrinks and eventually becomes too small to sustain life. In Mr Laing's case, the liver was also described as 'irregular', which meant that the surface of the liver had a scalloped contour consistent with cirrhosis. There was no focal lesion and so there was no sign of cancer. Dr Alexander was surprised that the spleen was not enlarged as it often is in advanced liver disease. Mr Laing also had moderate ascites, a collection of fluid in the abdomen, which was suggestive of liver failure and, from a clinical point of view, indicated that life expectancy was less than two

---

<sup>479</sup> Witness Statement of Mrs Annie Laing [WIT.003.0417] at 0418 and 0419. Mrs Laing says that this occurred on 2 June. The medical records indicate it was on 6 June [LAI.001.0177]

<sup>480</sup> Medical records [LAI.001.0177] and [LAI.001.0178]

<sup>481</sup> Referral letter dated 16 June 2003 [LAI.001.0038]

<sup>482</sup> Letter from Woolmanhill Hospital to GP dated 2 July 2003 [LAI.001.0037]

<sup>483</sup> Referral letter from GP to Woolmanhill Hospital dated 16 June 2003 [LAI.001.0038] at 0039

<sup>484</sup> Dr Alexander – Day 4, page 26; Letter from ARI to GP dated 19 July 2002 [LAI.001.0050] The letter was dictated on 18 June.

<sup>485</sup> Day 4, pages 27–28

<sup>486</sup> *Ibid* page 29

<sup>487</sup> *Ibid* pages 26–27

<sup>488</sup> Letter from Woolmanhill Hospital to GP dated 2 July 2003 [LAI.001.0037]; Letter from ARI to GP dated 6 August 2003 [LAI.001.0032]; Witness Statement of Annie Laing [WIT.003.0417] at 0419

<sup>489</sup> ARI Diagnostic Imaging report dated 24 July 2003 [LAI.001.1020]



years. On this occasion he had gallstones, which were missed previously on the ultrasound scan. These features told Dr Alexander that Mr Laing had advanced liver disease.<sup>490</sup>

**7.261** Mr Laing was re-admitted to the ARI on 30 July but deteriorated rapidly.<sup>491</sup> There was a picture of steady decompensation: his condition was no longer under control.<sup>492</sup> Mr Laing now had signs that implied an increasing risk of serious disease and death including bleeding, ascites and confusion.<sup>493</sup> Mr Laing had also developed pedal oedema (swollen feet), another feature of liver disease.

**7.262** Mr Laing was not able to go home and began to fade. A decision was taken that he should not be resuscitated and palliative measures were put in place. He died on 4 September 2003 with his family at his side.<sup>494</sup>

### The natural history of Mr Laing's infection

**7.263** The certified cause of death was 'Hepatitis C Related Liver Disease'.<sup>495</sup> Dr Alexander thought it should have been liver failure secondary to Hepatitis C and cirrhosis but that it was as accurate as it needed to be for the purpose of communicating the cause of death.<sup>496</sup>

**7.264** Dr Alexander explained some of the mechanisms involved in Mr Laing's final illness. He had jaundice. Although the precise mechanism by which jaundice is caused is not very clear, essentially bilirubin (a bile pigment which is orange or yellow) is not cleared by the liver and is instead pumped back into the circulation resulting in what is known as a 'jaundiced appearance' (typically yellowish pigmentation of the skin and eyes). Jaundice was a sign of the liver's response to injury. Cachexia (wasting) occurred: in advanced liver disease the body starts to use its own store of fat and muscle as a source of energy rather than food and muscle bulk is lost. Mr Laing lost all fat and looked thin, a feature of very late disease. Portal hypertensive gastropathy occurred. Blood normally travels from the gut into the liver, a soft organ, under low pressure. If the liver becomes distorted and scarred it is hard for the blood to get from the gut into the liver. It starts to go backwards and seek other routes. The stomach, downstream of the pressure effect, becomes very distended, thickened with blood. The gut comes under high pressure and that makes it develop varices (varicose veins) which can bleed.<sup>497</sup>

**7.265** Dr Alexander said that understanding of the natural history of Hepatitis C in older patients is no longer as it was initially thought. As now understood, an individual infected with Hepatitis C at nearly 67, as Mr Laing was, was likely to experience relatively rapid progression of disease. Most early experience was based on non-A, non-B Hepatitis (NANB Hepatitis) transfusion-related liver disease prior to the introduction of Hepatitis C testing. In those circumstances the majority of people died of diseases related to the reason for which they had been transfused, not to the hepatitis that arose as a result. As a result, there was an artificially skewed view of what NANB Hepatitis/Hepatitis C did to patients. It was not until the introduction of testing for Hepatitis C in 1991 that it was realised that many people had very different disease outcomes from that which had been previously described. The real picture was described about five or six years later.<sup>498</sup>

---

<sup>490</sup> Day 4, pages 29–30

<sup>491</sup> Letter from ARI to GP dated 12 September 2003 [LAI.001.0031]

<sup>492</sup> 'Decompensation' is the failing condition of an organ, such as the liver.

<sup>493</sup> Dr Alexander – Day 4, page 31

<sup>494</sup> Letter from ARI to GP dated 12 September 2003 [LAI.001.0031]

<sup>495</sup> Death Certificate [LAI.001.1068]

<sup>496</sup> Day 4, pages 32–33

<sup>497</sup> Day 4, pages 34–35

<sup>498</sup> Ibid pages 36–37

**7.266** Dr Alexander had extensive research experience. His laboratory's work on the effect of ageing (measuring people's 'biological age') and outcome is discussed in Chapter 16, *Knowledge of Viral Hepatitis 3 – 1986 Onwards*, at paragraph 16.65. In short, physical changes in the structure of DNA as people grow older makes the DNA vulnerable to damage. The same mechanism affects Hepatitis C–positive patients, once they reach a certain biological age. If the patient does not have an effective immune system, they cannot cope with Hepatitis C so that the virus takes a stronger grip.<sup>499</sup> The immune system begins to be impaired generally when one gets to around 60; in an HCV- positive patient that process is accelerated and response to treatment is also affected. Dr Alexander's laboratory found that the biological age at which treatment was significantly less likely to be effective – the treatment cut-off age – was 58. Mr Laing's age is a particular indication that he would not have benefited from antiviral treatment.<sup>500</sup>

### Source of infection

**7.267** As discussed in paragraphs 7.235 and 7.240, it was clearly established that Mr Laing contracted Hepatitis C from the blood transfusion received at the time of his surgery for cancer in 1990. He died of the complications of that infection. At the time of his surgery in 1990, donated blood was not screened in the UK for Hepatitis C: screening was introduced in 1991. There was an issue for the Inquiry whether, had HCV screening been in place in Scotland, the donation that infected Mr Laing would have been identified and not used.

**7.268** After HCV was identified in 1988, its genetic characteristics became the subject of intense research.<sup>501</sup> Variations in those characteristics were identified which were sufficient to define genetic sub-groups, or 'genotypes', which differ from others of the same virus, although not sufficiently to be considered different viruses. The genes of individual genotypes, like other organisms in the body, define their 'genomes'. The immune system responds to the activity of a virus by producing antibodies, proteins that seek to neutralise part of the virus. Antibodies remain in the body and, with appropriate technology, can often be identified. With modern, sophisticated technology, the genotype of the virus can be determined by scanning for particular antibodies to the virus.<sup>502</sup>

**7.269** At the date of Mr Laing's surgery in 1990, early tests had been devised for screening donors' blood for HCV. The tests, known as enzyme-linked immunoabsorbent assays (ELISAs), were chemical products developed by pharmaceutical companies from components that would react with antibodies to HCV if they were present in a sample of serum, producing a change of colour.<sup>503</sup> More sensitive second-generation ELISA tests were used in screening blood donors from autumn 1991.

**7.270** First-generation ELISAs targeted two specific areas of HCV that, as events were to prove, were characteristic of Genotype 1, which was particularly prevalent in the USA but were not present, so far as is material for present purposes, in Genotype 3 of the virus.<sup>504</sup> Technically, the first-generation tests were directed against the NS4 region of the virus, a non-structural region of the virus found in Genotype 1. So the components used for

---

<sup>499</sup> Ibid pages 42–44 and 46–47

<sup>500</sup> Ibid pages 42–44 and 46–47

<sup>501</sup> See Chapter 13, *Knowledge of Viral Hepatitis Now* and Chapter 16, *Knowledge of Viral Hepatitis 3 – 1986 Onwards*

<sup>502</sup> Dr Dow – Day 4, pages 54–61

<sup>503</sup> Ibid pages 85–86

<sup>504</sup> Ibid pages 62–64

first-generation tests could detect only Genotype 1 efficiently. They did not detect many Genotype 2 or 3 cases at all well.<sup>505</sup>

**7.271** In the result, the first-generation tests initially introduced for Hepatitis C screening of blood donations appeared relatively successful in identifying Hepatitis C-positive material in the USA but relatively unsuccessful in the UK where there was a high prevalence of Genotype 3 HCV.

**7.272** It became of interest to identify the HCV genotype of the donor whose blood was transfused to Mr Laing. This was in order to determine whether the infection might have been detected and the donation deferred – that is withdrawn from use for transfusion – if routine screening of blood donations had been carried out at the time of Mr Laing's transfusion in August 1990.

**7.273** The infected donation was traced through the national look-back process, as already noted. The donor had a blood transfusion in the 1960s or 1970s and may have acquired infection at that time, which was long before issues of testing for Hepatitis C became relevant.<sup>506</sup> A retained serum sample was found to be Hepatitis C-positive, using a second-generation ELISA test, on 8 January 1992. Research identified the genotype of the virus in question as Genotype 3.<sup>507</sup> Specifically, the donor genotype had high concentrations of four positive antibodies involved in the fight against Hepatitis C. Components of the second-generation tests targeted specific parts of the virus genome (components C22 and C33) found in Genotype 3.

**7.274** In March 1992, as part of a research project in which Dr Brian Dow<sup>508</sup> was involved, the same sample of the donation was re-tested using the Abbott first-generation test which had been available at the time of the original donation in some Scottish virology laboratories. The sample tested negative for Hepatitis C.<sup>509</sup> If the donation had been tested at the time it was given and transfused to Mr Laing, the first-generation tests then available would have been negative. The blood would have been banked and used for clinical purposes, as it was in the event in the course of Mr Laing's surgery.<sup>510</sup>

### Surrogate testing

**7.275** Before the introduction of the first-generation ELISAs, blood could be screened using tests which were not directly related to Hepatitis C itself but used assays that might give an indication that the subject may have been infected with Hepatitis C. These are known as 'surrogate' tests.<sup>511</sup> They were not conclusive on the presence of HCV or its antibody but indicated signs associated with infection. Observation had shown that in patients who had Hepatitis C there was a high correlation with raised levels of alanine amino transferase (ALT), a liver enzyme. One surrogate test therefore targeted ALT levels. There was also a reasonable correlation between having Hepatitis C and also having the

---

<sup>505</sup> Ibid pages 58–59

<sup>506</sup> Ibid page 78

<sup>507</sup> Ibid page 53; Dr Dow's amended report [PEN.012.0344]

<sup>508</sup> Now retired, Dr Dow was Consultant Clinical Microbiologist of the SNBTS Microbiology Unit, Glasgow. In 1992, he was Principal Clinical Scientist of the Microbiology Unit.

<sup>509</sup> Dr Dow – Day 4, page 65; The research project was reported in 1993: McOmish et al, 'Detection of three types of hepatitis C virus in blood donors', *Transfusion*, 1993; 33, [PEN.001.0018]

<sup>510</sup> Dr Dow – Day 4, page 65

<sup>511</sup> A surrogate marker is a directly measurable physical entity (usually measured in a blood test) that correlates (has a statistical association) with a disease where it is not possible to test directly for the disease or where any direct test would be problematic. See Chapter 27, *Surrogate Testing of Donated Blood for non-A, non-B Hepatitis* for more detailed discussion.

antibody to Hepatitis B core antigen (anti-HBc).<sup>512</sup> The other surrogate test accordingly targeted anti-HBc.

**7.276** Within the same research project in 1992 referred to in paragraph 7.274 above, Dr Dow and his colleagues therefore looked at surrogate testing. They carried out anti-HBc testing and found that the sample from the donor involved in Mr Laing's case was one of those which was anti-HBc negative. Dr Dow concluded that the result would have been the same had the donation been tested at the time of donation.<sup>513</sup> Dr Dow's research project had investigated the ALT levels in 90 donations but the donation in question was not among those investigated for ALT.<sup>514</sup> Subsequently, however, Dr John Gillon, SNBTS, was able to access and follow up the records of the donor whose blood was implicated in Mr Laing's infection with Hepatitis C. The records showed that the donor's ALT level was tested on four occasions, in February and August 1992, in December 1993 and in October 1994. On each occasion the level was well within normal limits. Dr Dow concluded that it was likely that the implicated donation would have given a normal ALT value if the donor's blood had been tested in August 1990.<sup>515</sup>

**7.277** The question whether ALT surrogate testing should have been introduced in Scotland in the period before introduction of the anti-HCV assay was extensively debated and is discussed at length in Chapter 27, *Surrogate Testing of Donated Blood for non-A, non-B Hepatitis*. In the circumstances, however, ALT testing of the donated blood would not have produced counter-indications to the use of the donation in Mr Laing's case.

**7.278** It was submitted that Mr Laing's case raised systemic issues related to the use of blood from people who had received transfusions; about the non-introduction of surrogate testing in Scotland; and about the screening of donations.<sup>516</sup> There is no basis for the view that, given what was known in 1990, donors who had themselves received a donation should have been excluded from donating at that time. There are systemic issues for the Inquiry relating to the non-introduction of surrogate testing. However, the decisions, and the failures to reach decisions, that had the result that surrogate testing was not adopted in Scotland, could not have influenced Mr Laing's case. All of these issues are dealt with in Chapter 27, *Surrogate Testing of Donated Blood for non-A, non-B Hepatitis*. Similarly, had screening of blood donations been in place in the summer of 1990, the kits used would have been first-generation ELISAs and would not have detected Hepatitis C in the donation which subsequently infected Mr Laing. Mr Laing's death from complications of his infection with Hepatitis C, having survived serious and potentially fatal cancer, was a personal tragedy for Mrs Laing and her family. That is the light in which it should continue to be seen.

### **Mr Laing's treatment as a patient**

**7.279** Dr Alexander considered that Mr Laing's treatment had been exemplary.<sup>517</sup> In this case, the summary of his views in his report is the best expression of the position:

The short interval of just six years between acquisition of hepatitis C virus infection and documentation of cirrhosis at liver biopsy and the seven years

---

<sup>512</sup> Dr Dow – Day 4, pages 67–68

<sup>513</sup> Dr Dow – Day 4, pages 70–71; Dr Dow's amended report [PEN.012.0344] at 0345

<sup>514</sup> Ibid page 70

<sup>515</sup> Dr Dow's amended report [PEN.012.0344] at 0345

<sup>516</sup> Closing Submission [PEN.019.0777]

<sup>517</sup> Day 4, page 42

that followed thereafter to his death, are consistent with what we now know about the natural history of hepatitis C virus infection. The proportion of patients that go on to develop cirrhosis and the rate at which cirrhosis develops subsequently are greatly accelerated in the elderly and in particular in men over 60. The fact that he had been overweight earlier in life may have been an additional confounding factor increasing his chance of becoming cirrhotic and increasing the rate at which the disease would progress. The first large publications drawing attention to the importance of age on the progression of liver fibrosis were published around 1997 and would have been discussed in abstract form, probably in the preceding few months. Thus the information that was provided to Mr Laing at the time of his biopsy in 1996 was probably 'best known practice'.

The fact that he was told that his disease was benign and was likely to remain so may well have influenced his decision not to accept the offer of anti viral therapy and it seems clear to me from the letters around that time that he was likely to have been told that the Interferon- $\alpha$  treatment was not likely to offer him a cure. I agree that was certainly true at the time and the response rate to treatment with Interferon- $\alpha$  in our centre was just 9% of cases ... with an even lower rate in the elderly and those with cirrhosis.

I do think, however, that the biopsy ... is likely to have been under reported in terms of the stage of fibrosis and that the possibility that the biopsy might have represented a higher stage of fibrosis was not appreciated by the clinicians. A fragmented biopsy, such as that in this case, is not one on which to base a prognosis with confidence.

It must be noted that Mr Laing survived 13 years after his diagnosis of carcinoma of the rectum with Duke's C histology, which is an astonishing outcome. I do not feel that even if there had been a better indication of his fibrosis stage in 1996 that it would have been possible to modify the natural history of his hepatitis C virus infection as the treatment available at that time was relatively ineffective and more so in elderly males with cirrhosis. If he had presented now with Pegylated Interferon and Ribavirin available the chances are that he would not have responded to treatment and if I was asked now to consider treatment I would very likely not offer him treatment with Pegylated Interferon and Ribavirin, the best available current therapy, because of his age and cirrhosis and the low probability of a response.<sup>518</sup>

**7.280** It is a matter of agreement on the part of Mrs Laing and the other 'patient interest' core participants that there appear to have been no reasonable precautions whereby Mr Laing's death might have been avoided once he had contracted Hepatitis C.<sup>519</sup>

## Conclusions

**7.281** Factors contributing to the death of Mr Laing were:

- (i) Mr Laing died from Hepatitis C-related liver disease.

---

<sup>518</sup> Report on Alexander Black Laing [LAI.001.1125] at 1127–1128

<sup>519</sup> Closing Submission [PEN.019.0777]

**7.282** Infection with Hepatitis C:

- (ii) Mr Laing was infected with Hepatitis C as a result of transmission of blood at the time of his surgery for Duke's C carcinoma on 7 August 1990.
- (iii) The surgery saved his life. It was never suggested that surgery could have been carried out without transfusion.
- (iv) The donor's infection was discovered in the course of the UK national look-back programme for transfusion-related Hepatitis C in 1995 and the blood used in Mr Laing's operation was traced to the infected donation in the follow-up stages of that investigation.
- (v) The donor's infection probably resulted from the transfusion of an infected donation in the 1970s. In 1990, there was no requirement for a policy of excluding recipients of previous blood donations from themselves donating blood.
- (vi) In 1990, anti-Hepatitis C testing was in its infancy and had not been adopted to screen blood donations in the UK.
- (vii) If the first-generation ELISA tests that were available at the time in 1990 had been used, the donor's Hepatitis C would not have been discovered.
- (viii) Surrogate testing for anti-HBc was not in use but, if it had been, it would not have given rise to an inference of possible Hepatitis C: the infected donation, when retrospectively tested, was negative for anti-HBc.
- (ix) Surrogate testing using ALT levels was not in use, but if it had been it would not have given rise to an inference of possible Hepatitis C: the donor had normal levels of ALT on two occasions in 1992, once in 1993 and once in 1994.

**7.283** Progression of disease:

- (x) Mr Laing's Hepatitis C progressed as would have been predicted by current understanding of the disease in a man of his age.

**7.284** Mr Laing's management as a patient:

- (xi) Mr Laing's management as a patient was an illustration of exemplary care.

## **Victor Tamburrini**

### **Introduction**

**7.285** Mr Victor Tamburrini was born on 27 April 1957. He died at the Royal Infirmary of Edinburgh on 17 November 2004, aged 47 years. The certified causes of death were liver transplant graft failure and recurrent Hepatitis C.<sup>520</sup>

### *The recovery of Mr Tamburrini's health records*

**7.286** Health records for Mr Tamburrini were recovered from the Glasgow Royal Infirmary (GRI), the Greater Glasgow and Clyde Community Alcohol Service and the Royal Infirmary of Edinburgh (RIE). In addition, relevant transfusion related records were obtained from the SNBTS. The Inquiry was unable to recover the full GP records of Mr Tamburrini.

**7.287** Mr Tamburrini's GP records were obtained by the Crown Office and Procurator Fiscal Service (COPFS) in January 2007 following a request by Messrs Thompsons, solicitors, on

---

<sup>520</sup> Death certificate [TAM.001.2946]

behalf of Mrs Tamburrini, to Strathclyde Police, for sight of the records.<sup>521</sup> Mrs Tamburrini was pressing for a Fatal Accident Inquiry (FAI) in to her husband's death. While Mr Tamburrini's other health records continued to be held by the COPFS, from which they were recovered by the Inquiry, the GP records had been returned to the NHS National Services Scotland Practitioner Services. It is likely that they were returned in 2007.<sup>522</sup> That department destroyed the original GP records on 16 June 2009.<sup>523</sup>

### *The destruction of Mr Tamburrini's original GP records*

**7.288** In ordinary course, destruction of medical records conforms to the 'Guidance for the Retention and Destruction of Health Records' issued by the former Scottish Office in 1993. In the case of GP records, the guidance recommends a retention period of three years after a patient's death.<sup>524</sup> If the guidance had been followed, Mr Tamburrini's GP records would have been destroyed on receipt by Practitioner Services or shortly thereafter: the three-year retention period had long expired.

**7.289** In January 2009 Crown Counsel instructed that there should be no FAI into Mr Tamburrini's death.<sup>525</sup> However, Scottish Ministers continued to consider referring Mr Tamburrini's death to this Inquiry and that was done on 13 November 2009. Destruction of the GP records therefore occurred while consideration was still being given to the reference of Mr Tamburrini's death to the Inquiry.

**7.290** How that came about is unclear. The GP records appear to have been returned to Practitioner Services<sup>526</sup> before the decision to instruct no proceedings in relation to an FAI and there has been no explanation why the COPFS took that step while retaining other medical records. So long as a decision on an FAI remained to be reached, the GP records were potentially required as evidence and the COPFS should have been aware of that possibility. At the time the COPFS was not aware of the Scottish Government Health Directorate document retention policy.<sup>527</sup> However, it is clear that the records remained available in the hands of Practitioner Services after the decision by the COPFS on FAI proceedings.

**7.291** The destruction of the records by Practitioner Services remains unexplained. However, at the time of their destruction a summary of the GP records was prepared.<sup>528</sup> In addition, the hospital records include correspondence with Mr Tamburrini's GP. The Inquiry is satisfied that the records produced to it were sufficient to enable the investigation of his death. The lack of the original GP records did not inhibit the investigation.

### **Initial symptoms and diagnosis of Hepatitis C Virus infection**

**7.292** How and when Mr Tamburrini acquired infection with Hepatitis C is not known. Mr Tamburrini married for the second time on 8 March 1991. His widow, Mrs Jean Tamburrini, had limited information about his medical history before they met in 1987. She knew that he had been in a car accident and had suffered serious burns in September

---

<sup>521</sup> Letter from Deputy Crown Agent to the Inquiry dated 22 December 2010 [PEN.001.0303]

<sup>522</sup> Ibid

<sup>523</sup> Ibid Letter from Central Legal Office to Inquiry dated 23 November 2010 [PEN.001.0246]; Letter from Practitioner Services to CLO dated 11 November 2009 [PEN.001.0245]

<sup>524</sup> [http://www.sehd.scot.nhs.uk/mels/1993\\_152.htm](http://www.sehd.scot.nhs.uk/mels/1993_152.htm), last accessed 08/01/15

<sup>525</sup> Letter from Deputy Crown Agent to the Inquiry dated 22 December 2010 [PEN.001.0303]

<sup>526</sup> Ibid [PEN.001.0303]

<sup>527</sup> Ibid [PEN.001.0303]

<sup>528</sup> Summary of records [TAM.001.1459]

1984. In general, however, her evidence related to the period from 1987 onwards. In the circumstances she was unable to provide an insight into possible dates of infection before 1987.

**7.293** Mr Tamburrini was diagnosed with Hepatitis C in September 2001.<sup>529</sup> By then he had signs and symptoms strongly suggestive of severe liver damage. That would provide the latest date by reference to which estimates of the duration of infection might be made on the basis of knowledge of the natural history of the disease. There was, however, evidence that, in retrospect, indicated he was developing liver disease at an earlier period.

### *Early signs and symptoms*

**7.294** At Christmas 1991, Mr Tamburrini felt unwell and could not stop falling asleep. He was doing heavy work at a fruit market as a porter or deliveryman, however, and the possible significance of his condition only became apparent later.<sup>530</sup>

**7.295** In about 1994 or 1995 he worked for his uncle in a factory for around 10 months. The work was hard and physical and he had difficulty in maintaining the energy levels required and had to leave the job. He then began working in licensed premises owned by his brother-in-law, first as a barman and then, from about 1997, as bar manager. He suffered from lethargy and slept a lot but his employer was supportive and accommodated him.<sup>531</sup>

**7.296** In 1998, Mr Tamburrini was feeling unwell: he had suddenly begun to put on weight, experienced heartburn and had poor appetite. His ankles and abdomen were swollen and he was increasingly lethargic.<sup>532</sup> In May 1998, he went to see his GP complaining of a painless swelling in his right breast.<sup>533</sup> It was recorded that there had been no trauma or serious illness in his recent medical history. He was referred to the GRI where he was seen at the professorial breast clinic. In the referral form, the GP noted that Mr Tamburrini had mentioned a habit of consuming large quantities of alcohol. The hospital report to the GP following examination on 15 July noted that Mr Tamburrini had a history of alcohol abuse. Atypical gynaecomastia (benign enlargement of breast tissue in males) was diagnosed in the right breast and it was proposed that the affected area should be removed. The left breast did not present with similar swelling.<sup>534</sup> On admission on 10 December 1998, it was found that the lump in the right breast which had been noticed first was not palpable and that a lump had developed in the left breast. On the following day bilateral subcutaneous mastectomy was carried out.<sup>535</sup> Mr Tamburrini was discharged from hospital on 15 December 1998 with a note stating that he was well and was to be followed up in clinic.<sup>536</sup>

**7.297** Gynaecomastia can be observed in men with advanced liver disease from any cause. Not infrequently it is also seen, in the absence of cirrhosis, in men who are putting on weight, as Mr Tamburrini was, and in heavy drinkers.

---

<sup>529</sup> See paragraph 7.302

<sup>530</sup> Witness Statement of Mrs Jean Tamburrini [PEN.001.0309]

<sup>531</sup> Ibid [PEN.001.0309] at 0310; Affidavit of Bernard Fisher [PEN.018.1559]; Mrs Jean Tamburrini – Day 1, pages 14-15

<sup>532</sup> Witness Statement of Mrs Jean Tamburrini [PEN.001.0309] at 0310

<sup>533</sup> GP's request to the GRI for out-patient consultation dated 2 June 1998 [TAM.001.2583]

<sup>534</sup> Letter from the GRI to GP dated 17 July 1998 [TAM.001.2582]

<sup>535</sup> GRI careplan [TAM.001.2907]

<sup>536</sup> Letter from the GRI to GP dated 20 January 1999 [TAM.001.2574]



**7.298** On 27 January 1999, Mr Tamburrini was admitted to the Lister Department of Surgery, at the GRI, as an emergency patient, complaining of severe epigastric (abdominal) pain. He gave a history of diarrhoea about a week earlier. His pain had gradually increased and on admission he had mildly raised serum amylase (an enzyme produced by the pancreas) but no other indicators of severe disease. An ultrasound scan disclosed some large stones in his gallbladder. There was a diagnosis of '(?)Viral induced acute pancreatitis'. He was discharged well, to be followed up in the clinic.<sup>537</sup> He was reviewed on 24 February 1999, found to be well and discharged without further follow-up.<sup>538</sup>

### *Towards a diagnosis of liver disease*

**7.299** In 2000, Mr Tamburrini again began to put on weight around his abdomen, gave up exercise because he could not manage it and, on holiday, was depressed and grumpy. He had swollen ankles and could not wear normal shoes.<sup>539</sup> In 2001, the Department of Oral Medicine at the Glasgow Dental Hospital and his GP each separately referred him to the GRI for examination. The Department of Oral Medicine referred him specifically to the Haematology Department and he was seen at Dr Isobel Walker's clinic. The GP's referral letter reported a history of previous admissions and findings and described the basis of the current referral as 'recently developed moderate/severe oedema of both legs', the abnormal accumulation of fluid, clinically apparent as swelling. It reported that Mr Tamburrini's liver function tests were deranged and provided recent values. The referral letter from the Department of Oral Medicine noted 'peri-orbital oedema [swelling around the eyes] and bilateral ankle swelling' in addition to the oral problems for which he had been examined.<sup>540</sup>

**7.300** Dr Lorna McLintock of the Department of Haematology reported to the Dental Hospital on 8 August 2001.<sup>541</sup> She noted that the abnormal blood parameters included elevated mean corpuscular volume (MCV), thrombocytopenia, mild eosinophilia and mild reticulocytosis.<sup>542</sup> She thought that Mr Tamburrini's blood parameters all related to liver disease but wished further tests to be carried out. Dr David Mutimer, a Consultant Hepatologist who provided expert testimony to the Inquiry, said that the features reported by Dr McLintock were all seen in patients with advanced liver disease, which was therefore indicated at that time.<sup>543</sup> MCV is a measure of the size of the red blood cells and a high MCV is found typically in patients with cirrhosis, particularly when due to alcohol.<sup>544</sup> Thrombocytopenia (a decrease in the level of platelets in the blood), eosinophilia (a decrease in another blood component, eosinophii) and reticulocytosis (an increase in immature red blood cells) are also seen in patients with cirrhosis or advanced liver disease.<sup>545</sup>

**7.301** Mr Tamburrini was reviewed by Dr McLintock on 5 September 2001.<sup>546</sup> She again found his liver function test results to be elevated. She reported to his GP that Mr Tamburrini 'obviously' had significant liver disease. She sent blood for autoantibody serology and hepatitis serology.

---

<sup>537</sup> Letter from the GRI to GP dated 3 March 1999 [TAM.001.2572]

<sup>538</sup> Letter from the GRI to GP dated 5 March 1999 [TAM.001.2573]

<sup>539</sup> Witness Statement of Mrs Jean Tamburrini [PEN.001.0309] at 0311

<sup>540</sup> Letter from the Glasgow Dental Hospital to the GRI dated 18 June 2001 [TAM.001.2540]; Letter from GP to the GRI dated 8 June 2001 [TAM.001.2570]

<sup>541</sup> Letter from the GRI to the Glasgow Dental Hospital dated 8 August 2001 [TAM.001.2542]

<sup>542</sup> 'Thrombocytopenia' refers to a shortage of platelets. The letter referred to 'thrombocytosis' and was corrected by Dr Mutimer. Eosinophilia and reticulocytosis refer to the replacement of red cells by the bone marrow: Day 1, page 97

<sup>543</sup> Day 1, pages 96–97

<sup>544</sup> Ibid page 96

<sup>545</sup> Dr Mutimer – Day 1, page 97

<sup>546</sup> Letter from the GRI to GP dated 31 October 2001 [TAM.001.2553]

### *Diagnosis with Hepatitis C*

**7.302** A Hepatitis C test, using polymerase chain reaction (PCR) technology, proved positive<sup>547</sup> and on 26 September 2001 Mr Tamburrini was told that he had contracted Hepatitis C.<sup>548</sup> Mrs Tamburrini was also tested for the presence of the Hepatitis C virus (HCV): she was not infected.<sup>549</sup> Dr McLintock noted that Mr Tamburrini did not feel that he had a history of any high-risk behaviour associated with the transmission of Hepatitis C.<sup>550</sup> Blood tests performed at that time strongly suggested severe liver damage: the results were consistent with cirrhosis and hepatic decompensation. The MCV score was again very high at 111.<sup>551</sup> Dr Mutimer thought that the blood test results would be consistent with cirrhosis and hepatic decompensation due to the effect of alcohol, to Hepatitis C or to a combination of the two.<sup>552</sup> Mr Tamburrini thereafter attended Dr AJ Stanley's Liver Clinic at the GRI before being referred to the Liver Transplant Unit (LTU) at the RIE in February 2002.<sup>553</sup> Mr and Mrs Tamburrini began to understand that the condition was serious.

### **Possible cause of HCV infection**

**7.303** There are two main groups of causes of HCV infection. The first group comprises transmission of infection during health care, by transfusion of infected blood, blood components or blood products, or hospital-acquired transmission, for example by needle-stick injury. The second group comprises causes of infection outwith a healthcare setting. Overwhelmingly the commonest cause of infection in the second group, in Scotland, has been intravenous drug use and sharing HCV-infected materials. More rarely, HCV may have been acquired from contaminated tattooing or body piercing equipment. These possibilities will be explored in light of the fact that Mr Tamburrini already had cirrhosis at the latest in 2001 when he was aged 44.

**7.304** Mr Tamburrini's medical records were examined to ascertain whether there was evidence of medical procedures that might have involved blood transfusion and created a risk of transmitting infection. The records were examined specifically in an attempt to identify a date of transmission. The examination was not limited to the period within which he might be thought to have acquired infection.

### *Possibility of infection during an appendicectomy in December 1968*

**7.305** Mr Tamburrini had an appendicectomy as a child, in 1968.<sup>554</sup> That was the first occasion on which he might have had a blood transfusion. The appendicectomy was noted elsewhere in his medical records.<sup>555</sup> There was no reference to transfusion or to any event of an exceptional nature at the time of the operation that might have indicated a need for transfusion. The appendicectomy scar, in itself unremarkable, was noted throughout the records without comment.

---

<sup>547</sup> 'Polymerase Chain Reaction' test (see Glossary); Regional Virus Laboratory Test result form dated 12 September 2001 [TAM.001.2703]

<sup>548</sup> Witness Statement of Mrs Jean Tamburrini [PEN.001.0309] at 0311

<sup>549</sup> Ibid at 0312

<sup>550</sup> Letter from the GRI to GP dated 28 October 2001 [TAM.001.2559]

<sup>551</sup> Dr Mutimer's report [PEN.010.0310] at 0311

<sup>552</sup> Ibid at 0313

<sup>553</sup> Letter from the GRI to GP dated 9 December 2001 [TAM.001.2557]; Letter from the GRI to the RIE dated 14 February 2002 [TAM.001.2565]

<sup>554</sup> Summary of GP records printed on 6 January 2005 [TAM.001.1459] at 1460

<sup>555</sup> eg GRI careplan dated 10 December 1998 [TAM.001.2907]

**7.306** Professor Willem van Aken was asked to express an opinion on the likelihood of transfusion at the time of the procedure. Professor van Aken was, until retirement, Director of the Board of the Central Laboratory of the Netherlands Red Cross Blood Transfusion Service and had a long and distinguished record in that service. He was well qualified to comment on the use of blood transfusion for surgical procedures at the relevant period. In his view it would have been a rarity for anyone ever to have received a transfusion of blood in the course of an appendicectomy in 1968. It would happen only very seldom and only when there was a complication and major bleeding. Most appendicectomy procedures would not have required the transfusion of blood.<sup>556</sup>

**7.307** As a medical scientist, Professor van Aken could not rule out the possibility that there had been a blood transfusion. On the evidence as a whole, however, there is no basis for a finding that Mr Tamburrini did have a blood transfusion in 1968. The records do not disclose any complication or major bleeding. Bare possibility could not support a finding that there was a transfusion in the face of Professor van Aken's evidence.<sup>557</sup>

**7.308** On a balance of probabilities, Mr Tamburrini was not transfused at the time of his appendicectomy and that procedure cannot have been the occasion of transmission of infection.

#### *Possibility of infection during treatment for burns in 1984*

**7.309** On 7 September 1984, Mr Tamburrini was admitted to the burns unit of the GRI having sustained extensive surface area burns as a result of a vehicle fire: the accident Mrs Tamburrini knew about. He was transfused with six units of Plasma Protein Solution (otherwise Stable Plasma Protein Solution, SPPS), an albumin preparation, each recorded as having come from a specific batch of product numbered 1194 released by the SNBTS on 10 August 1983.<sup>558</sup> Transfusion of SPPS was a standard procedure in the circumstances, in this application much safer than plasma or whole blood.<sup>559</sup> Severe burns involve the loss of fluid from the circulation: in the vicinity of the burn, blood vessels become dilated and leak protein-rich fluid, creating a risk of shock. Blood pressure drops and there tends to be an urgent need to restore blood volume and to increase osmotic/oncotic pressure, which is a composite of the protein content in the blood and the resistance provided by tissue. In some patients the albumin level in the blood drops. SPPS specifically restores albumin as part of the process of increasing the volume of circulating blood. Mr Tamburrini recovered, and was discharged on 6 October 1984.<sup>560</sup>

**7.310** The transfusion of SPPS was the second event that provided a focus for investigation as a possible source of transmission of HCV infection. In the UK, and in Scotland in particular, SPPS was prepared at the material time in accordance with requirements set out in a monograph contained in the British Pharmacopoeia (BP) issued in 1980.<sup>561</sup> The batch from which the SPPS administered to Mr Tamburrini was drawn was prepared in that way.<sup>562</sup> The critical, penultimate stage in the process was described in the monograph:

---

<sup>556</sup> Professor van Aken – Day 2, page 20

<sup>557</sup> Ibid

<sup>558</sup> GRI IV therapy prescription sheet [TAM.001.2462]; Dr Cuthbertson – Day 1, page 123; Joint statement of Drs Perry and Cuthbertson on SPPS Batch No 1194 dated 4 March 2011 [PEN.011.0048] at 0051

<sup>559</sup> Professor van Aken – Day 2, pages 20–22

<sup>560</sup> Letter from the GRI to GP dated 10 October 1984 [TAM.001.2591]

<sup>561</sup> Excerpt from the BP (referred to as Plasma Protein Fraction) [PEN.001.0259]; Statement of Drs Perry and Cuthbertson on SPPS Batch No 1194 dated 4 March 2011 [PEN.011.0048] at 0049

<sup>562</sup> Dr Cuthbertson – Day 1, page 123 et seq

The albumin fraction, prepared by a suitable fractionation technique, is dissolved in water .... The solution is sterilised by *Filtration*, distributed aseptically in sterile containers, and sealed so as to exclude micro-organisms. It is then heated to, and maintained for ten hours at, 59.5° to 60.5° so as to prevent the transmission of hepatitis.<sup>563</sup>

**7.311** The records relating to the batch were comprehensive.<sup>564</sup> The product in question was pasteurised at 60°C for 10 hours.<sup>565</sup>

**7.312** The production process was described in detail by Dr Bruce Cuthbertson, currently Quality Director of the SNBTS.<sup>566</sup> 'Albumin' is the term used to describe a product that contains in excess of 95% albumin protein. SPPS must contain in excess of 90% albumin protein.<sup>567</sup> There is a 'purity' distinction between the products but there is no difference in terms of risk of transmission of hepatitis viruses. Both products are pasteurised by heating at 59.5°C to 60.5°C for 10 hours.<sup>568</sup>

**7.313** Albumin has had an almost unblemished record of safety in clinical use since its introduction in 1940 by the US Army for the battlefield treatment of trauma.<sup>569</sup> Albumin products have only twice been reported to transmit hepatitis: the first time in an experiment carried out on human volunteers in the 1940s when pasteurised and unpasteurised albumin doses were administered (those who received unpasteurised doses were infected with Hepatitis B while those who received the pasteurised product were not);<sup>570</sup> the second time, which again involved transmission of Hepatitis B, in 1973.<sup>571</sup> After full investigation it was shown that, in that instance, the pasteurisation process was defective. Pasteurisation was carried out in a bulk tank, after which the preparation was decanted into containers. The structure of the bulk-pasteurisation tank allowed for pockets of material to remain inadequately mixed with the remaining material and thus to fail to be subject to the complete heating cycle.<sup>572</sup> Professor van Aken gave further details of the 1973 incident.<sup>573</sup> Albumin has never been reported to transmit Hepatitis C.<sup>574</sup>

**7.314** The BP stipulation for pasteurisation in the final container addressed the risk illustrated by the 1973 incident.<sup>575</sup> The process requirements ensured that after sealing there was no prospect of there being incomplete pasteurisation or of the product being re-contaminated.<sup>576</sup>

**7.315** Professor van Aken was asked to comment on whether the word 'prevent' was apposite in the sentence from the BP: 'It is then heated to, and maintained for 10 hours at 59.5°C to 60.5°C so as to prevent the transmission of Hepatitis'. He had no doubt or uncertainty about the use of the word 'prevent' in this context.<sup>577</sup>

---

<sup>563</sup> Excerpt from the BP [PEN.001.0259]

<sup>564</sup> SNBTS record for SPPS Batch No 1194 [PEN.001.0260]

<sup>565</sup> Statement of Drs Perry and Cuthbertson on SPPS Batch No 1194 dated 4 March 2011 [PEN.011.0048]

<sup>566</sup> Day 1, page 121 et seq; Statement of Drs Perry and Cuthbertson on SPPS Batch No 1194 dated 4 March 2011 [PEN.011.0048]

<sup>567</sup> Dr Cuthbertson – Day 1, page 123

<sup>568</sup> Excerpt from the BP [PEN.001.0259]

<sup>569</sup> Dr Cuthbertson – Day 1, page 132

<sup>570</sup> Ibid page 133

<sup>571</sup> Ibid page 133; Pattison et al., 'An outbreak of Type B Hepatitis associated with transfusion of Plasma Protein Fraction', *American Journal of Epidemiology*, 1976; 103/4:99[LIT.001.3122]

<sup>572</sup> Ibid [LIT.001.3122] at 3127; Dr Cuthbertson – Day 1, page 133

<sup>573</sup> Day 2, pages 47–49

<sup>574</sup> Dr Cuthbertson – Day 1, page 134

<sup>575</sup> Professor van Aken – Day 2, page 49; Report [PEN.001.0306] at 0307

<sup>576</sup> Dr Cuthbertson – Day 1, page 133

<sup>577</sup> Professor van Aken – Day 2, pages 27–28; Excerpt from the BP [PEN.001.0259]

**7.316** Dr Cuthbertson explained that pasteurisation was the end stage in the production process.<sup>578</sup> Fractionation of plasma extracted various proteins using a variety of biochemical techniques, principally cold ethanol fractionation. The SPPS produced was sterile-filtered to remove bacteria and was then dispensed into bottles in an aseptic filling suite. The bottles and stoppers had already been sterilised separately at 121°C for 15 minutes and held in sterile conditions until used. Four hundred millilitres of liquid were placed in each bottle, the stopper was inserted and an aluminium overcap was put on top. The caps were then sealed. The bottles were crated, reserving two for quality control. The crated bottles proceeded to pasteurisation in a chamber commissioned and developed by the Protein Fractionation Centre (PFC, the manufacturer of blood products in Scotland). The bottles were sprayed with hot water for pre-wash, to remove any protein that might have been deposited on their exterior surfaces in the course of filling or handling. Thereafter the bottles were rapidly heated to 60°C for 10 hours.<sup>579</sup>

**7.317** Professor van Aken commented generally on the process of fractionation and in particular on the distribution of virus particles over the range of products.<sup>580</sup> It had been shown that the distribution was uneven, with some fractions containing more contamination than others.<sup>581</sup> Albumin was produced from a fraction that had been found to contain only a minute quantity of Hepatitis C virus after the fractionation process.<sup>582</sup> The major contributor to viral inactivation, however, was the pasteurisation process which followed fractionation. The position relative to the pasteurisation step was summed up by Brian Erstad and others in an article for the journal *Pharmacotherapy*:

Both HSA [human serum albumin] and PPF are manufactured with pasteurization procedures that have led to an excellent viral safety record based on 50 years of clinical use .... The pasteurization process is effective in eradicating known viral pathogens when good manufacturing practices are followed.<sup>583</sup>

**7.318** Professor van Aken's report stated that published studies had shown that heating of albumin for only 10 minutes at 60°C results in levels of virus inactivation and reduction, recognised as providing a very high margin of safety. He pointed out that the pasteurisation of albumin for 10 hours at 60° C is 60 times longer than is needed to inactivate hepatitis viruses.<sup>584</sup>

**7.319** He added in oral evidence:

The WHO [World Health Organization] expert committee on plasma products ... has addressed this issue in a very extensive report in which all these papers here are included, and one of the conclusions is in fact that ten minutes at 60 degrees Celsius results in a virus reduction of more than 16 logs, which means that ... it is about a risk of one in 16 millions that still a virus is not inactivated. So it goes well beyond our imagination that there is still some virus left after that period of time.<sup>585</sup>

---

<sup>578</sup> Dr Cuthbertson – Day 1, pages 133 and 138

<sup>579</sup> Ibid Day 1, pages 135–138; Statement of Drs Perry and Cuthbertson on SPPS Batch No 1194 dated 4 March 2011 [PEN.011.0048]

<sup>580</sup> Day 2, pages 35–36 and 38

<sup>581</sup> Ibid page 36; Yei et al, 'Partitioning of hepatitis C virus during Cohn-Onclay fractionation of plasma', *Transfusion*, 1992; 32/9:824–828) [LIT.001.3218]; Scheiblaue et al, 'Prevalence of Hepatitis C virus in plasma pools and the effectiveness of cold ethanol fractionation', *Clinical Therapeutics*, 1996; 18/B:59–70) [LIT.001.3131]

<sup>582</sup> Day 2, pages 36–37 and 40

<sup>583</sup> Erstad, 'Viral infectivity of albumin and plasma protein fraction', *Pharmacotherapy*, 1996; 16/6:996–1000) [LIT.001.3117]

<sup>584</sup> Professor van Aken's report [PEN.001.0306] at 0307

<sup>585</sup> Day 2, pages 44–45; Professor van Aken's report [PEN.001.0306] at 0308

**7.320** The original batch records for batch 1194, from which the SPPS used to treat Mr Tamburrini came, were examined to ascertain the procedure in the particular case. They showed that the pasteurisation cabinet was checked and found to be operating satisfactorily. The loading of the crates was recorded. The temperature was monitored by a Honeywell probe placed in a representative bottle in each crate of 10 bottles. The run was timed and the temperature maintained throughout was recorded as 60°C. The procedure was recorded in detail and explained in oral testimony by Dr Cuthbertson.<sup>586</sup> He noted that this was before the digital age: the data were recorded on charts. There was an independent check that the probes were in fact reading at 60°C. The procedure confirmed that the bottles were all behaving consistently.<sup>587</sup>

**7.321** The completed bottles were placed in cages, security-sealed, labelled with the individual batch number and placed in incubation for two weeks at about 30°C. Albumin is a good medium for bacterial contamination<sup>588</sup> and this procedure allowed any bacterial contamination that might be present to grow and become evident. Dr Cuthbertson had signed off the microbiology test results at the time.<sup>589</sup> It was only after quality control on a sample of pasteurised bottles, which included demonstration that the product had been effectively pasteurised, that the product was released for inspection.<sup>590</sup> The caps were inspected to ensure their integrity and the bottles were inspected under direct light and polarised light to look for the presence of visible contamination. Pasteurisation changes the characteristics of albumin from clear to opalescent. Rejection was a common occurrence. From the specific batch in question, 110 bottles were rejected. Most of these will have been because of the presence of fibres in the bottle. Once all the bottles had been inspected they were released for labelling and packing (or discarded had they failed the inspection).<sup>591</sup>

**7.322** Professor van Aken carried out an independent review of the records relating to the particular batch.<sup>592</sup> The procedures followed the guidance to pasteurise in the final individual containers as set out in the BP and in WHO guidelines.<sup>593</sup> His conclusions were:

The batch of SPPS administered to Mr Tamburrini was manufactured using methods which were at the time (and still are) widely recognised as being capable of eliminating any risk of virus transmission.

The records of batch number 1194 indicate that its manufacture, and in particular its pasteurisation, was carried out according to recognised industry and pharmacopoeial standards.

The answer to the query therefore is that the transmission of hepatitis C by SPPS is most unlikely ....<sup>594</sup>

---

<sup>586</sup> Day 1, pages 126–130; SNBTS record for SPPS Batch No 1194 [PEN.001.0260]

<sup>587</sup> Day 1, page 129

<sup>588</sup> Dr Cuthbertson – Day 1, pages 135–139

<sup>589</sup> Ibid page 131

<sup>590</sup> Ibid pages 139–140

<sup>591</sup> Ibid pages 141–144

<sup>592</sup> Professor van Aken's report [PEN.001.0306]; Professor van Aken – Day 2, pages 26–53

<sup>593</sup> 'Guidelines on viral inactivation and removal procedures intended to assure the viral safety of human blood plasma products', Annex 4 to *WHO Technical Report*, Series No. 924, 2004 [LIT.001.3143]

<sup>594</sup> Professor van Aken's report [PEN.001.0306] at 0308

**7.323** He was asked why he did not say 'impossible' and added in oral evidence:

Well, 'impossible' is a word which I use only very rarely because I have learned through my career that some events you can judge to be highly unlikely or even further, but you have to be cautious, so I cannot oversee the whole chain of events which was related to this incident because it is a chain of events; it doesn't stop with the manufacturing. It is also what happened during the administration, what happened in the hospital, which I cannot oversee, which I have no reports about, which I have no data about. So that's why I thought it would be more accurate to say "highly unlikely".<sup>595</sup>

**7.324** Absolute proposition, positive or negative, has to be avoided generally in scientific analysis.<sup>596</sup>

**7.325** Reviewing the medical history, Dr Mutimer agreed with the view that it was extremely unlikely that Hepatitis C was acquired as a consequence of administration of that plasma.<sup>597</sup>

### *Possibility of infection due to manufacturing deficiencies*

**7.326** The Medicines Inspectorate found a number of deficiencies in buildings and facilities at the Edinburgh PFC on an inspection in 1981 and also deficiencies in manufacturing practices in a further inspection in 1988.<sup>598</sup> The 1981 Medicines Inspectorate report highlighted: (i) inadequate space in some production and storage areas; (ii) unsatisfactory processing conditions; (iii) poor surface finishes; (iv) unsatisfactory work flow patterns which could lead to product mix-up; and (v) unacceptable staff movements through production areas which could lead to contamination of components and products. The 1988 Medicines Inspectorate report highlighted: (i) staff structure; (ii) a need for review of documentation; (iii) a need to expedite the expansion of premises; and (iv) a need to remedy inadequacy of storage areas.

**7.327** Suspicion arose in the minds of some interested parties that the deficiencies identified in the 1981 report might have been connected to possible contamination of the SPPS used in Mr Tamburrini's case, or cast doubt on the identification of the materials used in his treatment. The specific question put by Messrs Thompsons, Solicitors, representing the patients, relatives and Haemophilia Society, was 'whether there is any potential link between the documented unsatisfactory state of affairs at Liberton in the 1980s and the possible infection of Mr Tamburrini with Hepatitis C as a result of the transfusion in September 1984'.<sup>599</sup> Professor van Aken was asked to consider these issues. He produced a supplementary report on them and gave oral evidence.<sup>600</sup>

**7.328** Professor van Aken set the scene.<sup>601</sup> The inspections were part of the ongoing process of implementing good manufacturing practices in a range of NHS premises where blood products for intravenous use were being manufactured at the beginning of the 1980s. That process took considerable time, especially in buildings and with facilities that

---

<sup>595</sup> Professor van Aken – Day 2, page 53

<sup>596</sup> Ibid

<sup>597</sup> Dr Mutimer – Day 1, page 110; Dr Mutimer's report [PEN.010.0310] at 0313 and 0315

<sup>598</sup> Medicine Inspectorate 1981 Report [SNB.005.6826]; Medicine Inspectorate 1988 Report (draft only) [SNB.008.8791]

<sup>599</sup> Letter from Thompsons to Inquiry Solicitor dated 24 February 2011 [PEN.010.0386]

<sup>600</sup> Professor van Aken's supplementary report [PEN.011.0001]; Day 2, pages 56–57

<sup>601</sup> Ibid Day 2, pages 54–56

were constructed before the statement of manufacturing practice was written: it is easier to design facilities if one has a statement of manufacturing practice than it is to adapt something that already exists. He said that it was easily forgotten that, at that stage, 'the whole issue about safety and quality was different from now' and the introduction of good manufacturing practice was a major change, not just in the pharmaceutical industry but also in plasma fractionation. It required, on the one hand, that facilities were adapted and that equipment was changed and, on the other hand, that personnel were trained in a completely different way. A cultural as well as practical change had to happen. That could not be done overnight: time was required.<sup>602</sup> It is clear that the reports were part of an evolving scheme of regulatory oversight that involved the prescription of work required to upgrade facilities to meet new standards.

**7.329** Professor van Aken's initial view on the question posed by Messrs Thompsons was that, while he could not completely discount the proposition, he thought it highly unlikely that the noted problems with the PFC's production facilities had contributed to Mr Tamburrini's infection.<sup>603</sup> The evidence of Dr Cuthbertson was then disclosed to him,<sup>604</sup> which clarified the factual situation. The question posed had suggested to him that viral inactivation studies and manufacturing had not been carried out in separate environments (that is, in separate rooms) but they had, in fact, been separated: measures had been taken to reduce, minimise or completely avoid risk in this area.<sup>605</sup> The risk of mis-labelling and of mixing heated and unheated products had been considered. Dr Cuthbertson's statement gave him 'a good feeling that there is no question of mix-up between material which was pasteurised and material which was not pasteurised'.<sup>606</sup> The visual inspection step was common to all manufacturing facilities and the differences between pasteurised and non-pasteurised albumin products could be clearly seen.<sup>607</sup> He then referred to the possibility that batches could have been contaminated by the re-use of pH probes, especially if they had been used in 'virus-spiked' samples for experimental purposes. The process requirement of pasteurisation of already-sealed bottles excluded that, as did the fact that the Hepatitis C virus, which had not yet been isolated, could not have been in use at the PFC in 1983 in a way that might have contaminated probes.<sup>608</sup> He concluded that the potential link suggested in Messrs Thompson's question was 'impossible'.<sup>609</sup>

**7.330** He confirmed his views in answer to questions by Counsel representing the patients, relatives and the Haemophilia Society.<sup>610</sup> There is no basis for a view that a deficiency in plant or in the manufacturing processes at the PFC caused the issue of a product that may have caused Mr Tamburrini's infection.

**7.331** While in this context few scientific propositions can be expressed in terms of mathematical certainty, totally excluding alternative possibilities, it is, scientifically, most unlikely that the SPPS administered to Mr Tamburrini transmitted Hepatitis C. In conventional legal terms it was established, beyond reasonable doubt, that SPPS did not transmit Hepatitis C to Mr Tamburrini.

---

<sup>602</sup> Day 2, pages 54–55

<sup>603</sup> Professor van Aken's Supplementary report [PEN.011.0001]

<sup>604</sup> As set out in statement of Drs Perry and Cuthbertson SPPS Batch No 1194 dated 4 March 2011 [PEN.011.0048]

<sup>605</sup> Professor van Aken – Day 2, pages 56–57 and 60–62

<sup>606</sup> Day 2, page 59

<sup>607</sup> Ibid pages 59–60; Dr Cuthbertson – Day 1, pages 141–142

<sup>608</sup> Day 2, pages 63–64

<sup>609</sup> Ibid page 65

<sup>610</sup> Professor van Aken – Day 2, pages 65–67



### ***Possibility of infection in the course of surgery in 1998***

**7.332** The next possible candidate for transmission of infection that was explored was blood transfused on 14 December 1998 following Mr Tamburrini's surgery on 11 December 1998.<sup>611</sup> The mastectomy carried out was complicated by haemorrhage and he required evacuation of a haematoma and blood transfusion.<sup>612</sup> He was transfused with three units of packed red cells, one each from batches 707090QX, 611185X8 and 631627X1. A fourth unit from batch 707135Q3 was pierced and discarded unused.<sup>613</sup> He was discharged on 15 December.<sup>614</sup>

**7.333** Mr Tamburrini was diagnosed with cirrhosis in November 2001 and his liver failed to the extent that he required a transplant in October 2002, only some three years and ten months after the December 1998 operation. Dr Bathgate's view was that, in Mr Tamburrini's case, even four years was 'far too short' a period for liver failure as a result of his acquisition of Hepatitis C infection in 1998 to have developed.<sup>615</sup> Dr Mutimer's opinion was that the chances of acquiring Hepatitis C from a blood transfusion in 1998 were 'extremely low indeed' and he noted that, as mentioned in the GP's referral letter of 2 June 1998,<sup>616</sup> Mr Tamburrini already had abnormal liver function tests.<sup>617</sup> As referred to in paragraph 7.297, the gynaecomastia and other symptoms exhibited by Mr Tamburrini in 1998 were suggestive of existing liver disease.

**7.334** There were factors other than the issue of time that also tended to exclude the possibility of infection in 1998. Dr Myrtle Peterkin, clinical consultant to the West of Scotland Blood Transfusion Service, was contacted in September 2001 by Dr McLintock and agreed to follow up Mr Tamburrini's transfusion in 1998 as a possible source of his HCV infection. She investigated the sources of the blood components (packed red cells) transfused, and available to be transfused, to Mr Tamburrini in the course of the surgical procedures undertaken. She traced the process from the request for blood to cover the operation through to the record of transfusion. The respective donors' donating histories were traced and the history of the screening of those donations was reviewed.<sup>618</sup> Finally, the archived samples of the donations were repeat-tested with a PCR test for Hepatitis C.<sup>619</sup> Dr Peterkin reported on the outcome of her investigation in a letter of 17 October 2001 to Dr Isobel Walker.<sup>620</sup>

**7.335** In oral evidence, Dr Peterkin explained that this was a specific investigation. In ordinary course, the SNBTS did not trace or record the patients to whom blood and blood products were administered; rather, hospital blood banks recorded such use.<sup>621</sup> She was provided with details of the pack numbers derived from Mr Tamburrini's hospital record sheet and traced the records back from there. The records provided a complete audit trail from the transfusion of identified pack or batch numbers of individual units of red cells, prescribed and infused by named clinicians and countersigned by nursing staff, which were

---

<sup>611</sup> Dr Mutimer's report [PEN.010.0310] at 0311

<sup>612</sup> GRI careplan [TAM.001.2907]

<sup>613</sup> GRI IV Therapy prescription sheet [TAM.001.2918]; GRI blood bank record [TAM.001.2463]

<sup>614</sup> Medical notes from 15 December 1998 [TAM.001.2912]; Discharge letter from the GRI to GP dated 20 January 1999 [TAM.001.2574]

<sup>615</sup> Day 1, pages 74–75; Report [TAM.001.2380] at 2388

<sup>616</sup> GP's request to the GRI for out-patient consultation dated 2 June 1998 [TAM.001.2583]

<sup>617</sup> Dr Mutimer – Day 1, page 110

<sup>618</sup> Day 2, pages 3 and 7–10

<sup>619</sup> Ibid page 10

<sup>620</sup> Dr Peterkin's letter to Dr Walker [TAM.001.2396]

<sup>621</sup> Day 2, page 3

correlated with records of the issue of the materials from the SNBTS.<sup>622</sup> From the records, the identities of the individual donors and the date of the donations were identified.<sup>623</sup> Dr Peterkin described what happened next with reference to one of the units:

It is important in cases like this that we don't just focus on the one donation; that is really critical. The index donation, which is why I highlighted it in bold, so that you can refer back to that – but as it were, to make assurance doubly sure that we are not missing any marker of infectivity, we look at the entire donating record. We actually retrieve archive samples from all the donations given and probe these donations as well for the specific markers that relate to the case in point.

So in this case we are talking about a possible Hepatitis C transmission and this is why we look at all those donations with specific references to the Hepatitis C virus, and ... all of the donations which were checked are Hepatitis C PCR negative, including the one that was given to the patient, and this donor had given two donations prior to November 1998, and so this is the full record of this donor that we have looked at.<sup>624</sup>

**7.336** The same procedure was carried out with each of the relevant units. The donations had been screened by anti-HCV screen when they were given. On this occasion the archived samples were also screened by HCV PCR test with negative results. Mr Tamburrini did not acquire Hepatitis C from red cells transfused at the time of surgery in December 1998.

### *Other possibilities*

**7.337** Excluding transfusion as a cause of infection does not exclude entirely the possibility of infection having been transmitted in hospital. Dr Mutimer commented:

We tend to forget that just being in hospital and having procedures done to us is associated with a risk of – transmission of infection, and that includes Hepatitis C infection. So although the blood products that he has been given are unlikely to be a cause of Hepatitis C transmission, you can never exclude the possibility that he came into contact with Hepatitis C infection during his medical care, not necessarily those inpatient admissions even; it could have been dental or medical treatment that he had at any time in his early life.<sup>625</sup>

**7.338** Dr Mutimer thought that Mr Tamburrini's teenage years might define a period of his life when he was more likely to have come into contact with Hepatitis C.<sup>626</sup> There are some issues relating to that estimate, given that it involved an assumption about experimentation with intravenous drug use, or association with others who used such drugs, for which there was no evidence. However, setting aside the speculation about drug use, Dr Mutimer's epidemiological data support the opinion that Mr Tamburrini may have been infected in his early teens. While that might indicate a period when transmission was more likely, it does not help identify the means of infection. The Inquiry heard no evidence concerning any other possible means of infection.

---

<sup>622</sup> GRI blood bank record [TAM.001.2463]; GRI IV Therapy prescription sheet [TAM.001.2918]; Day 2, pages 5–7

<sup>623</sup> Day 2, pages 7–9

<sup>624</sup> Ibid pages 9–10

<sup>625</sup> Day 1, page 114

<sup>626</sup> Ibid page 113

**7.339** The written closing submission submitted on behalf of patient interest core participants in relation to Mr Tamburrini's death states: 'In the circumstances the evidence that was heard by the Inquiry did not demonstrate even on the balance of probabilities how Mr Tamburrini came to be infected with Hepatitis C'.<sup>627</sup> That is an accurate statement.

**7.340** While the possibility of hospital-acquired transmission cannot be excluded absolutely, however, the evidence did establish, albeit to varying standards of probability, that none of the NHS procedures identified in Mr Tamburrini's case transmitted his Hepatitis C infection.

### **Possible date of infection with HCV**

**7.341** Having regard to the whole evidence covering this period, there is no room for doubt that Mr Tamburrini had well-developed Hepatitis C infection and cirrhosis by the end of 2001.<sup>628</sup>

**7.342** In a large statistical population of patients infected with Hepatitis C, the median time lapse between infection and cirrhosis of the liver in patients who do not have aggravating factors is about 30 years. At that stage half of infected patients will have developed cirrhosis and half will have less serious damage to the liver.<sup>629</sup> Men may progress more quickly than women. Consumption of alcohol will accelerate the progression to cirrhosis, as more fully discussed at paragraphs 7.345–7.346 below. In patients who acquired HCV infection under the age of 40, it is very rare for cirrhosis to be seen within 10 years of infection and it is uncommon to see it within 20 years of infection. Dr Mutimer's expertise in this area is extensive and his evidence is accepted as reliable. He had particular experience of patients requiring liver transplant procedures in Birmingham. He said:

[I]f I think of the patients that we transplant in Birmingham who have Hepatitis C, who look a little bit like Mr Tamburrini, then the majority of those will have been infected in their early adult years, late teens, early 20s. There will be a history of significant alcohol consumption, not necessarily alcoholism, and the average age at which they come to transplantation is approaching 55.<sup>630</sup>

**7.343** The extent to which Mr Tamburrini consumed alcohol was controversial and it is necessary to consider some of that evidence to ascertain whether it helps to determine at least an approximate period of time during which he was probably infected with Hepatitis C. In Mr Tamburrini's case, cirrhosis was diagnosed positively in November 2001.<sup>631</sup> He was approximately 44 years and seven months of age. At the date of his first liver transplant, in October 2002, he was 45 years of age, 10 years younger than the average age among Dr Mutimer's group of comparable patients infected in their teens or early twenties: Mr Tamburrini's Hepatitis C progressed to serious liver disease at a relatively early age. The duration of his underlying liver disease cannot be determined on the basis of these facts alone but they suggest a rapid progression of disease relative to the average.

**7.344** Progression to cirrhosis by the end of 2001, assuming a 30-year progression, would suggest a possible date of infection in about 1971, when Mr Tamburrini was about 14 years. Mr Tamburrini's teenage years appear to define the earlier end of the spectrum of

---

<sup>627</sup> Patient interest core participant's closing submissions [PEN.019.0783] at 0785

<sup>628</sup> Dr Mutimer's Report [PEN.010.0310] at 0311; Letter from the GRI to GP dated 13 December 2001 [TAM.001.2564]

<sup>629</sup> Dr Mutimer – Day 1, page 111

<sup>630</sup> Ibid page 112

<sup>631</sup> Letter from the GRI to GP dated 13 December 2001 [TAM.001.2564]

possibilities. The later end of the spectrum depends on whether alcohol was a contributory factor in the progression of his liver disease. If alcohol did accelerate the progression of the disease, he may have been infected in the later 1970s or early 1980s, in his early twenties, assuming a period of progression of 20–25 years, on the basis of the ranges provided by Dr Mutimer.

**7.345** The most complete scientific explanation of the role of alcohol in the progression of Hepatitis C was given by Professor Thomas. He said:

[I]t's now an accepted fact ... that alcohol increases the level of replication of Hepatitis C and, as a consequence, the liver damage that you see in someone who has Hepatitis C and is in addition taking significant amounts of alcohol, those two factors are synergistic; in other words, they cause more liver damage than the sum of the damage due to the alcohol and the Hepatitis C ... [B]efore we had ways of treating patients with Hepatitis C, one important thing to say was that you can slow down the progression of your Hepatitis C if you reduce your alcohol intake, and the ideal scenario would be that you would be abstinent from alcohol.<sup>632</sup>

**7.346** It was well understood by the later 1990s that significant alcohol consumption was associated with more rapid liver disease progression following Hepatitis C infection and with a higher likelihood of development of cirrhosis in those infected with Hepatitis C virus in young adulthood.<sup>633</sup> That alcohol might have, not merely an additive, but a synergistic effect on the progression of Hepatitis C virus infection was suggested around 2004–05 as a result of studies of factors that altered understanding of the effectiveness of replication of the virus.<sup>634</sup> 'Significant' was not quantified in this context. The official guidance set out in the Scottish Intercollegiate Guidelines Network (SIGN) publication 'Management of hepatitis C – A national clinical guideline' published in 2006 and repeated in the updated version published in 2013, is that: 'Even moderate amounts of alcohol (within government recommended guidelines) have been associated with increased liver fibrosis compared to those who abstain'.<sup>635</sup>

**7.347** The issue for the purposes of this discussion is whether Mr Tamburrini's consumption of alcohol assists in determining the period within which he acquired Hepatitis C infection. Detailed analysis of his medical records showed a pattern of persistent alcohol use over a period. The earliest reference to 'alcohol consumption in excess' dates from 1995.<sup>636</sup> From then until March 2002 there are about 10 instances of reports that expressly, or by reasonable implication, indicate that statements were made by Mr Tamburrini that he had been consuming significant quantities of alcohol.

**7.348** Dr McLintock's letter of 8 August 2001 (referred to above in paragraph 3.300), following examination at the GRI Haematology Clinic, narrated that Mr Tamburrini had reported his alcohol consumption as at least 20 units of alcohol per week and

---

<sup>632</sup> Day 52, pages 17–18. The evidence of a relationship between alcohol consumption and Hepatitis C progression is discussed in Chapter 13, *Knowledge of Viral Hepatitis Now*, at paragraphs 13.75–13.81.

<sup>633</sup> Freeman et al, 'Estimating progression to cirrhosis in chronic Hepatitis C virus infection,' *Hepatology*, 2001; 34:809–816 [LIT.001.4365]

<sup>634</sup> Evidence of Professor Thomas – Day 53, pages 42–43. The synergism of alcohol was discovered as a result of work on the 'Replicon' model of Hepatitis C by Bartenschlager.

<sup>635</sup> SIGN Guideline 2006 (paragraph 8.4) [PEN.018.0298] at 0317; SIGN Guideline 2013 ( paragraph 9.4) [LIT.001.5550] at 5574

<sup>636</sup> Summary of GP Records 1968–2004 [TAM.001.1459] at 1460

frequently more, normally of beer and red wine.<sup>637</sup> Dr McIntock reviewed Mr Tamburrini on 5 September 2001. On this occasion he reported mild success in cutting down his alcohol intake.<sup>638</sup> When seen at the Gastroenterology Clinic in November 2001, following Dr McIntock's reference, Mr Tamburrini is recorded as reporting a five-year history of drinking approximately 80 units of alcohol per week, which he claimed to have cut down by that date.<sup>639</sup> He was thought 'clearly' to have decompensated chronic liver disease from a combination of alcohol and Hepatitis C.<sup>640</sup>

**7.349** On 17 December 2001, Mr Tamburrini was seen at the GRI Liver Clinic by Dr Stanley. He was said to have been keeping fairly well and to have reduced alcohol consumption to a glass of wine every week or two.<sup>641</sup>

**7.350** In January and February 2002, Mr Tamburrini attended the GRI Gastroenterology Unit for tests and was referred to the Liver Transplant Unit (LTU) at the RIE for assessment for transplantation.<sup>642</sup> He reported that he had been off alcohol for three months.<sup>643</sup> After attendance at the LTU on 25 February 2002, the discharge report dated 5 March sent to Mr Tamburrini's GP and copied to Dr Stanley commented on a number of matters including the consumption of alcohol.<sup>644</sup>

**7.351** The letter of 5 March 2002 provided a careful and detailed professional review of Mr Tamburrini's history to the end of February 2002. It indicated that his period of abstinence was shorter than reported at the end of 2001 and followed a long period of sustained drinking: 100 units a week of wine and beer over the previous eight years. He had managed to remain abstinent for about six weeks in November and December 2001 but had relapsed at Christmas time and at that stage he was drinking five to six units per week.<sup>645</sup> On his referral from Liaison Psychiatry, at the RIE, to Psychiatry at Parkhead Hospital, Glasgow it was noted that, on review of the GRI notes, Mr Tamburrini had been told to abstain from alcohol on at least two occasions. He was asked by the transplant team to abstain completely.<sup>646</sup>

**7.352** At that time, Mr Tamburrini was referred to the Community Alcohol Service of Greater Glasgow Primary Care NHS Trust where he was seen by a Community Psychiatric Charge Nurse, Audrey Ewing (later Audrey Russell, after her marriage). There, he gave an account of seven years of heavy drinking which had escalated to 50–100 units of alcohol per week over five days when he had worked in the public house trade. Before that he drank very little. He said that, when very young, he had experimented with drugs, later identified as amphetamines and cannabis.<sup>647</sup> He did not keep follow-up appointments at the Community Alcohol Service, cancelling many.<sup>648</sup> By August, however, he had completed all relapse-prevention sessions and his support from the Service was terminated.<sup>649</sup>

---

<sup>637</sup> Letter from the GRI to the Glasgow Dental Hospital dated 8 August 2001 [TAM.001.2542]. See also Dr McIntock's letter to the GRI Gastroenterology dated 20 September 2001 which reported similar consumption [TAM.001.2545]

<sup>638</sup> Letter from the GRI to GP dated 31 October 2001 [TAM.001.2553]

<sup>639</sup> Letter from the GRI to GP dated 9 December 2001 [TAM.001.2557]

<sup>640</sup> *Ibid* at 2558

<sup>641</sup> Letter from the GRI to GP dated 15 January 2002 [TAM.001.2562]

<sup>642</sup> Letter from the GRI to the RIE LTU dated 14 February 2002 [TAM.001.2565]

<sup>643</sup> Letter from the GRI to GP dated 15 February 2002 [TAM.001.2566]

<sup>644</sup> Letter from the RIE LTU to GP [TAM.001.2524]

<sup>645</sup> *Ibid* [TAM.001.2524]

<sup>646</sup> Letter from the RIE to the Parkhead Hospital, Glasgow dated 6 March 2002 [TAM.001.0905]

<sup>647</sup> Letter from the Community Alcohol Service to the RIE dated 10 April 2002 [TAM.001.0898]. The Community Alcohol Service details form [TAM.001.3074] at 3097. Efforts by the Inquiry team to trace Audrey Ewing (Russell) to obtain her evidence were unsuccessful, as set out in the transcript of Day 1, pages 82–83.

<sup>648</sup> Letter from the Community Alcohol Service to the RIE dated 9 May 2002 [TAM.001.0897]

<sup>649</sup> Letter from the Community Alcohol Service to the RIE dated 12 August 2002 [TAM.001.3076]

**7.353** While the reports show wide variation in the volume of alcohol reportedly consumed, the overall picture presented was of significant and sustained consumption. As reported by Dr Seonaid McCallum of the Department of Psychological Medicine, at the RIE, to Dr Jauhar, Consultant Psychiatrist, at the Parkhead Hospital, on 6 March 2002, psychiatric examination disclosed that:

Initially Mr Tamburrini denied that he had an alcohol problem but during ... interview he admitted that indeed, although he had managed to stop drinking, sustained abstinence was a problem for him. He also had limited insight into the effect excess alcohol can have in conjunction with hepatitis C and was unaware that it can cause accelerated liver failure. I felt that at the end of the interview he was beginning to show some motivation and insight into his alcohol problem. He did not give a history of alcohol dependency, rather his problem was one of harmful alcohol use.<sup>650</sup>

**7.354** As reported by Dr McCallum, Mr Tamburrini had given a history of drinking 50–100 units of alcohol per week. He had achieved a six-week period of abstinence before Christmas which he had been unable to maintain. Dr Mutimer considered that psychiatric assessment as perhaps the most expert undertaken during Mr Tamburrini's psychological assessment for liver transplantation.<sup>651</sup> His evidence is accepted. It is to be noted that Dr McCallum's view was that Mr Tamburrini's problem was of harmful alcohol use, particularly in the context of his HCV infection, of which he was unaware until 2001. It is nowhere suggested that he was 'an alcoholic' or otherwise dependent on alcohol.

**7.355** Dr Mutimer said of Mr Tamburrini:

In my opinion, both hepatitis C virus infection and alcohol caused cirrhosis and subsequent hepatic decompensation. It is not possible to determine the relative contributions of hepatitis virus infection and alcohol to his liver damage. The duration of his hepatitis C infection is unknown. It is possible that he was infected with hepatitis C at a young age ....It is also possible that he was infected at a much later date .... At times in his life, his alcohol intake was excessive and certainly sufficient to cause liver damage. His reported (or at least documented) alcohol consumption varies quite significantly. Perhaps the most expert assessment would have been undertaken during his psychological assessment for liver transplantation. That assessment stated that he consumed 50 to 100 units of alcohol per week for eight years.<sup>652</sup>

He underwent liver biopsy in August 2002. The liver biopsy showed that he had a micronodular cirrhosis and that the changes were consistent with chronic hepatitis virus infection. At that time, there were no particular signs of alcoholic liver damage. This observation is not surprising and does not exclude alcohol as a significant cause of his liver damage. It seems likely that he was abstinent from alcohol during all of 2002 and that his alcohol consumption during the last quarter of 2001 was not excessive. I believe that the histological changes associated with alcoholic liver damage could have resolved during his

---

<sup>650</sup> Dr McCallum's letter [TAM.001.0905]

<sup>651</sup> Dr Mutimer's report [PEN.010.0310] at 0313

<sup>652</sup> The psychological assessment carried out by Dr McCallum [TAM.001.0905] refers to 50–100 units per week and to 'drinking to excess over the last 5 years'. The reference to drinking 100 units a week over eight years is in the letter from Dr MacGilchrist's registrar dated 5 March 2002 [TAM.001.2524]. Dr Mutimer has conflated the two sources.

period of abstinence. Indeed the hepatologists in Edinburgh would have been encouraged by the histological appearances which would have reassured them that there was no significant recent alcohol intake. In summary, I believe that hepatitis C and alcohol contributed to his liver disease.<sup>653</sup>

**7.356** Dr Bathgate and Dr Mutimer both commented on consumption of alcohol as a possible factor which might have contributed to Mr Tamburrini's underlying liver disease. Dr Bathgate described experience in south east Scotland which indicated that alcohol was the major co-factor seen in cases such as Mr Tamburrini's.<sup>654</sup> Dr Mutimer was more positive: Mr Tamburrini's underlying liver disease was secondary to HCV infection and alcohol. He was, however, unable to determine their relative contributions.<sup>655</sup>

**7.357** The reports of alcohol consumption were not challenged as inaccurate records of what Mr Tamburrini told medical staff. It was submitted that the basis on which the amounts were 'estimated' was not known but the written records indicate that they reflect what Mr Tamburrini told the physicians and other relevant health care professionals, including Nurse Audrey Ewing. The reports were clearly not believed by the family's wider circle, however. Mrs Tamburrini and friends of the family submitted affidavits in which they stated variously that Mr Tamburrini did not drink heavily.<sup>656</sup> Mrs Tamburrini has stated that in the late 1980s her husband did not drink during the week, except perhaps for celebrations, and did not drink excessively. When he began working in licensed premises, he would have a couple of beers with his friends but they did not have money to drink heavily. She did not recall any increase in his drinking when he began bar work. They had both abstained in 1996 for a period. She comments that the family are incredulous that it should be recorded in the medical records that he drank 50–100 units of alcohol a week.<sup>657</sup> Mr Charlie Cunningham never saw Mr Tamburrini drink to excess. He would have a couple of drinks in a night club. He did not recall any escalation in his drinking when he started working in the bar.<sup>658</sup> Mr Stephen Clocherty said that, at the fruit market, because of the early start, Mr Tamburrini would not have been able to stay out late drinking. He did not see any change when Mr Tamburrini went to work in the bar. He thought that it was 'pure nonsense' to say that he drank 50–100 units of alcohol a week.<sup>659</sup> Mr Fisher, the owner of the establishment where Mr Tamburrini worked, said that no one drank at work. During the week they would have a bottle of beer while tidying up. At weekends they would sometimes have two or three drinks before going home. He remembered Mr Tamburrini being advised to stop drinking before his first transplant. He never saw him drink anywhere near 50–100 units of alcohol a week.<sup>660</sup>

**7.358** There are three significant problems with this evidence. In the first place, some of it does not relate to the period over which Mr Tamburrini is likely to have been developing liver disease. Mrs Tamburrini met her husband in 1987.<sup>661</sup> Mr Fisher knew him as brother-in-law of Mrs Tamburrini and speaks of no earlier acquaintanceship.<sup>662</sup> Mr Cunningham and Mr Clocherty knew Mr Tamburrini from school and from work but speak of very

---

<sup>653</sup> Dr Mutimer's report [PEN.010.0310] at 0313

<sup>654</sup> Day 1, page 75

<sup>655</sup> Report [PEN.010.0310] at 0310 and 0313

<sup>656</sup> Affidavits of Mrs Jean Tamburrini [PEN.018.1544], Charlie Cunningham [PEN.018.1549], Stephen Clocherty [PEN.018.1547] and Bernard Fisher [PEN.018.1559]

<sup>657</sup> Affidavit of Mrs Jean Tamburrini [PEN.018.1544]

<sup>658</sup> Affidavit of Charlie Cunningham [PEN.018.1549]

<sup>659</sup> Affidavit of Stephen Clocherty [PEN.018.1547]

<sup>660</sup> Affidavit of Bernard Fisher [PEN.018.1559]

<sup>661</sup> Statement of Mrs Jean Tamburrini [PEN.001.0309]

<sup>662</sup> Affidavit of Bernard Fisher [PEN.018.1559]

general impressions only. Secondly, in the nature of things, the witnesses could never give more than impressions from observation of Mr Tamburrini's drinking when they were present. Thirdly, standing the records, the evidence contradicts what Mr Tamburrini himself told medical staff. Balancing these statements against contemporaneous records of Mr Tamburrini's own statements, the witnesses' affidavits cannot be accepted as reliable evidence of Mr Tamburrini's consumption of alcohol over the period when he was developing significant liver disease, which probably began long before 1987.

**7.359** Further, the evidence is misdirected so far as the issues before this Inquiry are concerned. It has not been suggested that Mr Tamburrini was generally adversely affected by alcohol, or drank to excess in any conventional sense that implies drunkenness. As noted above, Dr McCallum's view was that Mr Tamburrini's problem was of harmful alcohol use, particularly in the context of his Hepatitis C virus infection. In the progression of HCV-related liver disease, even moderate alcohol consumption may play a part in accelerating damage. On his own reports there were clearly long periods when Mr Tamburrini drank alcohol regularly.<sup>663</sup> He frequently reported consumption, inconsistently as to amount, at periods when his developing symptoms could have been related, in whole or in part, to his alcohol habit. The conditions reported in Mr Tamburrini's medical records and described above frequently have plausible associations with alcohol.

**7.360** It is not possible to quantify precisely the effect of alcohol in the progression of Mr Tamburrini's liver disease. However, accurate estimates of quantity are unnecessary in light of the expert evidence led. On the evidence of the medical records, there was a pattern of alcohol consumption over a period of years that was highly likely to have accelerated the progression of liver disease due to his infection with Hepatitis C. It made it more likely that he would become one of the minority of those infected at a young age (under 30 years) who develop cirrhosis sooner rather than later.

**7.361** Given a relatively short period of progression from infection to cirrhosis, the history narrated above nevertheless indicates that alcohol was a contributory factor. That was the view of the medical witnesses, which is accepted.

**7.362** As set out in paragraphs 7.299–7.300 above, Mr Tamburrini's abnormal blood parameters found in 2001 were thought by his clinicians at the time to be indicative of liver disease. Dr McLintock thought that their most likely cause was liver disease probably caused by alcohol. Mr Tamburrini had reported his consumption to her as 20 units per week.<sup>664</sup> Dr Mutimer commented that, in Mr Tamburrini's case, the gynaecomastia reported earlier in 1998 would be consistent with alcoholic liver damage, with HCV infection, and also with damage due to both alcohol and HCV infection. His MCV recorded at that time was in keeping with alcohol excess.<sup>665</sup> Some medications used to treat patients with advanced liver disease can also cause gynaecomastia but there is no record of Mr Tamburrini taking such medications at the time.<sup>666</sup> The medical evidence was consistent: by the end of 2001 there was established liver disease, consistent with the consumption of alcohol and Hepatitis C.

**7.363** In January 1999, when suffering from acute pancreatitis, Mr Tamburrini was advised to abstain from alcohol. Choledocholithiasis (the presence of stones in the bile

---

<sup>663</sup> Dr Mutimer's report [PEN.010.0310] at 0313

<sup>664</sup> Letter from the GRI to the Glasgow Dental Hospital dated 8 August 2001 [TAM.001.2542]

<sup>665</sup> Dr Mutimer's report [PEN.010.0310] at 0311

<sup>666</sup> Dr Mutimer – Day 1, pages 94–95



duct) and excess alcohol consumption are both important causes of acute pancreatitis. Either might have precipitated the episode of pancreatitis he had at this time.<sup>667</sup> From the contemporaneous medical records, his pancreatitis was clearly thought to be related to some extent to his drinking, although it was formally recorded that it might have been due to preceding viral infection.

**7.364** As discussed at paragraph 7.355, it is accepted that Mr Tamburrini was abstinent from alcohol from late 2001 until his death in November 2004. Alcohol did not contribute to the failure of either the first or second liver transplant grafts received by Mr Tamburrini or cause, or contribute to the cause of, his death. It is accepted that the cause of death was unrelated to alcohol consumption. The progression of his liver disease following transplantation was independent of those factors.

**7.365** In summary, consumption of alcohol was a contributory factor in the progression of Mr Tamburrini's liver disease to cirrhosis at a relatively young age.

### Later progression of disease

**7.366** On 12 November 2001, an abdominal ultrasound scan was carried out at the GRI liver clinic.<sup>668</sup> There were changes consistent with liver cirrhosis and it was decided to proceed to Magnetic Resonance Imaging (MRI) scan.<sup>669</sup> The MRI scan on 20 November 2001 showed underlying cirrhotic change in the liver, with liver cirrhosis, especially in the right lobe. There was no underlying focal mass and no evidence of hepatoma (liver cancer)<sup>670</sup> and there was no overt portal hypertension (high blood pressure around the liver).<sup>671</sup> However, albumin levels indicated advanced liver impairment and raised alphafetoprotein (AFP) levels suggested the possibility of hepatoma despite the negative scans.<sup>672</sup> Dr Stanley reported to Mr Tamburrini's GP on 13 December that there were a few spider naevi (visible red lines on the skin indicative of cirrhosis of the liver) on examination but no definite ascites (fluid in the abdomen, a marker of liver function).<sup>673</sup>

**7.367** On 28 November 2001, Mr Tamburrini was reviewed at the GRI Haematology Clinic by Dr Maclean. It was noted that significant macrocytosis (abnormally large red blood cells indicative of anaemia) persisted.<sup>674</sup> On 17 December, he was seen at the Liver Clinic by Dr Stanley. He was said to have been keeping fairly well. Rising AFP levels were still of concern and thought to indicate the need for a liver biopsy.<sup>675</sup> On 8 January 2002, Dr Stanley noted an AFP level of 366 and thought the rising pattern suggested hepatoma.<sup>676</sup> Dr Mutimer explained that the magnitude of the AFP level was informative. If it was in the thousands, that almost always meant that there was liver cancer. When it was in the hundreds, as it was in Mr Tamburrini's case, then it could simply be associated with an inflamed liver rather than with cancer but tests would be performed to exclude the possibility of liver cancer.<sup>677</sup> Investigations proceeded on 7 February 2002. A contrast enhanced three phase scan and an ultrasound scan confirmed underlying liver cirrhosis but there was no

---

<sup>667</sup> Dr Mutimer's report [PEN.010.0310] at 0311

<sup>668</sup> Report of ultrasound scan [TAM.001.2699]

<sup>669</sup> Letter from the GRI to GP dated 9 December 2001 [TAM.001.2557] at 2558

<sup>670</sup> Hepatoma is primary hepatocellular carcinoma.

<sup>671</sup> Report of MRI scan [TAM.001.2697]

<sup>672</sup> Letter from the GRI to GP dated 13 December 2001 [TAM.001.2564]; Dr Mutimer – Day 1, page 106; Dr Bathgate – Day 1, page 31

<sup>673</sup> Letter from the GRI to GP dated 13 December 2001 [TAM.001.2564]

<sup>674</sup> Letter from the GRI to GP dated 20 December 2001 [TAM.001.2563]

<sup>675</sup> Letter from the GRI to GP dated 15 January 2002 [TAM.001.2562]

<sup>676</sup> Letter from the GRI to GP dated 25 January 2002 [TAM.001.2561]

<sup>677</sup> Day 1, page 106

underlying hepatic mass. Gastro-oesophageal varices and varices along the lesser curve of the stomach were identified. The impression was of underlying liver cirrhosis, with overt portal hypertension (pressure within the portal vein from the liver is increased and may lead to bleeding) but no hepatoma.<sup>678</sup> Dr Stanley wrote to Mr Tamburrini's GP on 15 February with these results.<sup>679</sup>

**7.368** On 14 February 2002, Dr Stanley referred Mr Tamburrini to Dr Simpson, consultant hepatologist at the RIE LTU for assessment.<sup>680</sup> At that time, there remained some concern that Mr Tamburrini had developed primary liver cancer.<sup>681</sup> Dr Stanley was concerned about a rising level of AFP in his blood test, an indication of possible hepatocellular cancer. That was a legitimate concern at the time but events were to show that Mr Tamburrini did not have hepatocellular cancer. Dr Stanley reported that two ultrasound scans, an MRI scan and a contrast CT scan<sup>682</sup> had been carried out which disclosed liver cirrhosis, varices, and stones in the gall bladder but no splenomegaly (enlargement of the spleen). No scan had shown evidence of underlying hepatocellular cancer but ascites and poor synthetic liver function were noted.<sup>683</sup>

**7.369** Mr Tamburrini was admitted to the RIE LTU on 25 February 2002.<sup>684</sup> Dr MacGilchrist's registrar reported to Mr Tamburrini's GP, copied to Dr Stanley, following discharge on 2 March 2002. The discharge letter, dated 5 March, commented on past medical history, as understood at the time, clinical findings, test results and consumption of alcohol.<sup>685</sup> Comprehensive tests were carried out. Mr Tamburrini was cytomegalovirus (CMV) and Hepatitis C positive.<sup>686</sup> Dr Bathgate thought that the results showed moderate impairment of liver function at this stage.<sup>687</sup> Cirrhosis was confirmed during the assessment for liver transplant. Because Mr Tamburrini reported that he was still drinking alcohol he was thought not to be a suitable candidate for transplant: prior to becoming eligible for listing for liver transplant, a period of abstinence (usually six months) is required. In the meantime, other tests were carried out to follow up the risk of hepatoma.<sup>688</sup> It seems clear that Mr Tamburrini remained abstinent from alcohol from this time, as instructed.

**7.370** He was reviewed at the RIE LTU on 4 April 2002.<sup>689</sup> His AFP level had fallen. A CT scan using Lipiodol, a contrast medium, was carried out shortly before his clinic appointment and the results were 'against him having hepatocellular carcinoma'.<sup>690</sup> A triple-phase CT scan carried out on 21 June did not indicate any focal abnormality of his liver.<sup>691</sup> He was to be reviewed in six weeks.<sup>692</sup> Mrs Tamburrini recollected that monthly reviews were arranged.<sup>693</sup> In July, his AFP had risen again and Dr Stanley asked the LTU to ensure early reassessment.<sup>694</sup>

---

<sup>678</sup> Report of scan [TAM.001.2695]

<sup>679</sup> Letter dated 15 February 2002 [TAM.001.2566]

<sup>680</sup> Letter from the GRI to RIE LTU [TAM.001.2565]

<sup>681</sup> Dr Mutimer's report [PEN.010.0310] at 0311; Dr Bathgate – Day 1, page 31

<sup>682</sup> Computerised tomography scan, sometimes also known as CAT scan.

<sup>683</sup> Letter from the GRI to RIE LTU dated 14 February 2002 [TAM.001.2565]; Dr Bathgate – Day 1, pages 31–33

<sup>684</sup> Witness Statement of Mrs Jean Tamburrini [PEN.001.0309] at 0312

<sup>685</sup> Letter from LTU RIE to GP dated 5 March 2002 [TAM.001.2524]

<sup>686</sup> Ibid [TAM.001.2524] at 2525

<sup>687</sup> Day 1, page 35

<sup>688</sup> Letter from LTU RIE to GP dated 5 March 2002 [TAM.001.2524] at 2525

<sup>689</sup> Letter from LTU RIE to GP dated 9 April 2002 [TAM.001.0900]

<sup>690</sup> Ibid [TAM.001.0900]; Dr Bathgate – Day 1, page 35

<sup>691</sup> Letter from RIE LTU to GP dated 26 August 2002 [TAM.001.0881]

<sup>692</sup> Ibid [TAM.001.0881] at 0883

<sup>693</sup> Witness Statement of Mrs Jean Tamburrini [PEN.001.0309] at 0312

<sup>694</sup> Letter from the GRI to the RIE LTU dated 3 July 2002 [TAM.001.2533]

**7.371** He was seen at the LTU on 4 July 2002. His AFP level was seriously raised, as were other levels. The recent CT scan results were thought to indicate that the AFP level indicated ongoing Hepatitis C activity rather than the presence of a tumour. Further review in two months was arranged.<sup>695</sup> Dr Bathgate thought that the AFP level noted on 4 July was quite concerning.<sup>696</sup>

**7.372** Mr Tamburrini was re-admitted to the LTU on 13 August 2002 for formal liver transplant assessment. After extensive review, including liver biopsy, Dr MacGilchrist's registrar reported at length to Mr Tamburrini's GP. There was cirrhosis with mild ongoing inflammation thought to be due to Hepatitis C. He was CMV and HCV positive. The conclusion at that stage was that there was increasing active viral replication but no indications of hepatocellular carcinoma and transplantation was to be delayed as long as possible in view of the fact that he was asymptomatic of liver disease.<sup>697</sup>

### *The decision to proceed with a liver transplant*

**7.373** Mr Tamburrini next attended the LTU on 10 October 2002. By this stage, Dr Simpson noted that he was becoming more symptomatic. He was increasingly tired and having to sleep during the day. He was not sleeping at night. He was getting night cramps. The reversal of his sleep pattern was an indication of early encephalopathy (brain dysfunction).<sup>698</sup> His weight was increasing and he felt swelling in his ankles and abdomen. His AFP level had fallen further. Following examination it was decided to admit him on 17 October and list him for liver transplantation.<sup>699</sup>

**7.374** He was admitted on 17 October but found to be very unwell. Mrs Tamburrini explained that her husband's health had started to deteriorate rapidly by this point.<sup>700</sup> He had become confused and jaundiced. He complained of fever and abdominal pain over three days. On examination he was septic and had evidence of spontaneous bacterial peritonitis. He was treated intensively. At this stage, Mr Tamburrini signed a contract of alcohol abstinence and was officially put on the transplant waiting list and allowed home on 25 October.<sup>701</sup>

**7.375** However, on that day a suitable donor liver was found and he was re-admitted. He had a liver transplant on 26 October 2002. He required intensive care and treatment after the operation. There were complications of bacterial peritonitis and renal impairment (which resolved without the need for dialysis). He progressed to a good recovery and was allowed home on 15 November 2002.<sup>702</sup> No hepatocellular cancer was found in the explanted liver.<sup>703</sup>

### *Post-transplant observation*

**7.376** On 19 November 2002, Mr Tamburrini attended a planned post-operation review at the LTU. He complained of abdominal pain. Clinically, he appeared unwell and in obvious pain and was admitted for investigation.<sup>704</sup> There was free fluid within the abdomen.

---

<sup>695</sup> Letter from the RIE LTU to GP dated 24 July 2002 [TAM.001.2470]

<sup>696</sup> Dr Bathgate – Day 1, pages 40–41

<sup>697</sup> Letter from the RIE LTU to GP dated 26 August 2002 [TAM.001.0881]

<sup>698</sup> Disorder of the brain, a late complication of cirrhosis.

<sup>699</sup> Letter from the RIE LTU to GP dated 16 October 2002 [TAM.001.0878]

<sup>700</sup> Witness Statement of Mrs Jean Tamburrini [PEN.001.0309] at 0312

<sup>701</sup> Letter from the RIE LTU to GP dated 13 December 2002 [TAM.001.0876]

<sup>702</sup> Ibid [TAM.001.0874]

<sup>703</sup> Ibid [TAM.001.0874]

<sup>704</sup> Letter from the RIE LTU to GP dated 13 December 2002 [TAM.001.0872]

After extensive tests, it was found by ERCP procedure (endoscopic examination)<sup>705</sup> that there was a leak from his bile duct at the anastomosis, the biliary connection with the implanted liver. The ERCP was complicated by pancreatitis but the stricture was dilated and a stent was inserted to try to stop the leak. It was anticipated that he would require to be re-admitted for assessment of the need for further surgery of the anastomosis.<sup>706</sup> He was discharged home on 13 December. Dr Mutimer thought that inflammation from the recurrence of Hepatitis C and poor drainage via the bile duct as a result of the stricture were both relevant to subsequent damage of the implanted liver.<sup>707</sup>

**7.377** Mr Tamburrini attended Dr MacGilchrist's clinic on 17 December 2002. A report was sent to his GP.<sup>708</sup> On discharge, Mr Tamburrini remained generally well, with no abdominal pain and reduced drainage of fluid. The prospect of further surgery to renew the connection was kept open. He was reviewed on 14 January 2003 and an ultrasound examination showed a normal liver with no evidence of collection around his biliary tree.<sup>709</sup> He reported at a clinic appointment on 28 January feeling well and said that he was thinking of going back to work.<sup>710</sup>

**7.378** Mrs Tamburrini reported that, after discharge, her husband lost the previous excess fluid and recovered his normal condition. He received medication to prevent rejection of the implanted liver.<sup>711</sup>

**7.379** After a clinic visit on 27 February, Mr Tamburrini was admitted to the LTU for further examination on 10 March 2003. Tests confirmed that there was no obvious debris or stones. There was a suggestion of focal hepatic artery stenosis (narrowing), possibly at the anastomosis, with very turbulent flow. An ERCP procedure was carried out on 11 March. Ultrasound examination and ERCP showed that the bile duct was dilated above an anastomotic stricture. This required placement of a new endoscopic stent. Mr Tamburrini's bilirubin level fell slowly, which suggested that the endoscopic stent was providing biliary drainage.<sup>712</sup> Treatment of his possible hepatic artery stenosis was deferred.<sup>713</sup>

**7.380** Mr Tamburrini was reviewed in April and June 2003. It was decided to continue monitoring his condition.<sup>714</sup> On 24 July 2003, he was reviewed at the LTU when he reported feeling much better. At that stage, it was thought that his biliary stent should be removed in September.<sup>715</sup> It was arranged that he would be admitted for his annual biopsy following a holiday in October.<sup>716</sup> Mrs Tamburrini reported that, on 27 August 2003, at a family event, he was bloated and jaundiced.<sup>717</sup> The ERCP was repeated in September 2003. This showed that the anastomotic stricture persisted. The stent which had been placed six months earlier was not visible. In September it was decided that no further intervention should take place.<sup>718</sup>

---

<sup>705</sup> Endoscopic retrograde Cholangiopancreatography.

<sup>706</sup> Letter from the RIE LTU to GP dated 14 December 2001 [TAM.001.0869]

<sup>707</sup> Day 1, pages 107–108

<sup>708</sup> Letter from the RIE LTU to GP dated 31 December 2002 [TAM.001.0867]

<sup>709</sup> Letter from the RIE LTU to GP dated 21 January 2003 [TAM.001.0862]

<sup>710</sup> Letter from the RIE LTU to GP dated 4 February 2003 [TAM.001.0859]

<sup>711</sup> Ibid [TAM.001.0859]; Witness Statement of Mrs Tamburrini [PEN.001.0309] at 0313

<sup>712</sup> Letter from the RIE LTU to GP dated 17 March 2003 [TAM.001.0857]; Dr Mutimer's report [PEN.010.0310] at 0312

<sup>713</sup> Letter from the RIE LTU to GP dated 17 March 2003 [TAM.001.0857]

<sup>714</sup> Letter from the RIE LTU to GP dated 16 April 2003 [TAM.001.0842]; Letter from the RIE LTU to GP dated 25 June 2003 [TAM.001.0835]

<sup>715</sup> Letter from the RIE LTU to GP dated 4 August 2003 [TAM.001.0832]

<sup>716</sup> Ibid [TAM.001.0832]

<sup>717</sup> Witness Statement [PEN.001.0309] at 0313

<sup>718</sup> Letter from the RIE LTU to GP dated 11 September 2003 [TAM.001.0830]

**7.381** The couple went on holiday but Mr Tamburrini's sleeping pattern was disturbed and he again became jaundiced. His ankles and abdomen were swollen.<sup>719</sup> He was seen at the LTU on 6 November 2003. His symptoms of 'obstructive' jaundice were noted. Further tests were arranged with specific reference to the state of his hepatic artery.<sup>720</sup>

**7.382** Additional investigations were performed at about that time. These were highly technical. There were differing opinions about what was shown and in particular whether there was restriction of blood flow. The appearance of the biliary tree was similar to that shown on previous ERCP scans. There was a new finding of multiple upper abdominal fluid collections of uncertain nature. Liver biopsy showed established cirrhosis with evidence of recurrent and active Hepatitis C infection. It was decided to repeat ERCP and stenting across the anastomotic stricture. Antiviral treatment was also considered.<sup>721</sup> It was noted at that stage that his Hepatitis C was Genotype 1.<sup>722</sup> Dr Bathgate explained that Genotypes 1, 2 and 3 are commonly found in Scotland. Antiviral therapy for Genotype 1 usually requires 12 months with a success rate of less than 50%, whereas treatment for Genotypes 2 and 3 requires six months with an 80% success rate. Treatment is less effective in individuals with cirrhosis and after liver transplant.<sup>723</sup> Mr Tamburrini's prospects were relatively poor.

**7.383** On 4 December 2003, Mr Tamburrini was seen by Dr Bathgate and treatment of his Hepatitis C was discussed.<sup>724</sup> Poor liver function persisted. Dr Bathgate thought that Mr Tamburrini was unlikely to tolerate any treatment in his then existing state.<sup>725</sup> Options would be discussed in January. Dr Bathgate thought that treatment of the Hepatitis C would have to have been 'fairly aggressive', given his history.<sup>726</sup> In January 2004, his condition deteriorated seriously and he was confused, disorientated and jaundiced.<sup>727</sup> He was admitted on 13 January to the RIE. Again tests showed evidence of cirrhosis likely to be secondary to Hepatitis C. Hepatitis C had returned and he needed a second transplant.<sup>728</sup>

### **Second liver transplant**

**7.384** A donor liver became available on 4 February and he had a second liver transplant operation.<sup>729</sup> The surgeon found a dilated and thickened donor bile duct. There was also portal vein thrombosis. Dr Mutimer considered that the appearance of the donor bile duct suggested that biliary complications (in addition to the recurrent Hepatitis C infection) had probably contributed to the development of cirrhosis and graft failure.<sup>730</sup> He expanded on his views in oral evidence. He thought that, during the first year post-transplant, the team were clearly having problems with the bile duct. It was his impression that they thought they had largely resolved that problem but that the finding of the dilated, thickened bile duct at the time of re-transplantation suggested that perhaps that was a problem which had not, in fact, been completely resolved.<sup>731</sup>

---

<sup>719</sup> Witness statement of Mrs Tamburrini [PEN.001.0309] at 0313

<sup>720</sup> Letter from the RIE LTU to GP dated 13 November 2003 [TAM.001.0824] at 0825: the problem so noted was not restricted to obstruction. It indicated that the liver was working very badly and could properly have been described as 'cholestatic'.

<sup>721</sup> Letter from the RIE LTU to GP dated 8 December 2003 [TAM.001.0814] at 0815

<sup>722</sup> Specifically Genotype 1A. But the distinction between 1A and 1B is not relevant for present purposes. See Chapter 13, *Knowledge of Viral Hepatitis Now*, paragraph 13.14 for discussion of HCV genotypes.

<sup>723</sup> Dr Bathgate's report [TAM.001.2380] at 2382 and 2384; Day 1, page 56

<sup>724</sup> Letter from the RIE LTU to GP dated 15 December 2003 [TAM.001.0812]

<sup>725</sup> Day 1, page 56

<sup>726</sup> Letter from the RIE LTU to GP dated 15 December 2003 [TAM.001.0812]

<sup>727</sup> Witness Statement of Mrs Jean Tamburrini [PEN.001.0309] at 0314

<sup>728</sup> Letter from the RIE LTU to GP dated 3 March 2004 [TAM.001.0799]

<sup>729</sup> Witness Statement of Mrs Jean Tamburrini [PEN.001.0309] at 0314; Letter from the RIE LTU to the GRI dated 11 February 2004 [TAM.001.0804]. Letter from the RIE LTU to GP dated 3 March 2004 [TAM.001.0799]

<sup>730</sup> Dr Mutimer's report [PEN.010.0310] at 0312

<sup>731</sup> Day 1, pages 108–109

**7.385** Mr Tamburrini developed post-operative biliary peritonitis secondary to a leaking enterostomy. Further treatment and surgery was required. He made an eventual recovery from that admission<sup>732</sup> and was discharged on 28 February, with a recall date in March to consider antiviral treatment for Hepatitis C.<sup>733</sup> Mr Tamburrini was examined on 16 March 2004 and it was found that his liver function tests had deteriorated.<sup>734</sup> The clinicians were concerned that he was susceptible to aggressive Hepatitis C recurrence.<sup>735</sup> He was to be reviewed by Dr Bathgate, with in-patient ultrasound and liver biopsy examinations.<sup>736</sup> Thereafter, antiviral therapy with a combination of Interferon and Ribavirin was commenced during in-patient care between 23 and 29 March and he had a further liver biopsy. A report was sent to his GP: he was to return for review on 8 April. At this stage, Mr Tamburrini was seen by the specialist Hepatitis C nurse and told what to expect from the treatment.<sup>737</sup>

**7.386** Mr Tamburrini continued to attend hospital. On 22 April 2004, he was reported to be tired, lacking in energy and looking unwell although he did not complain of being depressed. In contrast, Mrs Tamburrini had noted that he was grumpy at this time.<sup>738</sup> Mr Tamburrini showed considerable fortitude throughout this period. The antiviral treatment caused diarrhoea. Balancing treatment against his tolerance was necessary.<sup>739</sup> His HCV level was measured on a number of occasions during antiviral therapy. Despite the therapy, his HCV level remained extremely high and there was no obvious improvement from the therapy.<sup>740</sup>

### *A grave prognosis*

**7.387** Mr Tamburrini was an in-patient at the RIE from 1 to 15 June 2004. Among the tests carried out, liver biopsy showed fibrosing cholestatic hepatitis (an aggressive type of Hepatitis C generally seen in patients who are immunosuppressed)<sup>741</sup> caused by recurrent Hepatitis C.<sup>742</sup> The prognosis was very grave and there were few options for treatment.<sup>743</sup> Antiviral therapy was increased and other elements of his therapy were re-balanced. He required the additional use of erythropoietin and other haematologic growth factors.<sup>744</sup> He was reviewed again, on 15 July and 6 September.<sup>745</sup> On 14 September liver ultrasound had been unable to detect flow in the portal vein. There was a cystic collection in the left lobe of the liver as well as splenomegaly and moderate ascites. A further liver biopsy was carried out. His treatment now involved the optimum dose of pegylated Interferon and Ribavirin, which he managed to tolerate well, but he required blood transfusions every two to three weeks to counter side-effects of the Ribavirin treatment.<sup>746</sup>

---

<sup>732</sup> Dr Mutimer's Report [PEN.010.0310] at 0312

<sup>733</sup> Letter from the RIE LTU to GP dated 3 March 2004 [TAM.001.0799]

<sup>734</sup> Letter from the RIE LTU to GP dated 1 April 2004 [TAM.001.0795]; Dr Bathgate – Day 1, page 61

<sup>735</sup> Dr Mutimer's report [PEN.010.0310] at 0312

<sup>736</sup> Letter from the RIE LTU to GP dated 1 April 2004 [TAM.001.0795]

<sup>737</sup> Ibid [TAM.001.0793]; Dr Bathgate – Day 1, pages 64–65

<sup>738</sup> Letter from the RIE LTU to GP dated 28 April 2004 [TAM.001.0789]

<sup>739</sup> Dr Bathgate – Day 1, pages 65–66

<sup>740</sup> Dr Mutimer's report [PEN.010.0310] at 0313

<sup>741</sup> Ibid

<sup>742</sup> Letter from the RIE LTU to GP dated 28 June 2004 [TAM.001.0781]

<sup>743</sup> Ibid [TAM.001.0781]

<sup>744</sup> Dr Mutimer's Report [PEN.010.0310] at 0313

<sup>745</sup> Letter from the RIE LTU to GP dated 22 July 2004 [TAM.001.0774]; Letter from the RIE LTU to GP dated 14 September 2004 [TAM.001.0768]

<sup>746</sup> Letter from the RIE LTU to GP dated 20 September 2004 [TAM.001.0762]; Dr Bathgate – Day 1, page 69

**7.388** Despite treatment, his condition deteriorated. On 7 October 2004, he was again admitted to the RIE. He was suffering from severe lethargy and fatigue, weight loss and significant depression. He had a fever and was treated with antibiotics. He developed increasing hepatic decompensation, with increasing ascites and episodes of recurrent encephalopathy. He required paracentesis, the drawing off of fluid. A third transplant could not be considered. The antiviral treatment was stopped. His care regime was changed from aggressive therapy to palliative care after discussion with Mrs Tamburrini. He died on 17 November 2004.<sup>747</sup>

### **Mr Tamburrini's treatment and management**

**7.389** Asked to comment on whether Mr Tamburrini's treatment and management were appropriate Dr Mutimer said in his report:

[Mr Tamburrini] clearly had significant liver damage prior to the diagnosis of Hepatitis C virus infection in October 2001. His medical attendants assumed that the abnormal liver function tests were due to the consumption of alcohol. The hospital admission with possible pancreatitis was also in favour of an alcoholic aetiology for the abnormal liver function tests. In general, alcohol-induced pancreatitis is only seen in patients with quite high levels of alcohol consumption. I cannot determine from the medical files if attempts were made to engage the patient with services that might modify his alcohol consumption. That would have been appropriate. Eventually, he developed overt liver failure. It was appropriate that he was screened for viral hepatitis. That confirmed hepatitis C infection. His subsequent management seemed entirely appropriate. He was advised to abstain from alcohol and largely achieved that. He underwent appropriate psychological assessment. He was placed on the liver transplant waiting list and underwent liver transplantation. All of that seemed quite appropriate. He had significant complications after transplantation. Those complications principally involved damage to the bile duct. This is a recognised complication after liver transplantation and attempts to investigate and manage the biliary problems seem entirely appropriate. It is possible, however, that inadequate drainage of the bile duct contributed to liver damage and the development of cirrhosis. It was quite reasonable to attribute the rapid development of cirrhosis (in the transplanted liver) to the hepatitis C infection. Certainly it would have made a significant contribution. It is recognized that re-transplantation for aggressive Hepatitis C infection can be associated with aggressive recurrence in the second transplanted liver. Therefore, it was quite reasonable and appropriate to plan for early antiviral therapy after re-transplantation. It was appropriate that antiviral therapy was deferred pending resolution of the early post-operative complications. Indeed, antiviral therapy was commenced six weeks after re-transplantation at a time when liver graft function was good and biopsy confirmed that little damage had been experienced.<sup>748</sup>

**7.390** In Dr Mutimer's opinion, antiviral therapy appeared to have been fully clinically justified: the physicians were concerned that aggressive Hepatitis C recurrence would lead to early graft damage and graft failure. The use of erythropoietin and growth factors

---

<sup>747</sup> Letter from the RIE LTU to GP dated 22 November 2004 [TAM.001.0740]; Dr Bathgate – Day 1, pages 70–72

<sup>748</sup> Dr Mutimer's Report [PEN.010.0310] at 0314

enabled the continued administration of antiviral therapy despite suppression of the bone marrow. Suppression of the bone marrow including the leucocytes may have contributed to infection. As the patient died, there was a complicated picture of marrow suppression, possible infection and serious liver damage. Dr Mutimer stressed that, while the drugs administered were 'very toxic', in his opinion there was nothing wrong in the decision to administer the drugs or in the way they were administered, under the circumstances.<sup>749</sup>

**7.391** Dr Mutimer concluded his assessment of the appropriateness of Mr Tamburrini's treatment and management:

Despite antiviral therapy, it appears that there was very aggressive hepatitis C recurrence with development of significant liver damage by June 2004. Under that circumstance, it was quite reasonable to persist with antiviral therapy. Unfortunately, antiviral therapy can have quite significant haematologic side effects. The patient would have been susceptible to infection. Susceptibility to infection would have been a consequence of liver dysfunction and bone marrow suppression. In summary, I believe that this man's treatment and management were appropriate.<sup>750</sup>

**7.392** That assessment of the position is accepted.

### Cause of death

**7.393** The cause of death as given in the death certificate was liver transplant graft failure and recurrent Hepatitis C.<sup>751</sup> Dr Bathgate agreed with the causes given.<sup>752</sup> In his opinion, the transplant graft failure was caused by Mr Tamburrini's Hepatitis C infection. Severity was a function of several factors, including the concentration of the virus and the age at which the patient's own liver had deteriorated. The younger a person was when infected, the worse the likely outcome following liver transplantation. It was likely that Mr Tamburrini was in that category. In Dr Bathgate's view, Mr Tamburrini was at 'the worst end of the spectrum' of Hepatitis C infection.<sup>753</sup>

**7.394** Dr Mutimer thought that the final cause of death was difficult to ascertain but that contributing factors were aggressive Hepatitis C recurrence and antiviral therapy. Available antiviral treatment was a challenge when given to patients who were as sick as Mr Tamburrini and who were receiving so many other medications. It was recognised that the toxicity of antiviral treatment was much greater in that setting than in giving the drugs to the average non-transplant patient with Hepatitis C. He thought that Mr Tamburrini did have significant side-effects from the antiviral drugs. Dr Mutimer used these drugs in treating his own post-transplant patients and they suffered many of the same problems. In his view, Mr Tamburrini died as a consequence of HCV infection and the antiviral therapy that was required in his case. Dr Mutimer's evidence that antiviral therapy, though appropriate, was a contributory factor to mortality is accepted.<sup>754</sup>

---

<sup>749</sup> Ibid [PEN.010.0310] at 0313–0314; Dr Mutimer – Day 1, page 115

<sup>750</sup> Ibid at 0314–0315; Dr Mutimer confirmed in evidence (Day 1, page 116) that the date of June 2003 given on page 0314 of his report should be June 2004.

<sup>751</sup> Death certificate [TAM.001.2946]

<sup>752</sup> Day 1, pages 71–72

<sup>753</sup> Dr Bathgate's report [TAM.001.2380] at 2387; Day 1, page 72

<sup>754</sup> Day 1, page 115; Dr Mutimer's report [PEN.010.0310] at 0313–0314



## Conclusions

**7.395** Factors contributing to the death of Mr Tamburrini were:

- (i) A clinically severe form of Hepatitis C.
- (ii) Acceleration of cirrhosis after the first transplant associated with problems at the site of the biliary anastomosis which probably led to hepatic artery impairment, local leak of bile and infection, and the portal vein thrombosis found at the operation for his second liver transplant.
- (iii) Profuse HCV replication after the second transplant probably associated with further biliary and vascular problems, which led to accelerating cirrhosis and fibrosing cholestatic hepatitis.
- (iv) Liver transplant graft failure.
- (v) The antiviral treatment given to prevent damage to the second graft.

**7.396** Infection with Hepatitis C:

- (vi) On the evidence available, with the exception of the possibility of hospital acquired infection, it was established to varying standards of probability that the known NHS procedures in Mr Tamburrini's case did not transmit Hepatitis C infection:
  - a. On a balance of probabilities, having regard to the whole evidence available, Mr Tamburrini was not transfused at the time of his appendicectomy operation in 1968.
  - b. It was proved beyond reasonable doubt that SPPS did not transmit Hepatitis C to Mr Tamburrini in 1984.
  - c. It was established beyond reasonable doubt that Mr Tamburrini did not acquire Hepatitis C from red cells transfused at the time of surgery in December 1998.
- (vii) No connection was demonstrated between any deficiency in plant or process at the PFC and the infection of Mr Tamburrini with Hepatitis C.
- (viii) On epidemiological grounds, it is likely that Mr Tamburrini acquired HCV infection in his late teens or early 20s.
- (ix) The cause of that infection is unknown.

**7.397** Progression of disease:

- (x) Mr Tamburrini had probably developed advanced liver disease by July 1998.
- (xi) His gynaecomastia was likely to have been a symptom of that disease.
- (xii) Consumption of alcohol was a contributory factor in the progression of Mr Tamburrini's liver disease to cirrhosis, and the need for the first transplant in October 2002.

**7.398** Mr Tamburrini's management as a patient:

- (xiii) Mr Tamburrini's care and management as a patient were appropriate.

**7.399** Alcohol as a cause of death:

- (xiv) Consumption of alcohol did not contribute to the failure of either the first or second liver transplant grafts received by Mr Tamburrini, or cause, or contribute to the cause of, his death. It is accepted that the cause of death was unrelated to alcohol consumption.

© Crown copyright 2015

An online version of the report is available at [www.penroseinquiry.org.uk](http://www.penroseinquiry.org.uk)

**ISBN: 978-0-85759-022-0 (Volume 1 of 5)**

**This Inquiry Report comprises an Executive Summary (ISBN: 978-0-85759-023-7), five volumes and a DVD**

Published on behalf of The Penrose Inquiry by APS Group Scotland, 21 Tennant Street, Edinburgh EH6 5NA  
DPPAS43828 (03/15)

THE  
PENROSE  
INQUIRY

# Final Report

**Volume 2:  
Knowledge of HIV/AIDS and Hepatitis C**

THE  
PENROSE  
INQUIRY

# Final Report

**Volume 2:  
Knowledge of HIV/AIDS and Hepatitis C**

Laid before the Scottish Parliament by the Scottish Ministers  
under section 26 of the Inquiries Act 2005.

March 2015  
SG/2015/15

© Crown Copyright 2015



This publication is licensed under the terms of the Open Government Licence v3.0 except where otherwise stated. To view this licence, visit [nationalarchives.gov.uk/doc/open-government-licence/version/3](https://nationalarchives.gov.uk/doc/open-government-licence/version/3) or write to the Information Policy Team, The National Archives, Kew, London TW9 4DU, or email: [psi@nationalarchives.gsi.gov.uk](mailto:psi@nationalarchives.gsi.gov.uk).

Where we have identified any third party copyright information you will need to obtain permission from the copyright holders concerned.

This publication is available at [www.penroseinquiry.org.uk](http://www.penroseinquiry.org.uk).

ISBN: 978-0-85759-022-0  
(Volume 2 of 5)

Published on behalf of The Penrose Inquiry by APS Group Scotland, 21 Tennant Street, Edinburgh EH6 5NA  
DPPAS43828 (03/15)

# CONTENTS

<b>Volume 2: Knowledge of HIV/AIDS and Hepatitis C</b>		Page
8	Knowledge of HIV/AIDS Now	399
9	Knowledge of the Geographical Spread and Prevalence of HIV/AIDS 1	415
10	Knowledge of the Geographical Spread and Prevalence of HIV/AIDS 2	449
11	HIV/AIDS Aetiology	491
12	HIV/AIDS: Response and Clinical Practice	535
13	Knowledge of Viral Hepatitis Now	589
14	Knowledge of Viral Hepatitis 1	627
15	Knowledge of Viral Hepatitis 2 – 1975 to 1985	649
16	Knowledge of Viral Hepatitis 3 – 1986 Onwards	691

## CHAPTER 8

### KNOWLEDGE OF HIV/AIDS NOW

#### Introduction

**8.1** As in the case of the Hepatitis C virus (HCV), discussed in Chapter 13, *Knowledge of Viral Hepatitis Now*, an understanding of the current knowledge of HIV infection and the progression to AIDS is necessary for a proper appreciation of the accounts provided by patients and their relatives of experiences of HIV infection, narrated in Chapter 5. The forms of drug therapy associated with the treatment of HIV infection, with particular reference to the side-effects of treatment, are also discussed.

**8.2** This chapter provides an account of what is known now, in 2014, about HIV infection and the AIDS complex of diseases, in particular in relation to the two affected groups identified in Chapter 2, *Patients at Risk*: bleeding disorder patients receiving therapy and patients infected by blood transfusion in the course of medical or surgical procedures.

**8.3** Unlike HCV infection, the AIDS epidemic, so far as it affected those groups, struck NHS patients over a relatively short period of time and the response of scientists and clinicians alike was rapid and concentrated. This chapter is correspondingly short.

#### HIV and AIDS: an overview

##### *Cellular immunodeficiency*

**8.4** The Acquired Immune Deficiency Syndrome (AIDS) was first reported in July 1981 as a new acquired cellular immunodeficiency, exclusively in homosexual men.<sup>1</sup> At that time, it was already known that disorders or disturbances of the immune system might arise from a variety of causes. Primary immune deficiency, with which the patient was born, or which developed without a known external cause, was an area of established clinical expertise in one or two centres in the UK.<sup>2</sup> Secondary immune deficiency was known to arise from certain drugs, cancers or viral infections. Cytomegalovirus and Hepatitis B virus (HBV) infection were both examples of viral infections already known to influence the immune system and, initially, there was speculation that one or the other of these, or possibly a new, more virulent strain of one or other of them, might be the causative agent of AIDS as many of the individuals affected were positive on testing for both of these viruses.<sup>3</sup> It was also suggested that recreational drugs used by the male homosexual population might be the cause, with amyl nitrate briefly proposed as a candidate.<sup>4</sup>

**8.5** In the course of 1982 a syndrome very similar to that reported in homosexual men was identified, again in the USA, first in intravenous drug users (IVDUs) and then in a few individuals with haemophilia. It was therefore suggested that blood-borne transmission was a possibility.<sup>5</sup>

---

<sup>1</sup> 'Kaposi's Sarcoma and *Pneumocystis* Pneumonia Among Homosexual Men – New York City and California', *MMWR*, 4 July 1981 [LIT.001.0766]

<sup>2</sup> Professor Lever – Day 26, pages 73–74

<sup>3</sup> Professor Lever's Report [PEN.015.0517] at 0519

<sup>4</sup> Report of the UK Haemophilia Directors' Hepatitis Working Party on AIDS [DHF.001.7178] at 7180. Professor Lever's Report [PEN.015.0517] at 0520. (See also Professor Ludlam – Day 18, page 109; Professor Ludlam's statement [PEN.015.0445] at 0447).

<sup>5</sup> Professor Lever's Report [PEN.015.0517] at 0520

**8.6** While other views have persisted and still persist, there is now a very strong general consensus that AIDS is a condition caused by a blood-borne virus, the Human Immunodeficiency Virus (HIV). Developments towards that consensus are discussed in Chapter 11, *HIV/AIDS Aetiology*. For present purposes, it is sufficient to note some key events and the short period of time over which they developed.

**8.7** The AIDS virus was first isolated in 1983 by researchers in France from a patient with enlarged lymph glands and was called 'lymphadenopathy-associated virus' (LAV).<sup>6</sup> It was not, however, generally accepted that this virus was the cause of AIDS until researchers in the USA reported, in 1984, on the isolation of what proved to be the same virus from a number of patients with AIDS.<sup>7</sup> The first US isolates were named 'Human T-cell Lymphotropic Virus Type III' (HTLV-III) because of an assumed association with two other viruses, previously identified by the same research group, that specifically attacked T lymphocytes – immunologically active white blood cells.<sup>8</sup> In 1986 the virus was renamed Human Immunodeficiency Virus (HIV) by the International Committee on Taxonomy of Viruses.<sup>9</sup> It is now widely agreed that HIV-1 is the principal agent of transmission of AIDS. In this discussion, where it is necessary to distinguish the disease from other immune deficiency conditions, the term HIV/AIDS will be used.

**8.8** HIV/AIDS emerged as the most serious issue for people with haemophilia and for those involved in treating them, or preparing products for their use, in the period 1981–85. By 1985, the virus, HIV, had been identified and steps could be taken to prevent its transmission by blood and blood products. Tragically, many patients were already infected and deaths from AIDS mounted among haemophilia patients during the late 1980s and beyond. From 1981–89, while non-A, non-B Hepatitis/Hepatitis C remained a problem both in relation to blood products and transfusion of whole blood and blood components, HIV/AIDS dominated the medical, scientific and political scene.

### *AIDS: the progressive deterioration of the body's immune system*

**8.9** AIDS is a condition which arises from the progressive deterioration of the body's immune system, leaving the patient prone to opportunistic infections and malignant diseases. The clinical manifestations of infection (the 'AIDS complex' of diseases) are very variable and widespread throughout the body but all ultimately stem from an impaired immune response. This can be the immune response to infections or a failure of the body's 'immune surveillance' of possible cancer cells. Since HIV can establish itself inside the body's lymphocytes for a period of time without damaging or destroying the lymphocytes, an individual can be 'HIV-positive', and infectious to others, while having no overt illness for a period of months or years.

**8.10** Many of the infections associated with HIV/AIDS are either rare or more severe than in patients who do not have HIV infection or AIDS. For example, tuberculosis bacilli (TB) probably appear randomly in the environment and many people may be exposed to

<sup>6</sup> Barré-Sinoussi et al, 'Isolation of a T-lymphotropic Retrovirus from a Patient at Risk of Acquired Immune Deficiency Syndrome (AIDS)', *Science*, 1983; 220:868–871 [LIT.001.0058]

<sup>7</sup> Gallo et al, 'Frequent Detection and Isolation of Cytopathic Retroviruses (HTLV-III) from Patients with AIDS and at Risk for AIDS', *Science*, 1984; 224:500–503 [LIT.001.3769]

<sup>8</sup> They were the third type of virus found by researchers that specifically attacked the T cells of humans, hence the designation HTLV-III.

<sup>9</sup> The Varmus Committee was convened by Dr Harold Varmus, Chair of the Retrovirus Study Group within the Vertebrate Virus Sub-committee of the International Committee on Taxonomy of Viruses. See: <http://socialarchive.iath.virginia.edu/xtf/view?docId=varmus-harold-cr.xml>. There are, in fact, known to be at least two main types of HIV viruses. HIV-1 is responsible for the worldwide pandemic of AIDS while HIV-2 is mainly confined to West Africa. (See Chapter 11 *AIDS Aetiology*, paragraph 11.10 for further brief discussion of HIV-1 and HIV-2).



them in small quantities from time to time. Normally, the immune system can deal with these few TB organisms and exposure does not lead to the development of tuberculosis, whether or not the individual has been vaccinated against the disease. In HIV patients, by contrast, exposure may lead to tuberculosis more readily and in a relatively severe form. The same situation arises with many other unusual pathogens, as well as various, usually extremely rare, forms of cancer – for example the vascular cancer Kaposi's sarcoma. As noted in Chapter 13, *Knowledge of Viral Hepatitis Now*, paragraph 13.118, it is also now known that, in individuals co-infected with HIV and HCV, the development of severe chronic liver disease from HCV occurs more frequently and more rapidly than if the patient is infected with HCV alone.

**8.11** Initially, diseases of the AIDS complex proved to be rapidly fatal in many cases once overt disease was diagnosed. There was fear of a pandemic and, in response, a huge investment in research into the condition and means of identifying infection and providing treatment.

### **Biology of HIV**

**8.12** HIV/AIDS plays a central role in this Report and some understanding of the biology of HIV is important in providing an insight into the clinical and epidemiological manifestations of the disease, which form one of the core themes of the Report. An account of the biology of HIV, much of it drawn from the written and oral evidence of Professor Andrew Lever, Professor of Infectious Diseases at Addenbrooke's Hospital, Cambridge, is therefore given here.

**8.13** In some viruses, genetic material has a DNA form: Hepatitis B is an example. DNA is a very stable molecule. It is easy to replicate very accurately. HIV is a ribonucleic acid (RNA) virus. RNA is a much less stable molecule than DNA. RNA viruses mutate (change their genetic information) much more readily.

**8.14** The processes by which viruses generally use the protein-synthesising machinery of a living cell to replicate (make new copies of themselves) are described in the context of HCV infection in Chapter 13, *Knowledge of Viral Hepatitis Now*.<sup>10</sup> Like other viruses, HIV can replicate only if it can attach to a cell and thereafter enter it. In order to do this the virus requires that the surface of the cell provides a suitable receptor to which the virus particle can 'dock'.

**8.15** Some individuals cannot be infected with HIV because they are effectively protected by a mutation of their lymphocyte cells which prevents HIV particles from docking. Other individuals are infected but appear to be able to maintain a normal immune response which suppresses the virus for many years. In each group variant genetic patterns may result in disease progress being inhibited.<sup>11</sup>

**8.16** Apart from such exceptional cases, the process typically begins when an HIV particle attaches itself to the surface of a cell bearing the immune recognition complex CD4 on its surface, and specifically the protein CCR5. This can be one of the protective cells in the blood that ingests infectious agents, known as macrophages, or it can be a particular type of lymphocyte, the T-helper lymphocyte, a type of white blood cell that plays a crucial role

---

<sup>10</sup> Chapter 13, *Knowledge of Viral Hepatitis Now*, paragraphs 13.22–13.23

<sup>11</sup> Professor Lever – Day 26, pages 20–21

in maintaining the function of the human immune system. After attaching to the cell, the virus converts its RNA into DNA by the use of an enzyme called reverse transcriptase. The viral DNA is transported to the cell's nucleus, where it is spliced into the human DNA.

### *The reproductive process*

**8.17** Once integrated into a cell, the virus may begin replicating immediately or may lie dormant within the infected cell for months, or even years. Cells do not malfunction on incorporation of the viral DNA: the viral DNA is very small, comprising about 10,000 individual nucleotides (the building blocks of DNA), a tiny number compared to the 30 million or so nucleotides that make up human DNA. Additionally, it almost always inserts in places which do not disrupt the normal functioning of the cellular DNA.<sup>12</sup> When the cell which the virus has entered becomes activated, it treats the HIV genes within it in much the same way as its own (human) genes. The virus DNA within the cell contains the data from which information is transcribed into RNA. When the RNA produced is trafficked out of the nucleus into the cytoplasm of the cell (the gel within the cell membrane) it carries a code which instructs internal cell sub-structures to assemble the amino acids required to produce the viral proteins of HIV. Where the transcription process is effective, the protein is a new RNA copy of the HIV virus.

**8.18** The result is that new HIV viral particles are formed and released, thereby starting the replication process all over again. HIV can replicate rapidly, with several billion new viruses made every day in a person infected with HIV. However, HIV is a very imperfect virus in terms of effective replication: it has a notoriously high 'particle to infectivity ratio'. Of the total number of virus particles to which an individual is exposed, only a very small minority are actually functional, capable of transmitting infection, and are harmful. An individual exposed to a million virus particles might only be exposed to 10 which could do any harm.<sup>13</sup>

**8.19** During replication HIV mutates and evolves. Reverse transcriptase often makes random mistakes in the transcription process from RNA to DNA. As a result, new types or strains of HIV (with slightly different DNA) develop in a person infected with the virus. Because of changes in the DNA the proteins of the virus will be different, making it harder for the individual's already compromised immune system to 'recognise' or to respond to and deal with the virus. By the time the immune system has developed antibodies to one strain, mutation has resulted in new strains, increasing the risk that the virus will evade the immune defences. On the other hand, many of the mutations that occur are lethal for the virus because they interfere with some important protein that the virus needs for survival.

**8.20** A further factor affecting the variability of HIV is that it can undergo a process of 'recombination'. Each virus particle carries two copies of its genes. During replication, the virus can take pieces from either copy to make up the final product. If a cell is infected with two different viruses, then sometimes the virus picks pieces from a copy of each. Then, when the recombination occurs, the resulting virus is a mixture of the genetic sequence of the two apparent viruses it came from and this also makes the virus extremely variable. This process probably has a more important impact on variability than the fact that the enzyme, reverse transcriptase, makes mistakes.<sup>14</sup>

---

<sup>12</sup> Ibid pages 12–13

<sup>13</sup> Ibid pages 62–65

<sup>14</sup> Ibid page 64

**8.21** In a person infected with HIV, the virus destroys billions of CD4 T-helper lymphocyte cells every day, eventually overwhelming the immune system's capacity to regenerate or fight infection.

**8.22** Professor Lever commented:

HIV has proven to be so far impossible to develop a vaccine against because it is hugely variable. Every time it replicates it mutates at least once and probably five or ten times.

Without being too technical, the virus ... is made up of RNA and there are about 10,000 individual nucleotides making up the RNA of the virus. We know that the enzyme that copies it makes a mistake about once every 10,000 bases, so it makes a mistake every time it replicates. Within an infected individual, even when they are well, they are producing around 10 to the 11th, which is 100 billion viruses every day, and they are mutating at the rate I mentioned, which means that in one infected person, every single one of the 10,000 nucleotides is being mutated at least once every day. So the variability of that virus is enormous.

....

This means that if you are infected once with HIV, you have a family of viruses which develop from that infection and certainly by sexual transmission, you probably only get infected by a small number, a handful of viruses. But you get a family that derive from that handful and rapidly become very large. If you are repeatedly exposed, you are going to be exposed to different variants, and because those variants can recombine, then the resulting diversity of viruses that you can get is going to be even larger.

So multiple exposures is a bad thing for increasing the diversity of the virus that your immune system has to encounter, and again this would be something which would not have been obviously predictable from other infections that we knew about [at the time of discovery of HIV].<sup>15</sup>

**8.23** At the start of the AIDS epidemic, it was known that in the case of some chronic infections, such as Hepatitis B, while some people were relatively poor at clearing the virus and a proportion of these became chronic carriers, the majority of healthy individuals did appear to be able to clear it and develop immunity from re-infection. This experience informed the common notion at the time that exposure to infectious agents usually gave a level of protection against further infection by the same virus. A perception had arisen that, having been exposed to a virus, it was not going to harm the individual to be exposed to the same virus again because either the immune system would have developed sufficient immunity to protect the individual completely or because it would help to suppress the second exposure. However, almost without precedent at the time, it was to emerge that, in the case of HIV, prior exposure to the virus gave no protection against infection on further exposure.<sup>16</sup> As noted in Chapter 13, *Knowledge of Viral Hepatitis Now*, a similar discovery was later to emerge in the case of HCV.<sup>17</sup> Immunity from further infection does

<sup>15</sup> Ibid pages 63–65

<sup>16</sup> Ibid pages 60–61

<sup>17</sup> Chapter 13, *Knowledge of Viral Hepatitis Now*, paragraph 13.38

not follow from clearance of infection with the virus. The more exposures there are, the more likely it is that the individual will be exposed to one which infects them successfully.

### **Transmission**

**8.24** HIV is found in the blood, semen and rectal and vaginal fluid of those infected with the virus. It cannot survive for very long outside the body. The main modes of transmission are: sexual intercourse; intravenous drug use (through the use of shared, contaminated needles); receiving a transfusion of infected blood or blood products; and perinatally (ie from infected mothers to their children at or around the time of birth, from infected maternal blood or through breast feeding). The route of infection affects the range of AIDS-related diseases to which the individual is exposed. Patients treated with blood products and others infected with HIV by blood-borne routes rarely presented with Kaposi's sarcoma, in contrast to gay men for whom this was an early and ongoing feature of AIDS.<sup>18</sup>

### **Testing**

**8.25** When an individual becomes infected with HIV, antibodies to the virus are produced but, unlike the case in most other infections, these antibodies have little or no ability to neutralise the virus. The antibodies are, however, used in laboratory tests as a marker for the presence of HIV. Tests which detect antibodies to HIV include enzyme-linked immunosorbent assay (ELISA) and Western blot tests. Detectable antibodies are usually produced within two to six weeks of infection, at which point a patient has 'seroconverted', although sometimes the period may be up to three months. Accordingly, the ELISA and Western blot laboratory tests may not detect infection in an individual who has been infected very recently with HIV (ie up to three months after infection, often referred to as the 'window period' between infection and seroconversion).

**8.26** A different type of test, polymerase chain reaction (PCR) tests, detect the presence of HIV itself, through detection of its genetic material, rather than the presence of antibodies to the virus. PCR testing may be undertaken to detect the presence of the virus before as well as after seroconversion and therefore may be used in the 'window' between the time the individual acquires HIV infection, and becomes infectious to others, and seroconversion. PCR tests are more time-consuming and expensive than ELISA and Western blot tests for antibodies, however, and are therefore unsuitable for use in screening large numbers of blood samples.

### **Symptoms and pathology**

**8.27** In the first few weeks after infection with HIV, most people experience few, if any, symptoms. A month or two after infection, individuals may experience a flu-like illness, including fever, headache, tiredness and enlarged lymph nodes in the neck and groin area. The symptoms usually disappear within a week to a month after their onset and are often mistaken for another viral infection such as glandular fever or influenza (flu). During this period, people are highly infectious. There then follows a period during which the body's immune system fights the virus and the disease remains clinically inapparent (clinically latent).

---

<sup>18</sup> Professor Lever – Day 26, pages 75–76. See Chapter 11, *AIDS Aetiology*, paragraph 11.43 for a possible explanation for the discrepancy between homosexual men and others with AIDS in relation to presenting with Kaposi's sarcoma.

**8.28** Over time, however, the immune system deteriorates to the point at which it is unable to fight off other infections. The rate of progression to symptomatic diseases associated with AIDS varies greatly from person to person and may take many years. Hence, when the disease was first reported, it was initially estimated that only a minority of patients infected with HIV would go on to develop AIDS.<sup>19</sup> It is now known, however, that, if untreated, the vast majority of patients who contract HIV are likely to go on to develop secondary 'opportunistic' infections or tumours (diseases of the 'AIDS complex') which, in the absence of treatment, are likely eventually to result in death.

### *Symptomatic disease*

**8.29** Understanding of the association between HIV infection and the symptomatic diseases identified in patients with AIDS has changed over time.<sup>20</sup> When HIV was recognised as causing AIDS, it was initially perceived that the effect was limited to the immune system and would therefore predispose the individual to infections and, as it turned out, infection-related cancers. Professor Lever explained the gradual progression of understanding from this point:

[A] number of additional medical conditions became apparent in patients with HIV infection, such as degeneration of the kidney, and HIV-associated brain disease, and it was realised that, by mechanisms which weren't always completely obvious, HIV was affecting other systems directly, and that when treatment for HIV came along and the virus load was successfully suppressed, these conditions would reverse.

That was a phase in which everything was potentially put down as attributable to HIV infection. More recently, I think, there is a more balanced feeling that a lot of what goes wrong in someone who is HIV-infected is HIV-related but that HIV-infected people get diabetes and get other conditions, so there is, I think, a more ready acceptance, particularly in the fact that the HIV population is now becoming an ageing population, that the diseases which affect ageing populations without HIV are affecting people with HIV.<sup>21</sup>

**8.30** Many cancers fall into that category. Professor Lever explained:

There is a general background increase in the incidence of almost all malignancies in patients with HIV because your immune system not only fights infections but has a role in eliminating malignant cells. So that if you have an advanced immunodeficiency and you lack the sort of lymphocytes which can recognise that a cell has become cancerous, then that cell has a greater chance of developing into a full-blown malignant tumour.<sup>22</sup>

**8.31** The 'age-related' risk in a long-term infected individual described by Professor Lever is still less than the risk of more directly virus-induced cancers, such as Kaposi's sarcoma or non-Hodgkins lymphoma, of which an increasing range has been identified.

<sup>19</sup> In 1986, for example, a UK Government advisory body stated that only 1 in 10 people with HIV were likely to go on to develop AIDS: DHSS Advisory Committee on Dangerous Pathogens, 'Revised guidelines on LAV/HTLV III – the causative agents of AIDS and related conditions' [DHF.002.1456] at 1463

<sup>20</sup> Professor Lever – Day 26, page 7

<sup>21</sup> Ibid pages 7–8

<sup>22</sup> Ibid page 146

**8.32** Within the group of infections that are HIV-related, the secondary infections that may develop include a variety of fungal, viral and bacterial infections of the mucous membranes and skin. However, a type of pneumonia caused by a fungal infection called *Pneumocystis jirovecii* (previously known as *Pneumocystis carinii* pneumonia and often still abbreviated to PCP) remains the most common life-threatening secondary infection in patients who progress from chronic HIV infection to AIDS.<sup>23</sup>

**8.33** AIDS may also affect the nervous system, not only with the development of secondary infections such as cerebral toxoplasmosis (leading to the formation of abscesses in the brain) but also directly as in progressive multi-focal leucoencephalopathy (progressive damage or inflammation of the white matter of the brain) and peripheral neuropathy (damage to the nerves of the peripheral nervous system). Patients may also suffer psychiatric disorders including depression.

**8.34** Without treatment, patients eventually develop end-stage disease, both secondary to having little immunity and from direct viral effect such as in progressive multi-focal leucoencephalopathy, and death becomes inevitable from one or more of the above or related conditions.

## Treatment

### *Drug therapy for HIV/AIDS*

**8.35** Throughout the 1980s, when the HIV/AIDS epidemic began, after the initial relatively asymptomatic period lasting for a variable number of years, people infected with the virus were unlikely to live longer than two or three more years from the time of the development of one or more of the AIDS-defining illnesses. Until 1986 there was no specific treatment for HIV. Patients were treated with the appropriate therapy for any HIV-related condition they presented with, such as PCP, thrush or a viral infection.<sup>24</sup> In general, without treatment, 50% of patients with AIDS survived one year but only 20% survived three years from the identification of an AIDS-defining illness.<sup>25</sup> Today, the prognosis for most of those infected with HIV is much better as a result of the availability of effective antiretroviral medication. There are six main groups of antiretroviral drugs presently available to treat the disease, each of which attacks the virus in different ways. The classes are: nucleoside reverse transcriptase inhibitors (NRTI); non-nucleoside reverse transcriptase inhibitors (NNRTI); protease inhibitors; fusion inhibitors; entry inhibitors and integrase inhibitors.<sup>26</sup> The development of drug therapy was initially slow but then accelerated, as indicated below.

**8.36** Zidovudine (also known as AZT), an NRTI drug, became available for patients on a named patient basis<sup>27</sup> from late 1986 and was licensed for use in 1987.<sup>28</sup> A study in 1986 suggested that patients with HIV had a longer rate of survival when prescribed Zidovudine and also that the rate of opportunistic infections was reduced.<sup>29</sup> Despite early

<sup>23</sup> Ibid pages 29–30

<sup>24</sup> Professor Leen – Day 33, pages 15–16; Professor Leen’s Report [PEN.012.1044]

<sup>25</sup> Professor Leen’s Report [PEN.012.1044] at 1056

<sup>26</sup> Ibid [PEN.012.1044] at 1055

<sup>27</sup> ‘Named patient basis’ meant that, if a clinician considered that a patient would benefit from a medication prior to it being licensed, the clinician could request access to the medication for this patient from the manufacturers. Professor Leen, Day 33, pages 20–21

<sup>28</sup> Professor Leen – Day 33, page 20. Zidovudine became available for the treatment of AIDS in Scotland on 1 April 1987: SHHD letter to General Managers [SNB.004.8395].

<sup>29</sup> Professor Leen – Day 33, page 20; Professor Leen’s Report [PEN.012.1044] at 1049. Though not specifically identified by Professor Leen, it is likely that the study was: Fischl et al ‘The efficacy of azidothymidine (AZT) in the treatment of patients with AIDS and AIDS-related complex. A double-blind, placebo-controlled trial’ *New England Journal of Medicine* 1987; 317(4):185–91

indications that it did inhibit the virus, clinical trials of the drug showed that it did not improve the long-term outlook for patients.<sup>30</sup> Between 1987 and 1993, two additional HIV drugs, Didanosine (DDI) and Zalcitabine (DDC) were undergoing clinical trials. These drugs were the same type of drug as Zidovudine (NRTIs). DDI and DDC were introduced in 1991 and 1992 respectively and clinicians started prescribing them to patients with HIV, again on a named patient basis. These, like AZT, tended to be used as single agent therapy (monotherapy).

**8.37** As stated above, HIV replicates very rapidly. As a result of this, Zidovudine (like the other NRTIs) on its own was not strong enough to completely prevent replication of the HIV virus and the treatment led to only a short-lived improvement in the patient's clinical condition.<sup>31</sup> For patients with late-stage AIDS, Zidovudine was associated with an improved prognosis of no more than two years.<sup>32</sup> In the event, monotherapy against the virus with any of these early drugs proved to be of little use. HIV quickly becomes resistant to a single drug and the drug stops being effective.<sup>33</sup> The early use of Zidovudine and disappointment at its lack of real efficacy is reflected in the accounts of patients and their families in Chapter 5.

**8.38** The practice of using drugs singly reflected the history of drug therapy in other diseases. There was a tendency to use each new drug one at a time; partly because they became available in that way, and partly because of a lack of perception at that time of the fact that some infectious agents can mutate to get around therapeutic agents. It has now become more generally accepted that more than one drug, working by more than one antiviral mechanism, should be used to provide additional hurdles for some viruses or other pathogens to overcome.<sup>34</sup> In the treatment of HIV infection, two or more antiretroviral drugs came to be prescribed at the same time, thereby reducing the rate at which resistance developed and making treatment more effective in the long term.<sup>35</sup> However, the view of Professor Clifford Leen<sup>36</sup> of these drugs was that, at the early stage of development of drug therapy, their effectiveness was '[p]retty poor actually. It was still a death sentence .... Even using two drugs ... still did not hold the virus at bay.'<sup>37</sup> As noted below at paragraph 8.43, from 1998 a combination of three different drugs came to be prescribed with the result of a great improvement in outcomes.

**8.39** Persistence with drug therapy is essential to its success. It is likely that 90–95% of prescribed treatment needs to be taken for the best chance of treatment to work.<sup>38</sup> Failing to adhere to this level of treatment results in the even more rapid emergence of drug resistance and the subsequent failure of HIV treatment and immunological deterioration.<sup>39</sup> When Zidovudine was first prescribed in 1987 it was recommended that the doses be taken every four hours. This meant that patients had to wake themselves up during the night to take a dose. This then had a knock-on effect on a patient's tiredness and must have

<sup>30</sup> Professor Lever – Day 26, page 143

<sup>31</sup> Professor Leen – Day 33, page 22; Professor Leen's Report [PEN.012.1044] at 1047

<sup>32</sup> Professor Leen's Report [PEN.012.1044] at 1056 and Professor Leen – Day 33, pages 21–22

<sup>33</sup> Professor Leen – Day 33, pages 24–25; Professor Lever – Day 26, page 144

<sup>34</sup> Professor Lever – Day 26, page 144

<sup>35</sup> Preliminary Report, para 2.63; Professor Leen's Report [PEN.012.1044] at 1047

<sup>36</sup> Professor Leen is Consultant Physician in Infectious Diseases and Honorary Professor at the University of Edinburgh.

<sup>37</sup> Professor Leen – Day 33, page 39

<sup>38</sup> Studies have shown that 90% to 95% of protease inhibitor therapy doses must be taken for optimal viral suppression. Professor Leen – Day 33, pages 53–54; Professor Leen's Report [PEN.012.1044] at 1049; Paterson et al, 'Adherence to protease inhibitor therapy and outcomes in patients with HIV infection' *Annals of Internal Medicine*. 2000; 133:21–30 [LIT.001.5525]

<sup>39</sup> Professor Leen's Report [PEN.012.1044] at 1063; Professor Leen – Day 33, pages 52–53

caused some anxiety about remembering to take the tablets on time.<sup>40</sup> The importance of full adherence to antiviral medication is now understood and patients receive adherence support from a number of professionals including clinical nurse specialists, dieticians, their doctor and sometimes a counsellor. In 2001, the British HIV Association issued guidelines about the adherence support a patient should receive. In contrast, those patients treated in the 1980s and early 1990s received very little support in adhering to their medication. There was, and is, difficulty in persuading children and teenagers in particular to take such medication.<sup>41</sup> Difficulties in keeping to quite complex treatment regimes for drugs are reflected in the evidence and statements of patients and relatives described in Chapter 5.

**8.40** These early treatments were also associated with many side-effects, affecting many organs, which added to patients' difficulties in adhering to therapy as well as having direct impact. These side-effects included headache, nausea, vomiting, diarrhoea, flatulence, skin rashes, liver inflammation, kidney stones, dysphoria (disquiet or restlessness), weird and sometimes frightening dreams, depressive symptoms, tiredness, poor sleep and body shape changes.<sup>42</sup> Didanosine can cause pancreatitis which can be debilitating. People with this condition have to fast and, if a patient is thin anyway from AIDS, they will become thinner due to this condition. Didanosine can also cause peripheral neuropathy (inflammation of the nerves) which can cause painful feet and hands.<sup>43</sup> Body shape changes are particularly distressing for patients. There are two different types of body shape changes that are seen. One change is fat loss, usually around the face and on the arms and legs. Patients' veins become prominent as a result of the fat loss in the arms, legs and buttocks. The facial fat loss is the most distressing as the patient appears to have lost weight and looks like an unwell AIDS patient with late-stage HIV disease. The other body shape change is fat accumulation around the belly and back of the neck. This can co-exist with the fat loss and the combination makes the patient's appearance quite abnormal.<sup>44</sup> Body shape changes can be stigmatising and distressing, often resulting in low self-esteem, isolation and depression, as reflected in the account of his illness described by the patient given the pseudonym 'Mark'.<sup>45</sup> These side-effects led many patients to stop their HIV medication.

### *Development in drug therapy from the early 1990s*

**8.41** Against this background, there was a clear incentive for research and the development of drug therapy and there was rapid development from the early 1990s.<sup>46</sup> Some of the principal developments are indicated in Table 8.1 below. Approval for use in the UK generally followed within a few months of approval by the Food and Drug Administration (FDA) in the USA.<sup>47</sup> The use of these drugs will be illustrated in Chapter 5, in the narrative of the experiences of individual patients.

<sup>40</sup> Ibid [PEN.012.1044] at 1062; Professor Leen – Day 33, pages 55–56

<sup>41</sup> Professor Leen – Day 33, pages 62–63

<sup>42</sup> Professor Leen's Report [PEN.012.1044] at 1058

<sup>43</sup> Professor Leen – Day 33, pages 26–27

<sup>44</sup> Professor Leen's Report [PEN.012.1044] at 1058-1059

<sup>45</sup> Chapter 5, *An Examination of the Effects of Infection with HIV on the Patients and Their Families, Including Treatment*, paragraph 5.294

<sup>46</sup> Professor Lever's Report [PEN.015.0517] at 0525

<sup>47</sup> Professor Leen – Day 33, page 40; Professor Lever's Report [PEN.015.0517] at 0525 from which the data are derived. Delavirdine has not been approved in the UK but is used on a named patient basis.



**Table 8.1: Development of Antiretroviral Drugs**

Year approved by US FDA	Name	Type
1987	Zidovudine	NRTI
1991	Didanosine	NRTI
1992	Zalcitabine	NRTI
1994	Stravudine	NRTI
1995	Saquinavir	Protease Inhibitor
	Lamivudine	NRTI
1996	Ritonavir	Protease Inhibitor
	Indinavir	Protease Inhibitor
	Nevirapine	NNRTI
1997	Delavirdine	NNRTI
	Nelfinavir	Protease Inhibitor
1998	Efavirenz	NNRTI
	Abacavir	NRTI
1999	Amprenavir	Protease Inhibitor
2000	Lopinavir + Ritonavir	Protease Inhibitor
2001	Tenofovir	NRTI
2003	Atazanavir	Protease Inhibitor
	Fosamprenavir	Protease Inhibitor
	Entricitabine	NRTI
	Enfuvirtide (T-20)	Fusion Inhibitor
2005	Tipranavir	Protease Inhibitor
2006	Darunavir	Protease Inhibitor
2007	Maraviroc	Entry Inhibitor
	Raltegravir	Integrase Inhibitor
2008	Etravirine	NNRTI

**8.42** The arrival of protease inhibitors from 1995–96 heralded a dramatic improvement in the treatment of HIV. The early drugs in the protease inhibitor class were associated with a tendency towards increased bleeding times, however, so that haemophilia patients often needed more clotting replacement therapy at the same time as their HIV treatment.

**8.43** The first British consensus statement on the treatment of HIV was published in *The Lancet* in April 1997 and revised in 1998. British guidance has been frequently updated since then.<sup>48</sup> In 1998 the British HIV treatment guidelines recommended the use of triple therapy in patients with HIV. This was the start of the Highly Active Anti-Retroviral

<sup>48</sup> Professor Leen's Report [PEN.012.1044] at 1045

Treatment (HAART) era.<sup>49</sup> Clinicians could now put together a 'cocktail' of three drugs to administer at the same time, severely restraining the ability of the virus to develop resistance.<sup>50</sup>

**8.44** Since then, further drugs have been developed, as noted in the table above. The wide range allows for additional flexibility in the selection of components of the dual and triple therapy prescribed. In addition, the way in which these newer drugs are formulated has allowed much simpler and better tolerated dosing regimes. The use of triple HIV combination therapy led to sustained suppression of HIV replication. This then allowed the immune system to reconstitute and, as a consequence, marked and sustained clinical improvement was expected. When full suppression of HIV replication is achieved, HIV drug resistance does not emerge.<sup>51</sup>

### *Treatment regimes and side-effects of therapy*

**8.45** For young people (and most of the haemophilia patients infected were boys), the treatment regimes could prove to be difficult. Apart from side-effects, the medication could be difficult to take and the routine was sometimes resisted. Some teenagers found the tablets difficult to swallow and found the taste unpleasant. They also had real problems in adhering to the regime and some stopped taking their medication regularly. Some tablets had to be taken with food but some patients could not manage to eat regularly. Patients were routinely advised that they should not discontinue drug therapy since, if they did, HIV symptoms would come back with a vengeance. In some cases, however, late teenaged boys stopped taking their medication. Some may have got to a point where they just decided to let nature take its course. Specific examples are described in Chapter 5. For immediate purposes, it is sufficient to note that these accounts give substance to the general observations of clinicians and others that adherence to drug therapy was, and remains, demanding.

**8.46** For many patients, young and not so young, side-effects of antiretroviral treatment were serious. Some patients developed thrombocytopenia (a reduction in the number of red blood cells) and treatment had to be suspended for a period. Examples are set out in Chapter 5.

**8.47** Since treatment regimes were demanding and side-effects could be debilitating, it became important for clinicians to know whether to persist with a particular course of treatment. In 1997, British HIV Association Guidelines for antiretroviral treatment of HIV patients recommended that 'viral load measurement' should be made widely available to physicians. Viral load is a test that measures the amount of HIV virus in the bloodstream. Originally available only in research laboratories, it first became generally available in clinics in August 1996.<sup>52</sup> Clinicians learned that if a patient's viral load was detectable while on the treatment, HIV drug resistance was likely to emerge. This test also allowed clinicians to explore responses to HIV drugs. They learned that if the patient was taking his/her medication appropriately and the HIV viral load was undetectable then, over time, their immune system would recover. Furthermore, if their viral load was undetectable, they were at much lower risk of developing new opportunistic infections.<sup>53</sup>

---

<sup>49</sup> Professor Leen – Day 33, page 46; Professor Leen's Report [PEN.012.1044] at 1051

<sup>50</sup> Professor Lever – Day 26, page 145

<sup>51</sup> Professor Leen's Report [PEN.012.1044] at 1047

<sup>52</sup> Professor Leen's Report [PEN.012.1044] at 1052

<sup>53</sup> Ibid [PEN.012.1044] at 1052; Professor Leen – Day 33, pages 47–48

**8.48** An 'HIV resistance test' started to become available from 2000 onwards. This test allows clinicians to predict which HIV drugs are likely to be most effective in their individual patients. Clinicians had quickly become aware that patients differed in terms of development of side-effects from medication, how the drugs were metabolised, how the drugs were absorbed or cleared from their body and how the drug–drug interactions affected drug levels in the individual patient's body. Adverse drug–drug interaction could lead to a failure of the drug combination to suppress HIV infections.<sup>54</sup>

**8.49** As noted in paragraph 8.9 above, the clinical manifestations of HIV infection are widespread: they can affect most organs of the body. In the early years of the epidemic, HIV-associated dementia and other significant neurological complications were serious and disabling consequences of HIV infection. It was therefore important to ensure that HIV drugs could get into the brain in sufficient volume so as to suppress HIV replication there. Similarly, the sexual transmission of HIV is thought to occur more readily if the amount of HIV is high in genital and rectal fluid. Therefore, choosing drugs which may achieve sufficient dilution in these fluids may reduce the risk of sexual transmission.<sup>55</sup>

### *The current situation*

**8.50** Currently, with almost 30 individual drugs from six drug classes to choose from, clinicians have considerable flexibility. Patients with HIV are well managed with these drugs and only a small number have run out of treatment options. At the present time, the majority of patients who are complying with treatment have fully suppressed HIV infection and those who are not controlling their virus almost always have adherence issues.

**8.51** Notwithstanding the increased range of drugs available, drug therapy does not cure people of HIV or AIDS: the virus is not completely eliminated from the body and starts replicating again if drug therapy is stopped.<sup>56</sup> Rather, the drugs suppress the virus, either by stopping the virus from replicating or by preventing it from binding to or entering human immune cells, or both.

**8.52** People undergoing treatment can still transmit the virus, however, and must continuously take antiretroviral drugs in order to maintain their health and to keep their infectivity suppressed. As noted in paragraph 8.22, there is currently no vaccine to prevent HIV infection nor is there a cure for HIV/AIDS. Professor Lever described the problem of developing a useable vaccine. Successful vaccines tend to replicate the natural immune response to infection: the vaccine triggers the same sort of immune response as does an individual who successfully clears the infection. He said:

The issue with HIV ... is that nobody who has been infected has ever developed an immune response which has cleared the virus from them completely. That's unique. And nobody has ever developed an immune response which completely protects them against a second infection. Both of those things relate, in part at least, to the fact that it is a very, very variable virus. It is not only that, because Hepatitis C is probably even more variable, but some people clear that.

It's also the fact that HIV integrates ... so it is difficult to find and eradicate.<sup>57</sup>

<sup>54</sup> Professor Leen – Day 33, page 48; Professor Leen's Report [PEN.012.1044] at 1053

<sup>55</sup> Professor Leen's Report [PEN.012.1044] at 1053 and 1054; Professor Leen – Day 33, pages 48–49

<sup>56</sup> Professor Leen – Day 33, page 50; Professor Leen's Report [PEN.012.1044] at 1054

<sup>57</sup> Professor Lever – Day 26, pages 148–9

**8.53** Professor Lever commented that the outlook for a protective vaccine was not good. Recent research suggested that a vaccine might conceivably be developed but that it would not be a conventional vaccine and would require regular administration.<sup>58</sup> By the close of the Oral Hearings of the Inquiry there remained uncertainty whether the reported research had progressed.

**8.54** Research continues in the area of gene therapy.<sup>59</sup> The discovery that the delta 32 mutation of the CCR5 protein on lymphocyte cells prevents infection with HIV<sup>60</sup> has led to the targeting of that particular protein as one of the suggested strategies for gene, as opposed to conventional drug-based, therapy.<sup>61</sup>

**8.55** Proof of concept of effective gene therapy has been provided in the case of Timothy Ray Brown (also known as 'the Berlin patient') who suffered from both leukaemia and HIV infection. It appears to be generally accepted that this recipient of a bone marrow transplant from a donor with both the same HLA type<sup>62</sup> and the CCR5 delta 32 mutation had the mutation passed on. Indications point to a functional cure.<sup>63</sup> However, the procedure – 'allogeneic haematopoietic stem cell transplantation' – is contra-indicated where the recipient does not have leukaemia (and, indeed, Brown experienced 'graft-versus-host' disease as a result of the transplantation). This isolated and quite exceptional case apart, effective gene therapy has not been developed to date.

### Morbidity and mortality

**8.56** Data for the impact of HIV/AIDS on NHS patients in Scotland receiving therapy for blood coagulation disorders and transfusions in the course of medical or surgical treatment are discussed in Chapter 3, *Statistics*. Mortality rates (reflecting the proportions of patients developing fatal conditions) were high and, among survivors, serious morbidity (reflecting severity of the illness) was very common. Very few indeed among those infected in the 1980s have had little serious ill health.

**8.57** In the UK as a whole, haemophilia patients were particularly severely affected. The United Kingdom Haemophilia Centre Doctors Organisation (UKHCDO) reported that in 2004, of a total population of 7250 male patients registered on the national database in 1985, 1246 (17.2%) were infected with HIV-1.<sup>64</sup> Among severely affected haemophilia patients, 65.8% of those with HIV had died between 1 January 1985 and 1 January 2000. The equivalent mortality for the mildly and moderately affected haemophilia patients with HIV was 59.9%.<sup>65</sup> Among the non-HIV-infected severely affected haemophilia patients alive in 1985, 18.3% had died by 1 January 2000 and 13.0% of the non-HIV-infected mildly and moderately affected patients had died by the same date. The difference in mortality between the infected and non-infected groups of patients appears to be largely attributable, directly or indirectly, to HIV/AIDS infection.

<sup>58</sup> Ibid pages 149–152

<sup>59</sup> That is, supplementing or directly modifying a patient's DNA as a pharmaceutical agent to treat disease.

<sup>60</sup> Professor Lever – Day 26, page 21

<sup>61</sup> Ibid page 20

<sup>62</sup> HLA types are discussed briefly in Chapter 13, *Knowledge of Viral Hepatitis Now*, paragraph 13.17

<sup>63</sup> Hutter et al, 'Long-Term Control of HIV by CCR5 delta 32/Delta 32 Stem-Cell Transplantation' *New England Journal of Medicine* 2009; 360(7):724–725 [LIT.001.5048]; Allers et al, 'Evidence for the cure of HIV infection by CCR5Δ32/Δ32 stem cell transplantation' *Blood* 2011; 117(10): 2791–2799 [LIT.001.4527]. (For an alternative view casting some doubt on the complete effectiveness of such a therapy, particularly in relation to 'T-cell reservoirs', see Nath et al, 'Eradication of HIV from the brain: reasons for pause' *AIDS* 2011; 25(5): 577–80 [LIT.001.4844])

<sup>64</sup> 'The impact of HIV on mortality rates in the complete UK haemophilia population'. *AIDS* 2004, 18:525–533; [LIT.001.1405]

<sup>65</sup> See Chapter 2, *Patients at Risk*, paragraphs 2.26–2.28 for a more technical discussion of the terms 'severely', 'moderately' and 'mildly' affected haemophilia patients.

**8.58** Among those infected, survival was strongly related to age at infection with HIV and the differences in mortality between HIV-infected and non-infected subjects were largely accounted for by HIV-related conditions. Without HIV infection, annual liver disease mortality (largely from HCV) remained below 0.2% throughout 1985–99. With co-infection (HIV plus HCV), liver disease mortality was 0.2% during 1985–90, and 0.8% during 1991–99. From 1997, after the introduction of effective treatment for HIV there were substantial reductions in annual mortality related to AIDS, though mortality from liver disease remained high. The risks in Scotland, as shown in Chapter 3, *Statistics*, were lower but still very significant.

### **Conclusion**

**8.59** It has to be emphasised again that the information about AIDS, its natural history and treatment, as discussed in this chapter, reflects the state of knowledge current at the close of the oral evidence heard by the Inquiry. Almost none of this would or could have been known before 1991. In particular, the understanding of clinicians and others at the time that patients were (often unbeknown) contracting HIV infection and suffering from AIDS-related conditions was very poor indeed in the first few years of the epidemic.

**8.60** Recognition of the new syndrome internationally and in Scotland; the emerging realisation that there was transmission by a blood-borne agent, posing risk to those undergoing blood transfusion or treatment with blood products; the identification of the virus; and the responses of scientists and clinicians to the threat posed to patients – the key issues identified in the Preliminary Report – remain for discussion in other parts of this Report (Chapters 9–12).

**8.61** However, the narrative of the current understanding of the natural history of HIV/AIDS takes on colour from the experiences of individuals exposed to the reality of the diseases. The impact on patients and their families is illustrated in the following chapters setting out the evidence provided to the Inquiry of their particular histories. The experiences described range between the extremes of patients who died of AIDS, either before effective drug therapy was available or notwithstanding therapy, and patients for whom treatment has been effective in arresting the progression of the disease. Some of the many witnesses who provided statements were invited to give oral evidence. The evidence of these witnesses, supplemented by the written accounts of others and, where possible and appropriate, by medical records, provides a telling picture of the wide impact of infection on the individuals affected and their families.



## CHAPTER 9

### KNOWLEDGE OF THE GEOGRAPHICAL SPREAD AND PREVALENCE OF HIV/AIDS 1

#### Introduction

**9.1** The impact of HIV/AIDS on National Health Service (NHS) patients receiving blood transfusions in the course of medical or surgical treatment or receiving blood, blood component or blood product therapy for coagulation disorders is part only of a much wider picture. The speed of response and the concentrated effort devoted first of all to understanding and then to dealing with AIDS, especially in the USA, reflected the apprehension that it was an epidemic threatening broad sectors of society.

**9.2** In a paper presented to a group of experts at the World Health Organization (WHO) on 14–16 April 1986, Dr John Ziegler, Director of AIDS Research at the American Veterans Administration Medical Center wrote:

The epidemic forces policy decisions in political, social, journalistic, and ethical spheres. The cause, prevention, and cure of AIDS has induced collaboration between clinicians, virologists, immunologists, molecular biologists, epidemiologists and sociologists. Thus this epidemic has, in five short years, mobilized a response from virtually every arena of human society.<sup>1</sup>

**9.3** In this chapter, the evolving picture will be examined from a narrow perspective, tracing developing knowledge of the incidence of diseases associated with HIV infection from the end of 1980, when cases of AIDS were first observed in the USA, to 1984, when testing for antibodies for HIV began to become available in the USA. This is with a view to providing context for the exploration of medical and scientific research into AIDS and the response to it, principally in the UK and the USA.

**9.4** However, it is appropriate also to take note, briefly, of the extent of the epidemic, particularly as it affected populations less able to respond to the challenges it presented, and still presents, than the cohorts with whom the Inquiry is particularly concerned.

#### A worldwide problem

**9.5** In 2006, the 25th anniversary of the emergence of AIDS in western countries, there were close to 40 million people around the world living with HIV infection and over 20 million people had died of HIV-related diseases. By 2009, the joint UNAIDS<sup>2</sup> and WHO publication *Global Facts and Figures* showed that since the beginning of the epidemic almost 60 million people had been infected with HIV and 25 million people had died.<sup>3</sup> By 2011, 30 years since HIV/AIDS was first discovered, 30 million people had died. The number of people living with the disease worldwide was estimated at 34.2 million, with a prevalence of 0.8% overall.<sup>4</sup> UNAIDS data showed wide variations in prevalence across regions, from 0.1% in East Asia to 5% in Sub-Saharan Africa. Western and central Europe were estimated to have 820,000 cases of infection, a prevalence of 0.2%. North America had 1.5 million cases, a prevalence of 0.5%.

<sup>1</sup> Ziegler, 'The Natural History of AIDS' in: Petricciani et al (eds), 1987, *The Safety of Blood and Blood Products in relation to AIDS*, The World Health Organisation: Tiptree, p.21 [LIT.001.5828]

<sup>2</sup> The Joint United Nations Programme on HIV/AIDS.

<sup>3</sup> UNAIDS/WHO *Global Facts and Figures* [LIT.001.5614]

<sup>4</sup> UNAIDS *Report on the Global AIDS Epidemic 2012* [LIT.001.5616]

**9.6** The epidemic in the UK, with particular reference to Scotland, is the context in which the Terms of Reference have to be addressed. Though a small part of the wider picture, it is not representative of it. The prevalence of the disease in the UK, and the response to it, has been materially different from the global picture. The emerging position in the USA usefully defines the wider context in which experience in the UK has to be seen. Along with other western countries, the USA and the UK have benefited from the investment of intellectual and financial resources not widely available in most areas with a high prevalence of infection.

**9.7** In the UK, AIDS surveillance began in 1982.<sup>5</sup> By the end of 2011, 120,756 people had been diagnosed with HIV, of whom 27,361 had developed AIDS and 20,335 had died.<sup>6</sup> The estimated prevalence of HIV in 2010 in the population of all ages was 0.15%: 0.18% in males and 0.09% in females. The Health Protection Agency (HPA) report for 2011 commented that the UK had a prevalence similar to other western European countries such as Ireland (0.2%), the Netherlands (0.2%) and Germany (0.1%), and lower than eastern and southern European countries such as Latvia (0.7%), Portugal (0.6%) and Spain (0.4%). Local social and environmental factors are reflected in those variations and, in geographical terms, a narrow field of study is required. However, it is not possible totally to isolate cases of infection in the UK from the wider world picture. A significant proportion of individuals diagnosed with HIV infection in the UK was originally infected abroad.<sup>7</sup>

**9.8** In the case of transfusion and blood disorder patients, experience was more clearly dependent on local factors: by definition NHS patients were treated in the UK. The risk of transmission of infection was related to the prevalence of infection in the donor population. Across western countries the picture varied. The prevalence of transfusion-transmitted AIDS in Australia was said in the mid-1980s to be 10 times greater than in the UK.<sup>8</sup> It was reported at that time that the prevalence of seropositivity<sup>9</sup> in the USA was 74% in people with Haemophilia A and 35% in people with Haemophilia B. In the USA, 15% of 'haemophilia wives' were seropositive, with the seroconversion rate still increasing.<sup>10</sup>

**9.9** By 1986, the Council of Europe had produced comparable data. For the UK, the data indicated positive findings in 896 (44%) of 2025 Haemophilia A patients tested and in 20 (6%) of 324 Haemophilia B patients tested. In severely affected Haemophilia A patients the proportion was 59%.<sup>11</sup> Comparative analysis of the widely divergent numerical data contained in these reports, even as between the USA and the UK, would not be helpful in tracing the history of the epidemic in Scotland.

**9.10** The numerical data on the prevalence of disease in Scotland are dealt with in Chapter 3, *Statistics*. The combined UK prevalence values are higher than comparable values for Scotland alone. The most up-to-date data available to the Inquiry indicate that for the UK, excluding Scotland, 1310 patients with bleeding disorders had tested positive for HIV by April 2012. Scotland has roughly 10% of the UK haemophilia population but

<sup>5</sup> HPA *HIV in the United Kingdom: 2011 Report* [LIT.001.4443] at 4448. See Paragraphs 9.36–9.38 below.

<sup>6</sup> House of Commons Library Standard Note SN/SG/2210, 25 October 2012 [LIT.001.5119] at 5121.

<sup>7</sup> *Ibid* [LIT.001.5119] at 5125, paragraph 3.2. The data relate to heterosexual exposure only.

<sup>8</sup> Report on XIXth Congress of ISBT and XX1st Congress of ISH, Sydney, Australia, May 1986 [SNF.001.3839] at 3841. For further details see Preliminary Report, para 8.179.

<sup>9</sup> That is, showing a significant level of HIV antibodies indicating infection with the virus.

<sup>10</sup> Report on XIXth Congress of ISBT and XX1st Congress of ISH, Sydney, Australia, May 1985 [SNF.001.3839] at 3846

<sup>11</sup> Extract from the Report of the Committee of Experts on Blood Transfusion and Immunohaematology – Berne 28-31 May 1986 [SNB.004.8127] at 8136. Preliminary Report, para 8.179



only 73 patients treated in Scotland tested positive, around 5% of the bleeding disorder patients infected with HIV.<sup>12</sup> Knowledge of these numbers would not emerge in the course of the period under discussion, 1981–1984.

## Origins of the disease

**9.11** AIDS was first reported in the USA in 1981. Data from the UK Haemophilia Centre Doctors' Organisation (UKHCDO) initially suggested that the first cases of HIV in haemophilia patients at Scottish centres were recorded retrospectively as having occurred in Aberdeen and Glasgow in 1982.<sup>13</sup> Earlier cases were identified and reported by Simon Garfield in his social history of HIV/AIDS, *The End of Innocence*.<sup>14</sup> The cases he noted appeared to demonstrate that AIDS was active in the USA and in the UK before 1981. Without verification, however, the reports gave no real insight into when AIDS first affected humans in western countries. It is clear, however, that none of these apparently isolated early cases was recognised or influenced medical and scientific thought when the first deaths in the modern epidemic came to light and were reported in 1981.

**9.12** Developments in the science of genetics and increasingly sophisticated technology applied to historic blood samples stored in the USA and the UK have now demonstrated that HIV infection had entered the population in the USA by 1978 and in the UK by 1979. Blood specimens retained from early studies of other conditions, and in particular Hepatitis B, were available for re-examination when appropriate technology was developed. Re-examination of specimens from a study of Hepatitis B infection in a cohort of homosexual men in San Francisco carried out between 1978 and 1984 disclosed HIV antibodies in samples dating from 1978.<sup>15</sup> Retrospective testing of samples from haemophilia patients in western Pennsylvania<sup>16</sup> and New York<sup>17</sup> also identified the first two cases of HIV seroconversion in that group of patients in samples from 1978. Similar testing in the UK has shown transmission of HIV to a haemophilia patient around June 1979.<sup>18</sup> Research into the origins of HIV continues.<sup>19</sup>

**9.13** The same technology has probably excluded one earlier date.<sup>20</sup> The death of a patient at the Manchester Royal Infirmary on 31 August 1959, aged 25, with a rare combination of symptoms, was reported in 1960 as a mystery.<sup>21</sup> In 1983 it was speculated that it might have been a case of AIDS.<sup>22</sup> In 1990, further study led to the conclusion that the patient

<sup>12</sup> Statistics – National Haemophilia Database – Bleeding disorder statistics for The Penrose Inquiry [PEN.019.0927] at 0961

<sup>13</sup> There is one unexplained retrospective test result from 1969 which appears to be unrelated to the events with which the Inquiry is concerned.

<sup>14</sup> The data are inconsistent and have not been verified. The 'Chronology of State Medicine etc' states that AIDS was first described in the USA in 1978. It also states that the first case of AIDS was reported in 1981: page 1, Introduction. Table 3, page 35, lists 'Cases of AIDS reported to the Regional Office of WHO as of 30 October 1983', and includes eight cases of AIDS in Europe before 1979, two cases in 1979, 10 cases in 1980 and 17 cases (including the first two cases in the UK) in 1981.

<sup>15</sup> Jaffe et al, 'The Acquired Immunodeficiency Syndrome in a Cohort of Homosexual Men: A Six-Year Follow-Up Study', *Annals of Internal Medicine*, 1985; 103:210–214 [LIT.001.1060]; Preliminary Report, para 2.48.

<sup>16</sup> Ragni, 'AIDS and treatment of hemophilia patients', *Plasma Therapy and Transfusion Technology*, 1988; 9:173–191 [LIT.001.0598]

<sup>17</sup> Evatt et al, 'Antibodies to human t-cell leukaemia virus-associated membrane antigens in haemophiliacs: evidence for infection before 1980', *The Lancet*, 1983; 698 [LIT.001.1196]

<sup>18</sup> Darby et al, 'Mortality Before and After HIV Infection in the Complete UK Population of Haemophiliacs', *Nature*, 1995; 377:79–82 [LIT.001.1301]. See also Machin et al, 'Seroconversion for HTLV-III since 1980 in British haemophiliacs', *The Lancet*, 1985; 336 [LIT.001.1195] for discussion of early seroconversion in UK haemophilia patients.

<sup>19</sup> In 2007, TP Gilbert and others published a study combining a range of phylogenetic, molecular, historical and epidemiological techniques, which traced the dispersal of HIV from Central Africa via Haiti to the USA, Europe (including the UK) and elsewhere. See Gilbert et al, 'The emergence of HIV/AIDS in the Americas and beyond', *Proceedings of the National Academy of Sciences*, 20 November 2007; Vol.104, No.47. [LIT.001.4483]. It is not necessary for present purposes to discuss these developments.

<sup>20</sup> Mentioned in the Preliminary Report at paragraph 2.48 footnote 37

<sup>21</sup> Williams et al, 'Cytomegalic inclusion disease and Pneumocystis carinii infection in an adult', *The Lancet*, 29 October 1960; 951–955 [LIT.001.3977].

<sup>22</sup> Williams et al 'AIDS in 1959?' *The Lancet*, 1983; 322;1136 [LIT.001.5504]

had HIV infection.<sup>23</sup> In 1995, however, US researchers cast doubt on the previous findings and speculated that they might have been due to cross-contamination of samples.<sup>24</sup> Further studies followed.<sup>25</sup> The conclusion of the Manchester scientists involved – two of whom had contributed to the *Lancet* article in 1983 – was negative: they agreed that the 1959 patient did not carry HIV. For them the case had again become a mystery. The final contribution to date is from Professor Hamilton and Mr Hooper, Oxford, who in 1996 again expressed the belief that the patient did not have AIDS.<sup>26</sup> The debate so far suggests that the case is not an early example of HIV infection, notwithstanding that the patient had signs and symptoms of diseases of the AIDS complex at his death. It illustrates the role of technology in developing understanding of the epidemiology of the disease and in particular the late date at which a measure of confidence in diagnosis was achieved.

**9.14** It can be said with greater confidence that knowledge of the emerging epidemic was disseminated first in 1981, with a great deal of literature published in and after June of that year. From the first clinical descriptions of the disease, concern began to grow. As seen from the perspective of staff at the Regional Haemophilia Centre, Glasgow Royal Infirmary (GRI), commenting on the early reports:

It was soon apparent that these cases represented the first reports of a new epidemic, one which medicine had not seen before, and one which has had dramatic consequences scientifically, medically and socially.<sup>27</sup>

**9.15** Within the UK, scientific and medical literature initially dealt mainly with experience in the USA and the literature most widely available to British scientists and doctors was published first in the USA and only later in the UK.

**9.16** In order for the Inquiry properly to understand the response to the epidemic as it affected those who received transfusions of blood and blood components and blood product therapy, it was necessary to trace the origins of the AIDS epidemic, and the publicity that it attracted, at least to the USA, and to place in context the emerging understanding of its impact on haemophilia and other patients. Knowledge of the groups at risk of infection quickly became widespread, while knowledge of the prevalence and natural history of AIDS-associated disease developed more slowly. The Preliminary Report set out much of the information recovered in chronological form and will not be repeated in detail.<sup>28</sup>

### **Early reports of infection in the United States of America: 1981–1982**

**9.17** Early reports in the USA presented a picture of rapidly increasing numbers of patients with perplexing signs and symptoms with high mortality and unknown cause. In *The Tragic History of AIDS in the Hemophilia Population 1982 – 1984*, Dr Bruce Evatt of the US Centers for Disease Control (CDC) wrote:

First apparent in the homosexual population in the USA in the last quarter of 1980, the disease possessed unusual properties that initially obscured

<sup>23</sup> Corbitt et al 'HIV infection in Manchester, 1959' *The Lancet* 1990; 336:51 [LIT.001.5505]

<sup>24</sup> Zhu and Ho, 'Was HIV Present in 1959?', *Nature*, 6 April 1995; 374:503 [LIT.001.5494]

<sup>25</sup> Corbitt and Bailey, 'AIDS in Manchester, 1959?' *The Lancet*, 1995, vol 345 1058 [LIT.001.4537]

<sup>26</sup> Hooper and Hamilton, '1959 Manchester Case of Syndrome Resembling AIDS', *The Lancet*, 1996; 347:189; *The Lancet*, 1996; 348:1363. [LIT.001.5507]

<sup>27</sup> Gracie et al, 'Acquired Immune Deficiency Syndrome: an Overview', *Scottish Medical Journal*, January 1985; Vol 30 [LIT.001.0829]; Preliminary Report, paragraph 8.140

<sup>28</sup> See Preliminary Report, paragraphs 8.4, 8.6-8.8, 8.10-8.13

it as a distinct infectious disease. Previously healthy victims had no specific symptoms but presented with either secondary infections or tumors associated with immune deficiency (i.e. *Pneumocystis carinii* pneumonia (PCP) or Kaposi's sarcoma)<sup>29</sup>. A long incubation time made it difficult to identify person-to-person spread. Laboratory methods needed to culture and identify the etiologic agent were lacking.<sup>30</sup>

### ***First reports: the association with sexual behaviour***

**9.18** The first US reports of AIDS created, for a time, an impression that the disease was a purely US phenomenon associated with sexual behaviour. The published history begins in 1981 when physicians in New York, Los Angeles and San Francisco reported previously healthy homosexual men with *Pneumocystis carinii* pneumonia (PCP). The Los Angeles cases were described in the *Morbidity and Mortality Weekly Report (MMWR)* for 5 June 1981.<sup>31</sup> That report is generally regarded as the first published recognition by a public health body of what was to become characterised in the 1980s as 'the AIDS epidemic'. Additional reports soon followed. Apart from the unusual nature of their illnesses, there was no common characteristic other than homosexual activity and in that respect the patients did not have a history of association with each other. As at 1981, the existence of what came to be known as AIDS was inferred from the constellation of very unusual tumours, such as Kaposi's sarcoma (KS), and other clinical signs and symptoms, including PCP, in patients who died fairly quickly after initial diagnosis.

**9.19** Kaposi's sarcoma in young homosexual men was brought to the notice of doctors in the UK in *The Lancet* of 19 September 1981 but it was reported as a US phenomenon.<sup>32</sup>

### ***A widening constituency: intravenous drug use***

**9.20** The range of people known to be at risk was extended when, on 10 December 1981, the *New England Journal of Medicine (NEJM)* reported PCP in seven intravenous drug users (IVDUs), only two of whom were homosexuals. It was suggested that IVDUs and homosexuals were at high risk for PCP but there was still an emphasis on male homosexuals as people particularly at risk.<sup>33</sup> At the time, the term 'Gay Compromise Syndrome' was coined for the 'newly recognised syndrome of opportunistic infections and/or KS in homosexual males'.<sup>34</sup>

**9.21** In terms of published intelligence, at the end of 1981 and continuing into 1982, reports in the *NEJM*, *The Lancet* and the *British Medical Journal (BMJ)* added to general knowledge that IVDUs were affected in addition to members of the male homosexual population.

<sup>29</sup> These diseases were known, but extremely rare and, outwith specific ethnic groups in the case of KS, usually only presented in immuno-compromised patients.

<sup>30</sup> Evatt, 'The tragic history of AIDS in the haemophilia population, 1982–84', *Journal of Thrombosis and Haemostasis*, 2006; 4/11:2295–2301 [PEN.016.1183] at 1185

<sup>31</sup> '*Pneumocystis* Pneumonia – Los Angeles', *Morbidity and Mortality Weekly Report*, 1981; 30: 250–2 [LIT.001.1026]. *MMWR* is published by the Centers for Disease Control and Prevention (CDC), a US government public health agency with its headquarters in Atlanta, Georgia. It is a publication which the Protein Fractionation Centre (PFC) in Edinburgh received; Preliminary Report, para 8.4. See also Dr Foster's evidence regarding subscription to the *MMWR*: Day 23, pages 6–7 and Dr Foster's Witness Statement [PEN.015.0101] at 0107

<sup>32</sup> Hymes et al, 'Kaposi's sarcoma in homosexual men – a report of eight cases', *The Lancet*, 1981; 318:598–600 [LIT.001.0768]; Preliminary Report, para 8.7

<sup>33</sup> Masur et al, 'An outbreak of community-acquired *Pneumocystis Carinii* pneumonia', *New England Journal of Medicine*, 1981; 305/24:1431–38 [LIT.001.0771]; Preliminary Report, para 8.8

<sup>34</sup> Brennan and Durack, 'Gay Compromise Syndrome', *The Lancet*, 1981:1338–1339 [LIT.001.0400]; Preliminary Report, para 8.8

### *A widening constituency: haemophilia patients*

**9.22** The earliest case of AIDS-related disease in a haemophilia patient, so far as is known to the Inquiry, was identified in October 1981. The case was not fully reported until February 1983 but the circumstances of a patient discussed by Professor Oscar Ratnoff of Cleveland, Ohio (one of the authors of the later report on the case) and Professor Charles Forbes, Director of the Regional Haemophilia Centre, Glasgow, at the end of 1981 were probably related to it.<sup>35</sup> Professor Ratnoff told Professor Forbes of haemophilia patients who were clearly ill with various opportunistic infections and tumours and of a patient of his who had a ‘funny immune problem in his blood’ and was obviously ill and eventually died.<sup>36</sup> He asked whether Professor Forbes had seen such cases (he had not, at the time). Thus at least one haemophilia clinician in Scotland had personal notice of the emerging problem, beyond the sexual context, from this time.

### *The first year*

**9.23** By June 1982, a year after the first report of AIDS, KS and opportunistic infections had been reported in 355 relevant cases in the USA.<sup>37</sup> The majority of the individuals infected (79%) were homosexual or bisexual men; 11% were heterosexual men; 4% were heterosexual women; and 6% were men of unknown sexual orientation. It was suggested that all of the cases were part of the same epidemic.

**9.24** In light of the oral evidence heard by the Inquiry, it would be wrong to imagine that the published reports communicated a clear account of the developing picture to the medical community generally. Across the professions experience was patchy: the patients were widely spread and few doctors would have had direct experience. Professor Andrew Lever, Professor of Infectious Diseases at Addenbrooke’s Hospital, Cambridge, distinguished those with direct experience, doctors looking after patients suffering from these infections and specialists such as epidemiologists with a specific interest, from clinicians generally. Individual physicians managing patients with AIDS and epidemiologists would have been trying to work out what was going on.<sup>38</sup> Professor Lever explained:

Mostly the people who saw the initial cases were seeing a lot of [them] ... or at least several, and it would have been an unusual phenomenon for anyone to have seen one of these and certainly very unusual for them to see two or three.<sup>39</sup>

**9.25** Experience was concentrated in a relatively small cohort of specialist practitioners. For most clinicians the published reports and comments would have described events of which they had no personal knowledge or experience. In the UK medical community, the impression was created, and persisted, that the disease was a US phenomenon.

### *The second year*

**9.26** Experience of AIDS was beginning to spread internationally, however. The cases of four Danish men who had developed KS or opportunistic infections were reported in July

<sup>35</sup> Professor Forbes – Day 17, pages 92–93; Professor Forbes’ Witness Statement [PEN.015.0254] at 0256. Professor Forbes’ recollection that this occurred in 1980 cannot be correct. The telephone conversation referred to must have been a year later.

<sup>36</sup> Professor Forbes – Day 17, pages 92–94

<sup>37</sup> ‘Epidemiologic Notes and Reports Update on Kaposi’s Sarcoma and Opportunistic Infections in Previously Healthy Persons-United States’, *Morbidity and Mortality Weekly Report*, 1982; 31/22:294, 300–301 [LIT.001.0566]

<sup>38</sup> Day 26, pages 37–38

<sup>39</sup> *Ibid* page 38

1982.<sup>40</sup> It was apparent that the syndrome was occurring in homosexual men in Europe as well as in the USA.

**9.27** In the same month, opportunistic infections among Haitian immigrants to the USA were reported.<sup>41</sup> At that time, the explanation for a concentration of cases in Haiti had not been documented and there was not a very clear idea about how the disease had arrived there.<sup>42</sup>

**9.28** On 16 July 1982, the *MMWR* reported three cases of PCP in haemophilia patients.<sup>43</sup> All were heterosexual males with no history of intravenous drug use. Two had died and one was critically ill. All had lymphopenia (abnormally low levels of lymphocytes, white blood cells important to the immune system) and the two who had been specifically tested had *in vitro* laboratory evidence of cellular immune deficiency. There had been a further material change in context moving away from an exclusive focus on the sexual behaviour of male homosexuals.

**9.29** By July 1982, the US Centers for Disease Control (CDC), and Dr Evatt in particular, were convinced by evidence of infection in haemophilia patients that AIDS was a blood-borne disease, though there was no direct proof. It is important to bear in mind, however, that there was no consensus at this stage that AIDS was even an infectious disease.

**9.30** In September 1982, it was reported again that intravenous drug use was a risk factor.<sup>44</sup> An update in the 'Current Trends' section of the *MMWR* stated that the incidence of AIDS had roughly doubled every half year since the second half of 1979. Among the 14 cases involving males under the age of 60 who were not homosexuals, IVDUs or Haitians, two (14%) had Haemophilia A. It was suspected that the eventual mortality rate of AIDS might be far greater than the overall 41% case-mortality rate noted for the total of 593 cases identified at that point. The editorial note suggested that Haemophilia A was perhaps a risk factor.

**9.31** There were further significant reports in the *MMWR* of 10 December 1982 of four more cases in the USA of heterosexual Haemophilia A patients with opportunistic infections, one suspected case in a 7 year old haemophilia patient and a report of a possible transfusion-related case of AIDS in a 20 month old child from San Francisco.<sup>45</sup> The editorial comment on the group of four patients stated:

These additional cases provide important perspectives on AIDS in U.S. hemophiliacs. Two of the patients described here are 10 years of age or less, and children with hemophilia must now be considered at risk for the disease. In addition, the number of cases continues to increase, and the illness may pose a significant risk for patients with hemophilia.<sup>46</sup>

<sup>40</sup> Gerstoft et al, 'Severe acquired immunodeficiency in European homosexual men', *British Medical Journal*, 3 July 1982; 285:17–19 [LIT.001.0229]; Preliminary Report, para 8.13.

<sup>41</sup> 'Opportunistic Infections and Kaposi's Sarcoma among Haitians in the United States' *Morbidity and Mortality Weekly Report*, 09 July 1982; 31/26:353-4, 360-1 [LIT.001.0562]

<sup>42</sup> Professor Lever – Day 26, page 39. Evidence that Haiti was the proximate source of the epidemic in the USA (and thereafter worldwide) has been produced: Gilbert et al, 'The emergence of HIV/AIDS in the Americas and beyond', *Proceedings of the National Academy of Sciences*, 20 November 2007; Vol.104, No.47. [LIT.001.4483].

<sup>43</sup> 'Pneumocystis carinii Pneumonia among Persons with Hemophilia A', *Morbidity and Mortality Weekly Report*, 16 July 1982; 31/27 [SGH.008.5097]; Preliminary Report, para 8.12

<sup>44</sup> 'Update on Acquired Immune Deficiency Syndrome (AIDS) – United States', *Morbidity and Mortality Weekly Report*, 1982; 31:353–361 [LIT.001.0540]

<sup>45</sup> 'Update on Acquired Immune Deficiency Syndrome (AIDS) among Patients with Hemophilia A', *Morbidity and Mortality Weekly Report*, 1982; 31:652–654 [SGH.008.5105].

<sup>46</sup> *Ibid* [SGH.008.5105] at 5108

**9.32** The infant from San Francisco had received multiple transfusions which had included platelets from a male found to have subsequently developed AIDS. The editorial note stated that several features of the infant's illness resembled those seen among adults with AIDS but warned that, since there was no definitive laboratory test for AIDS, any interpretation of the child's illness would need to be made with caution. It proceeded:

If the platelet transfusion contained an etiologic agent for AIDS, one must assume that the agent can be present in the blood of a donor before onset of symptomatic illness and that the incubation period for such illness can be relatively long ....

....

This report and continuing reports of AIDS among persons with hemophilia A raise serious questions about the possible transmission of AIDS through blood and blood products....<sup>47</sup>

**9.33** Discussion of the case of the infant at the Inquiry's Oral Hearings disclosed varying opinions of its significance: see Chapter 11, *AIDS Aetiology*, paragraphs 11.24–11.27.

**9.34** The initial reports of infections in homosexual men had left medical scientists in the USA unclear how the clustering of KS, PCP and other opportunistic infections were related. Over a short period of about 18 months, however, by autumn of 1982 thinking had moved on to the definition of a condition with specific signs and symptoms and identified groups at risk. People at risk in the USA included homosexual and bisexual men, IVUDs, heterosexual haemophilia patients, immigrants from Haiti and, more rarely, other heterosexual males and females without known risk factors.

### Response in the United Kingdom 1981–1982

**9.35** It should not be thought that the early US publications were immediately available in a practical sense, at or about the dates of their issue, to all clinicians and other doctors who would come to have an interest in the subject. The *MMWR* was a publication of particular interest to infectious diseases specialists. It was not likely to be widely read in ordinary course by many clinicians in the UK and, before AIDS became a matter of general interest, haemophilia clinicians and transfusion doctors (whether in the USA or in the UK) would not have been regular readers of the publication.<sup>48</sup> The early stages of the AIDS outbreak in the USA would have been known to some infectious diseases specialists from reading and soon from direct contact with patients or from discussion.<sup>49</sup> Haemophilia doctors also became aware of AIDS relatively quickly.

**9.36** The HPA 2011 Report, *HIV in the United Kingdom*, noted the first reports of AIDS in Los Angeles of 5 June 1981 and commented:

Ten days later, the first UK case of AIDS was reported in a young man with haemophilia followed by further reports of AIDS among homosexual men. These first reports prompted the creation of the UK's AIDS surveillance scheme in 1982.<sup>50</sup>

<sup>47</sup> 'Possible transfusion-associated acquired immune deficiency syndrome [AIDS] – California', *Morbidity and Mortality Weekly Report*, 1982; 31:652–654 [SGH.008.5105] at 5109–10

<sup>48</sup> Professor Ludlam – Day 18, page 95. See also: Dr Foster – Day 23, pages 6–7; Dr Foster's Witness Statement [PEN.015.0101] at 0107

<sup>49</sup> Professor Lever – Day 26, page 73

<sup>50</sup> HPA HIV in the United Kingdom: 2011 Report [LIT.001.4443] at 4448.

**9.37** The Inquiry's investigations have disclosed that the HPA Report, which was reviewed in January 2011 and again in November 2012, is inaccurate in this respect: there was no report of AIDS in a young haemophilia patient in the UK in June 1981. Public Health England, the successor to the HPA, has explained that the HPA confused the date of a sample from 1981, which was tested retrospectively when a haemophilia patient in Scotland was first diagnosed with clinical AIDS in 1994, with the date of first diagnosis.<sup>51</sup> The first reported case of clinical AIDS in the UK was the case of 'the Brompton patient'. *The Lancet* of 12 December 1981 published details of a 49 year old homosexual man (a frequent visitor to Florida), who had reported to Brompton Hospital. He was diagnosed with PCP and cytomegalovirus (CMV) but had no underlying immune deficiency.<sup>52</sup> Information was now circulating about AIDS in a UK patient, albeit one with US and homosexual associations.

**9.38** The Inquiry had the benefit of written and oral evidence from Dr Mark Winter, who became Consultant Haematologist at Kent and Canterbury Hospital in 1983. Dr Winter was a Senior Registrar at Guy's Hospital at the time of the Brompton Hospital case in 1981 and the topic was widely discussed among his colleagues.<sup>53</sup> Professor Lever was working with Dr David Webster at Northwick Park Hospital at the time. Although Professor Lever could not be certain, it appears highly likely that the patient from Brompton Hospital was transferred to Dr Webster's care and that he was one of the first two AIDS patients seen by Professor Lever in 1981–82. The second was a child recently arrived from the southern USA or the Caribbean.<sup>54</sup> The information given to Professor Forbes of Glasgow at the end of 1981 by Professor Ratnoff of what was probably the earliest case of AIDS-related disease in a (US) haemophilia patient known to a UK practitioner has already been mentioned in paragraph 9.22. A few doctors in the UK derived knowledge of the condition from direct contact with patients and from discussion with colleagues at the initial stages of the outbreak. As previously noted, surveillance of AIDS-related disease in the UK began in 1982.

**9.39** By the end of 1981, no cases had been seen in Scotland. Professor Forbes had received personal communication from Professor Ratnoff, and Professor Christopher Ludlam (Director of the Edinburgh Haemophilia Centre) was familiar with the literature.<sup>55</sup> It is not clear, however, how widely the emerging epidemic was known or studied at this point by Scottish haemophilia clinicians or other practitioners concerned with the use of blood, blood components or blood products. Early surveillance is more likely to have engaged physicians concerned with the diagnosis and treatment of AIDS-related diseases such as infectious diseases doctors, cardiologists, respiratory specialists and cancer doctors.

### *The Second International Symposium on Infections in the Immunocompromised Host*

**9.40** Information about the emerging epidemic was disseminated by a number of professional groups but not always shared on an interdisciplinary basis. In June 1982, the Second International Symposium on Infections in the Immunocompromised Host was held in Stirling. Professor Ian Hann, then at the Royal Free Hospital, London, but soon

<sup>51</sup> There were samples from Edinburgh (Chapter 3, *Statistics*, Table 3.16, case E22); the GRI (Chapter 3, *Statistics*, table 3.17, case G12) and Yorkhill (Chapter 3, *Statistics*, table 3.18, cases Y2, Y5 and Y14) taken in 1981 which subsequently proved positive for HIV antibodies on retrospective testing. None of these were known in 1981 or 1982 and they could not have prompted HIV/AIDS surveillance measures in 1982.

<sup>52</sup> Du Bois et al, 'Primary Pneumocystis Carinii and Cytomegalovirus infections', *The Lancet*, 12 December 1981; 1339 [LIT.001.0399]. So far as the Inquiry's investigations have disclosed, this was the first published reference to the syndrome in a British patient.

<sup>53</sup> Day 15, pages 110–111

<sup>54</sup> Professor Lever – Day 26, pages 73–74

<sup>55</sup> Day 18, page 91

to move to The Royal Hospital for Sick Children, Yorkhill, Glasgow (Yorkhill), attended.<sup>56</sup> One of his main interests at the time was infections in patients who had either immune deficiencies or, more commonly, leukaemia and cancers which made them very susceptible to infection. The symposium was to become the main regular meeting in the world of specialists dealing with such infections.<sup>57</sup> However at the time of the second meeting, it is unlikely that specialists in other fields were aware of its existence. Apart from Professor Hann, none of the haemophilia clinicians who gave evidence to the Inquiry attended the meeting or knew about it.<sup>58</sup> This provides a clear example of one of the consequences of professional demarcation: there is no evidence that information from the symposium was communicated by those attending to colleagues with different specialist interests.

**9.41** In relation to widening knowledge of AIDS in the UK, the timing of the meeting is instructive. AIDS was not on the programme for the Stirling symposium as originally prepared. The topic of AIDS in homosexuals and drug addicts came to the fore later and a special lecture, 'Acquired Immuno-Deficiency Syndrome: infection and neoplasia in homosexual men and intravenous drug addicts', was added.<sup>59</sup> The opening passage of the paper referred to experience in the USA and stated:

We are experiencing an alarming epidemic of an acquired immunodeficiency syndrome (AIDS) in certain cities in the United States. It is affecting homosexual men, intravenous drug abusers of either sex and Haitian refugees ....

We are seeing such cases on a regular basis in New York City .... AIDS patients are regularly seen in Los Angeles, San Francisco and other large cities in the United States and cases have also been reported from Europe.<sup>60</sup>

**9.42** At the symposium, AIDS patients were reported to have developed opportunistic infections, KS and other malignancies.<sup>61</sup> A high mortality rate was reported: 13 of 42 patients in New York had already died. PCP in particular was associated with high mortality. It was noted that those who took care of the patients realised how devastating this illness was.

**9.43** The paper did not mention haemophilia patients as being at risk. Professor Hann recollected, however, that there was a 'corridor discussion' of other possible groups of affected patients including a very small number with haemophilia.<sup>62</sup> The authors of the paper on AIDS were mainly from New York but also included Dr James Curran and others from CDC, Atlanta, who may have known of Dr Evatt's views (described in paragraph 9.29 above). Professor Hann's evidence is particularly telling. He remembered the meeting well as it was so shocking. At the time of the symposium, his interests did not include haemophilia and the 'corridor discussion' left him with the impression, as he moved into haemophilia care at Yorkhill at the beginning of 1983, that AIDS might possibly be relevant to his haemophilia patients; but, he said, AIDS was perceived at the time to be mainly a problem of sexual transmission and possibly also of intravenous drug use.<sup>63</sup>

<sup>56</sup> Comments from Professor Hann on excerpts from the 2nd International Symposium on Infections in the Immunocompromised Host [PEN.015.0270]; excerpts of a book on the symposium [LIT.001.3668]

<sup>57</sup> Professor Hann – Day 21, pages 39–40

<sup>58</sup> See, for example, Professor Forbes – Day 17, pages 100–101

<sup>59</sup> Second International Symposium on Infections in the Immunocompromised Host [LIT.001.3668] at 3685

<sup>60</sup> Ibid [LIT.001.3668] at 3685

<sup>61</sup> Ibid [LIT.001.3668] at 3688

<sup>62</sup> Day 21, page 44

<sup>63</sup> Ibid page 46



### *Official reaction*

**9.44** In UK government circles, the emerging problem was noted. On 16 July 1982, an internal Department of Health and Social Security (DHSS) memorandum advised that information had been received from the USA concerning the safety of US Factor VIII. The author of the memorandum (name redacted but probably written by a middle ranking official in the Department to another official who was medically qualified) stated that research was about to be published indicating that plasma taken from homosexual drug users contained a sort of virus and that, when the plasma was used for the production of Factor VIII, the virus could be passed on to haemophilia patients. It was claimed that '400 haemophilia patients in the USA [had] exhibited signs of the virus.' The memorandum noted that, with the UK's voluntary unpaid donor system, there was not the same problem of drug addicts being tempted to give blood for money. The author also noted, however, that about half of the concentrate used in the UK at this time was imported commercially from the USA.<sup>64</sup>

**9.45** In fact, up to the end of 1982, there was limited use of commercial concentrates by haemophilia centres in Scotland, with the exception of Yorkhill. Otherwise, the west of Scotland and the Edinburgh and east of Scotland centres used some commercial concentrates but mainly used Scottish concentrates or locally produced cryoprecipitate.<sup>65</sup> It is quite unclear where the 'information received from America' came from and the Inquiry has found no evidence to support the statement (from July 1982) that 400 haemophilia patients in the USA had exhibited signs of this virus. In fact, by coincidence, also on 16 July 1982 the *MMWR* published an account of the first three haemophilia patients in the USA thought to have AIDS.<sup>66</sup>

**9.46** In the UK, the Haemophilia Centre Directors began exploring the issue of AIDS in the autumn of 1982, remitting to Dr John Craske, who represented the Public Health Laboratory Service (PHLS), Withington Hospital, Manchester, the task of looking into the report from the USA of the syndrome in homosexual men and recently reported in three haemophilia patients. At that stage, the impression reflected in the minutes of the Directors' meeting of 13 September was that '[i]t appeared that there was a remote possibility that commercial blood products had been involved.'<sup>67</sup>

**9.47** Dr Frank Boulton, Deputy Director of the Edinburgh Blood Transfusion Centre, prepared a note of the Directors' meeting. In relation to AIDS, he stated:

This is a wasting disease with deficient cell-mediated immunity, possibly associated with an infectious element ....

Mortality 40-50%.

Three cases have occurred in haemophiliacs in the USA, possibly associated with parenteral drug abuse.<sup>68</sup>

<sup>64</sup> Memorandum [DHF.001.6744].

<sup>65</sup> See Chapter 20, *Haemophilia Therapy – Use of Blood Products*, Table 3 and Figure 8

<sup>66</sup> 'Epidemiologic notes and reports Pneumocystis carinii pneumonia among persons with Hemophilia A', *Morbidity and Mortality Weekly Report*, 1982; 31/27:365-7 [LIT.001.0559]

<sup>67</sup> Minutes of the 13th Meeting of UK Haemophilia Centre Directors, 13 September 1982 [SNB.001.7419] at 7428; *Morbidity and Mortality Weekly Report*, July 16 1982 [LIT.001.0559]; Preliminary Report, para 8.16

<sup>68</sup> Note of the Director's meeting [SNB.001.7494] at 7502

**9.48** Dr Boulton emphasised that the note did not express his personal opinion. He could not recollect who had suggested the association with 'parenteral drug abuse'.<sup>69</sup>

**9.49** Dr Winter was asked by the Inquiry about the reference to drug use in Dr Boulton's note; an association with drug use had not been mentioned in the *MMWR* of July. Dr Winter thought that there was a feeling at this time that only three haemophilia patients were affected, in the USA, and it was not absolutely certain that they were not part of some other risk group. He advised that a lot of attention was being paid to Germany where 'spectacularly high' quantities of imported Factor VIII were used. He said:

I think in fact the Bonn centre one year used more than every American centre put together, and one of the things that was said regularly at this time was, "If this is a new disease and it is in blood, why aren't the Germans getting it because, if anybody is going to get it, the Germans will."<sup>70</sup>

**9.50** Dr Craske asked the Directors to let him know if they had any cases of the syndrome. It was noted that the Hepatitis Working Party was considering the implications of the reports from the USA.<sup>71</sup> The Hepatitis Working Party was a UKHCDO group but had a wider membership than Haemophilia Centre Directors exclusively. Dr Craske was to have a pivotal role in collecting and disseminating intelligence on the disease among UK clinicians and scientists. Study of the prevalence of AIDS in the UK haemophilia population had begun but, subject to the 'remote possibility' that commercial blood products were implicated (a factor which would have had relevance in the UK generally but in England and Wales in particular), it was viewed as primarily a US problem at that stage and few haemophilia patients in the USA were affected. Professor Ludlam thought that the explanation for the assessment of risk as relatively low was that three only out of 20,000 haemophilia patients in the USA had been reported as being infected.<sup>72</sup>

**9.51** There was still a lack of communication of emerging knowledge among different professional groups in Scotland. As noted in the Preliminary Report, the minutes of the meetings of SNBTS Directors for 1982 did not disclose discussion of AIDS by Transfusion Directors at any meeting during the year.<sup>73</sup>

**9.52** At the end of 1982, therefore, there was emerging interest in the UK in AIDS but there was no general understanding that AIDS was a problem for Scotland or for any particular cohort or cohorts of potential patients.

### **Developments in the United States of America: 1983–1984**

**9.53** On 21 January 1983, an article in *Science* (published in the USA but one of the most widely-read and most prestigious science publications in the world) described a recent CDC workshop on the new immune disease.<sup>74</sup> Among topics discussed was the possibility that the disease might be spread through blood and blood products. The CDC had reported that haemophilia patients were at high risk of contracting AIDS. Dr Evatt, CDC, told the workshop that AIDS was the second leading cause of death for haemophilia patients in 1982.

<sup>69</sup> Day 24, pages 27–29

<sup>70</sup> Day 15, pages 126–7

<sup>71</sup> Minutes of the 13th Meeting of UK Haemophilia Centre Directors, 13 September 1982 [SNB.001.7419] at 7428

<sup>72</sup> Day 18, page 94

<sup>73</sup> Preliminary Report, para 8.17

<sup>74</sup> 'Health Officials Seek Ways to Halt AIDS', *Science*, 1983; 219:271–272; [LIT.001.1589]

**9.54** A widening range of people at risk was reported in the USA in 1983 and 1984. In January 1983 two cases of AIDS in the female sexual partners of IVDUs were reported.<sup>75</sup> Reports of infection in the Cleveland Hemophilia Center and other centres were published in the *NEJM* in February 1983.<sup>76</sup> All of the patients had a disorder resembling idiopathic thrombocytopenic purpura (a recognised autoimmune condition characterised by abnormally low platelet counts). Three out of four of the patients studied in 1981 and 1982 demonstrated evidence of impaired cell-mediated immunity. It appears highly likely that one of these was the patient discussed by Professors Ratnoff and Forbes at the end of 1981. Further cases of AIDS in haemophilia patients in the USA were reported in March 1983.<sup>77</sup> At the same time there were additional reports of immune abnormalities in young haemophilia patients who were otherwise apparently well.<sup>78</sup> An editorial in *The Lancet* for 2 April 1983 referred to reports from the USA of haemophilia patients, who had received Factor VIII concentrates, developing AIDS.<sup>79</sup> On 30 April, letters in *The Lancet* reported AIDS in 11 haemophilia patients in the USA and three in Spain who had received commercial concentrate.<sup>80</sup>

**9.55** A leaflet entitled *Facts about AIDS* was published by the US Public Health Service in September 1983.<sup>81</sup> The opening paragraph advised that AIDS was the number one priority of the US Public Health Service. Since 1981 the service had received reports of more than 2200 cases with a mortality rate of almost 40%. The leaflet included information about the nature and extent of AIDS, identifying who was at risk and giving advice on preventative measures. In the paragraph headed 'What causes AIDS?', it stated: 'The best evidence for transmission of AIDS through blood products is the occurrence of AIDS in a small number of hemophilia patients receiving large amounts of Factor VIII, a clotting substance in blood.' The leaflet included a number for a toll-free AIDS hotline where up-to-date information could be obtained.

### *Joint meeting of the World Federation of Hemophilia and the International Society for Thrombosis and Haemostasis*

**9.56** Dr Evatt reached a wide audience for his views at a joint meeting of the World Federation of Hemophilia and the International Society for Thrombosis and Haemostasis, held in Stockholm in June 1983. He reported that, by that date, the total number of confirmed AIDS cases in the USA was marginally higher than would be predicted from an exponential growth of the disease.<sup>82</sup> Haemophilia patients were in the group of infected people who developed opportunistic infections and there were 16 confirmed haemophilia patient cases in the USA (with eight dead by that date), three in Spain, one in Wales and one in Canada. Other delegates at the conference commented that there were more cases than that outside the USA (in Canada, Germany, Israel and Sweden) and that it was possible that these had not been confirmed by the CDC by that date. Of the 16 US haemophilia cases, one related to a mildly affected Haemophilia B patient.

<sup>75</sup> Historical Summary of AIDS in Haemophilia 1981–1985 [PEN.015.0468]; 'Epidemiologic Notes and Reports among Female Sexual Partners of Males with Acquired Immune Deficiency Syndrome (AIDS) – New York', *Morbidity and Mortality Weekly Report*, 1983; 31(52):697–8 [LIT.001.5539]; Professor Ludlam – Day 18, page 96

<sup>76</sup> Ratnoff et al, 'Coincident classic hemophilia and "idiopathic" thrombocytopenic purpura in patients under treatment with concentrates of antihemophilic factor (Factor VIII)', *New England Journal of Medicine*, 1983; 308:439–442 [PEN.016.1172]

<sup>77</sup> Historical Summary of AIDS in Haemophilia 1981–1985 [PEN.015.0468] at 0469

<sup>78</sup> *Ibid* [PEN.015.0468] at 0469

<sup>79</sup> 'Acquired immunodeficiency in haemophilia', *The Lancet*, 2 April 1983 [LIT.001.0408]; Preliminary Report, para 8.23

<sup>80</sup> 'Aids in haemophilia patients in Spain', *The Lancet*, 30 April 1983 [LIT.001.0403]. 'Factor VIII products and disordered immune regulation', *The Lancet*, 30 April 1983 [LIT.001.0911]; Preliminary Report, para 8.23

<sup>81</sup> Information leaflet [DHF.001.4724]

<sup>82</sup> Dr Foster's report of the meeting dated 15 July 1983 [SNF.001.3712]

**9.57** Further data on the developing picture worldwide was provided at a WHO conference held in Geneva in November 1983.<sup>83</sup> It was reported that it had been recognised by then that the cases already diagnosed had involved infection as early as 1978, implying a much longer incubation period before the appearance of significant disease than had previously been assumed. The fatality rate was high – less than 20% of those with AIDS were alive two years after diagnosis.<sup>84</sup>

**9.58** Data were updated to 5 December 1983 in the draft report of the conference.<sup>85</sup> AIDS cases in the USA reported to the CDC by that date were:

**Table 9.1: Patients at Risk, December 1983**

Patients at Risk	Cases	Males	Females
Homosexual or Bisexual	2052	2052	
Intravenous Drug Users	490	387	103
Others	326	240	86
<b>Total</b>	<b>2868</b>	<b>2679</b>	<b>189</b>

**9.59** In the USA, 0.7% of cases were in people with haemophilia and no other known risk factor and 1% of cases were in those who had received a blood transfusion in the previous five years.<sup>86</sup> There were, in addition, paediatric cases linked with blood transfusion in which sexual transmission could be ruled out.<sup>87</sup> The cases diagnosed were concentrated in five urban areas of the country.<sup>88</sup>

**9.60** The major part of the report dealt with surveillance, prevention and control of the disease. By this point there was no question that the USA was confronting a disease of epidemic proportions. Significantly, the draft report of the conference noted that the emerging epidemiological patterns in most western European countries were very similar to the pattern then established in the USA.

### *Further developments*

**9.61** The *MMWR* of 2 December 1983 noted that, based on CDC advice, as at 30 November 1983, 21 cases of AIDS had been reported among haemophilia patients in the USA, 19 among patients with Haemophilia A and 2 among patients with Haemophilia B. In addition, 7 cases from outside the USA had been brought to the attention of the CDC.<sup>89</sup>

**9.62** The retrospective studies referred to above (paragraphs 9.11–9.12), which were carried out on stored frozen blood samples of haemophilia patients using HTLV-III/HIV antibody assays, were enabled by the isolation and characterisation of the AIDS retrovirus in 1983 and 1984 and the development of antibody tests in and after 1984.<sup>90</sup> These revealed that,

<sup>83</sup> Preliminary Report, para 8.65

<sup>84</sup> Initial Report for Scottish Regional Transfusion Directors Meeting on 8 December 1983 [SNF.001.0552] at 0561

<sup>85</sup> Acquired Immunodeficiency Syndrome – An Assessment of the Present Situation in the World [SNF.001.2575]; Table 1 at 2607

<sup>86</sup> Ibid [SNF.001.2575] at 2577

<sup>87</sup> Initial Report for Scottish Regional Transfusion Directors Meeting on 8 December 1983 [SNF.001.0552] at 0565

<sup>88</sup> Ibid [SNF.001.0552] at 0561

<sup>89</sup> 'Current Trends Update: Acquired Immunodeficiency Syndrome (AIDS) Among Patients With Hemophilia – United States', *Morbidity and Mortality Weekly Report*, 1983; 32/47:613–5 [LIT.001.0551]

<sup>90</sup> Ragni, 'AIDS and treatment of hemophilia patients', *Plasma therapy & Transfusion Technology*, 1988, 9; 173 [SGF.001.1314] See, in particular, the table of dated seroconversions in Western Pennsylvania for the pattern. Chapter 29, *The Discovery of HIV and the Development of Screening Tests*, deals more extensively with the discovery of HIV.

in the USA, the peak in haemophilia patient seroconversion occurred in 1982 and 1983, with the earliest known seroconversions in 1978, shortly before the AIDS epidemic among homosexual men and intravenous drug users was first reported. By the end of 1983 and into 1984 the trends were becoming well established.

**9.63** Experience of AIDS in the USA had been discussed at a conference of combined clinical staffs at the US National Institutes of Health (NIH) Clinical Research Center, Bethesda, Maryland, on 23 June 1983. An edited summary of the proceedings was published in the *Annals of Internal Medicine* dated 1 January 1984, giving wide publicity to the discussion. The article observed that there had been a doubling of the number of patients afflicted every six months since the original reports in June and July 1981. It proceeded:

Because the incubation period for adults is generally felt to be greater than 1 year, the full scope of the syndrome has not yet been realized. However, the syndrome's pattern of transmissibility suggests that it will remain largely confined to the groups already affected, with minor intrusions into other populations not at high risk.<sup>91</sup>

**9.64** Four major risk groups were identified: homosexual and bisexual men; IVUDs with no history of homosexual activity; Haitian immigrants; and persons with haemophilia. A fifth group (3.8% of reported cases) comprised cases where no association was apparent or known. While numbers of individuals infected would continue to grow, the focus changed from reporting the prevalence of AIDS to the identification of the virus and then to tests for infection and to treatment.

**9.65** In relation to haemophilia patients, the situation was developing quickly. In July 1984, the first experimental antibody tests for the newly confirmed HIV became available in the USA. On 26 October 1984, the US CDC published an update on AIDS in people with haemophilia.<sup>92</sup> A total of 52 cases had been reported of haemophilia-associated AIDS in the USA. Thirty patients had died and only three diagnosed more than a year previously were still alive. The CDC had studied over 200 recipients of Factor VIII and 36 recipients of Factor IX concentrates containing materials from US donors. AIDS virus antibody rates of prevalence were 74% for Factor VIII recipients and 39% for Factor IX recipients.

**9.66** On 31 October 1984, Professor Elaine Eyster at the Milton S Hershey Medical Center, Pennsylvania State University, wrote to Dr Brian McClelland, Director of the Edinburgh Blood Transfusion Service, about work carried out by her team:

The data on sero conversion rates in 30 patients has not yet been put into abstract form or submitted for publication. I can tell you, however, that sero conversion began in 1979 when three of the 30 patients tested in 1983-84 became positive. The number steadily increased, with the big jump occurring in the year 1982.<sup>93</sup>

**9.67** Retrospective testing of stored serum samples was adding to the available knowledge of the history of transmission of infection.<sup>94</sup>

<sup>91</sup> Fauci *et al*, 'Acquired immunodeficiency syndrome: epidemiologic, clinical, immunologic, and therapeutic considerations', *Annals of Internal Medicine*, 1984; 100:92-106 [LIT.001.1573]

<sup>92</sup> 'Update: Acquired Immunodeficiency Syndrome (AIDS) in Persons with Hemophilia', *Morbidity and Mortality Weekly Report*, 1984; 33/42:589-91 [LIT.001.0460]

<sup>93</sup> Professor Eyster's letter to Dr McClelland [SNF.001.2512]

<sup>94</sup> Dr McClelland's reply 13 November 1984 [SNB.006.5999]

**9.68** By the end of 1984, the epidemic was well established in the USA, generally and in relation to haemophilia patients. The numbers of individuals infected were an indication of its extent but they were no longer relevant to whether there was a disease, or to diagnosis, or to treatment.

### Reports from outside the United States of America

**9.69** In the UK, the emerging epidemic was brought to the notice of the general public in media comment. An article published in *The Observer* in January 1983 entitled 'Mystery disease threat' stated: 'A commercial blood product imported into Britain from the United States may pose a grave threat to the health of haemophiliacs who inject it to encourage clotting'.<sup>95</sup> The article continued by saying that the product, Factor VIII concentrate, was being linked in the USA with a devastating new disease which caused a serious breakdown in the body's immune system. It was noted that the spread of the disease was described by officials at the CDC as 'an impending epidemic' among haemophilia patients. The article went on to describe how the disease had advanced from the homosexual community to include haemophilia patients.

**9.70** Data were made known to a significant number of UK doctors when Dr Craske's research up to the end of 1982 was reported informally on 24 January 1983 at a meeting held at Heathrow Airport chaired by Professor Arthur Bloom.<sup>96</sup> The report dealt mainly with experience in the USA. Dr Craske reported that the population groups affected by AIDS in the USA included promiscuous homosexuals, heroin addicts, immigrants into the USA from Haiti and haemophilia patients. Up to 10 December 1982, some 800 people had been reported as suffering from AIDS and there was a 45% mortality rate. Ten haemophilia patients in the USA had been affected, including a 7 year old child, and five had died. By that stage, only one or two cases of AIDS had been reported from the Communicable Disease Surveillance Centre (CDSC), based in Colindale, London.<sup>97</sup>

**9.71** Dr Craske's report would have provided important and well researched information to those attending the meeting. In the case of the US haemophilia patients, all had prolonged treatment with Factor VIII but there was no implication of one particular product or batch. It would have been clear that the problem was not limited to a single production process or event. Cases involving blood and blood product transmission had included platelet transfusions. An association with transfusion was explicit in some of the cases.

**9.72** Lack of understanding of the natural history of the disease was to have a bearing on the response of UK scientists and clinicians for some time. A report of the UKHCDO Hepatitis Working Party dated 1 March 1983 set out what was known of the origins of AIDS and the signs and symptoms of infection.<sup>98</sup> The report noted that the CDC had asked UK Haemophilia Centre Directors to report cases possibly associated with US commercial concentrates and that cases should also be reported to the CDSC. UK haemophilia clinicians were brought into the wider survey of the disease at this time.

**9.73** The report would not, however, have communicated the full extent of the implications for individuals with AIDS. It commented:

<sup>95</sup> *Observer* article, January 1983 [DHF.001.7108]

<sup>96</sup> See Preliminary Report, paragraphs 8.18 and 8.19 for further details.

<sup>97</sup> Notes of Meeting With Immuno at Heathrow Airport, 24 January – Hepatitis Reduced Factor VIII and Factor IX Concentrates for Haemophilia Therapy [SNB.001.4033] at 4035–6

<sup>98</sup> UKHCDO Hepatitis Working Party – The Acquired Immune Deficiency Syndrome (AIDS) [DHF.001.7178]

It is ... possible that the initial phase of the disease ... may not always progress to the final syndrome where marked depletion of the lymphoid cells is the most obvious appearance on histology of lymph nodes. It is therefore evident that the disease is not universally fatal and some patients may recover.<sup>99</sup>

**9.74** The natural history of AIDS was not then understood. Dr Winter commented that while, on the basis of the information then available, it was reasonable to suggest that not every patient infected with HIV would progress to AIDS, there was no basis for the statement that some might recover from AIDS: that was not the case, as events subsequently transpired.<sup>100</sup> The report understated the risk to patients and this was to be a continuing feature of comment for a time.

**9.75** Dr Peter Foster of the Edinburgh Protein Fractionation Centre (PFC – the manufacturer of NHS blood products in Scotland) gave a talk to Professor Ludlam's department on 8 March 1983 on methods for preparing non-infective blood products.<sup>101</sup> The talk was concerned primarily with avoiding or minimising the risk of transmission of hepatitis viruses although, among other problems of interest to blood product manufacturers, he referred to other infectious agents, including AIDS.<sup>102</sup>

**9.76** The Haemophilia and Blood Transfusion Working Group met on 22 March 1983.<sup>103</sup> There was concern that AIDS might appear in the UK and the Haemophilia Society was reported to be attempting to 'reassure its members and put fears of infection from blood products into perspective'. It was hoped that homosexuals and others at risk might be discouraged from being blood donors, although Transfusion Directors were reluctant to upset potential donors by asking questions to which they might take exception.<sup>104</sup> When asked whether enough concern had been expressed at this meeting, Professor Ludlam assured the Inquiry that there was concern and also 'bafflement'. He said that it was clear that it was a possibility, or even probability, that AIDS would come into England and Scotland.<sup>105</sup>

**9.77** Professor Forbes also attended this meeting and, although he had little recollection of the discussions, he recognised that there was a wave of tremendous anxiety about HIV infection and its transmission and, he told the Inquiry, depression in the patients who were being exposed to the possibility of infection. He continued:

I think most people thought that it undoubtedly would appear in the course of time, and already we were starting to look rather differently at our patients to see if they had any of the features that might be an early warning of AIDS.<sup>106</sup>

**9.78** On 28 March 1983, the UK National Institute for Biological Standards and Controls (NIBSC) was sufficiently concerned about the US position (where steps were being taken to avoid blood from high-risk groups in the preparation of certain blood products) that it suggested that the problem of AIDS should be considered at a meeting of the Committee on Safety of Medicines (CSM). The author (name redacted) of a letter of that date thought

<sup>99</sup> Ibid [DHF.001.7178] at 7182

<sup>100</sup> Dr Winter – Day 16, pages 34–35

<sup>101</sup> Outline of talk [SNB.007.3503]

<sup>102</sup> Ibid [SNB.007.3503] at 3507

<sup>103</sup> Minutes of the Haemophilia and Blood Transfusion Working Group [SNB.001.5183]

<sup>104</sup> Ibid [SNB.001.5183] at 5184

<sup>105</sup> Day 19, page 28

<sup>106</sup> Professor Forbes – Day 17, pages 103–104

it would be helpful if the Chairman of the Haemophilia Directors' group, Professor Bloom, could attend and advise the meeting. The author also requested the latest information on the surveillance of the condition in the UK.<sup>107</sup>

**9.79** Professor Bloom was frequently consulted at this time on matters relating to haemophilia patients. The CSM's functions were regulatory. The committee was concerned with the safety of medicines in general and this included the safety of blood. Any clinical investigation of the potential epidemic would have been carried out by the CDSC, the British equivalent of the CDC in the USA.<sup>108</sup>

**9.80** A report prepared by the Council of Europe dated 28 April 1983 summarised the AIDS situation in member states and other countries represented on the committee, as then reported.<sup>109</sup> The report was discussed at the meeting of the Committee of Experts on Blood Transfusion and Immunohaematology in Lisbon held between 16 and 19 May.

**9.81** Low numbers of infections were reported. The UK had eight possible cases, all males and almost all homosexuals. None followed the transfusion of blood or blood products. Most of the European countries reported fewer than five cases and, of those cases, the majority were homosexuals. Belgium had 15 cases affecting both male and female heterosexuals from Zaire (now the Democratic Republic of Congo). West Germany had the highest number of cases, 18, two of whom were haemophilia patients. The other European country to report several cases of AIDS in haemophilia patients was Spain, with three cases of haemophilia patients from the Andalusia region (two were brothers). Cases of AIDS in Canada were also included where there were 31 known patients, 16 of whom had died.

**9.82** The three Spanish cases were reported in *The Lancet* on 30 April 1983.<sup>110</sup> One patient had already died and a second was in hospital, seriously ill. The third had PCP, among other indications of advanced disease, but his general condition had improved with treatment. Prognosis for the survivors was not discussed but would not have been indicative of a benign outcome. Dr Spence Galbraith, Director of the CDSC in England and Wales, contacted the health authorities in Spain and discovered that the three patients had all received Factor VIII concentrate from the USA.<sup>111</sup> As noted below at paragraph 9.99, Dr Galbraith was to take a particular interest in following up these reports.

### **Press reports**

**9.83** On 1 May 1983 an article published in *The Observer* summarised the impact on the US population of 'America's newest and deadliest epidemic'.<sup>112</sup> The newspaper's US correspondent reported that more than 1350 patients in the USA had already been diagnosed as suffering from AIDS. No cure had been found and, given the long incubation period (up to three years), it was feared that thousands of people could be unwitting carriers. The most recent suspected victims were babies and adults who did not fall into any of the identified high-risk categories; it was feared that this disease was spreading to other groups within the community.

<sup>107</sup> Letter dated 28 March 1983 [DHF.001.7168]

<sup>108</sup> Dr Winter – Day 16, page 37

<sup>109</sup> Council of Europe Report [DHF.001.4394]

<sup>110</sup> 'AIDS in haemophilia patients in Spain', *The Lancet*, 30 April 1983 [LIT.001.0403]; Preliminary Report, paragraph 8.23

<sup>111</sup> Letter: 'Action on Aids' dated May 1983 [MIS.001.0005]

<sup>112</sup> *The Observer*, 1 May 1983 [DHF.001.4322]



**9.84** The article stated that more European sufferers had been identified, and that in France there were 29 patients, 13 of whom had died. Eleven haemophilia patients in Europe had been affected and this strengthened suspicions that AIDS could be passed on through blood. The US government was reported to be unwilling to stigmatise homosexuals, already a 'harassed minority', by banning them from donating blood. The US National Hemophilia Foundation, however, believed that this had to be the next step. The US government's official view, expressed by a spokesman for the Food and Drug Administration, was that: 'There [was] no clear cut evidence to show that AIDS [could] be transmitted through blood transfusion'.<sup>113</sup>

**9.85** Also on 1 May 1983, Susan Douglas, journalist for the *Mail on Sunday*, 'revealed exclusively' that two cases of AIDS in haemophilia patients had probably occurred in the UK already.<sup>114</sup> An accompanying opinion piece stated that '[t]he victims were not homosexuals but patients who had been treated with plasma imported from America'. The article continued with speculation that Britain would not be self-sufficient in producing 'this special kind of blood' until 1986. The paragraph concluded with the comment: 'Fortunately there is an alternative. It can be bought from Switzerland'.<sup>115</sup>

**9.86** The tone of an article in *The Daily Mail* on 2 May was equally uncompromising.<sup>116</sup> It stated: 'Government health experts have begun investigating the possibility that Britain is importing blood products from America contaminated with the killer homosexual disease AIDS'. The article concluded: 'According to the Department of Health, the advantage of using imported blood products far outweighs the "slight possibility" that AIDS could be transmitted to patients through [Factor VIII]'.<sup>116</sup>

**9.87** *The Daily Express* also published an article on 2 May and described AIDS as 'The new killer-disease'.<sup>117</sup> The focus of this article was fear of the unknown and fear that it could be a more general sexually transmitted disease also affecting heterosexuals. Dr Vernon Coleman (medical author and researcher) was quoted at the end of the article: 'If we could discover exactly what AIDS is – indeed, IF it is – we might be able to do something to counter it'.

**9.88** These publications caused concern generally and particularly amongst at-risk groups, including haemophilia patients.

### The position of the Haemophilia Society

**9.89** With AIDS now reported and discussed in the UK popular press and the media generally, anxiety grew among people at risk. Anxiety was spread not only by the facts but also by the tone of media comment. Prompted by the media coverage to date, and in particular the *Mail on Sunday* article of 1 May 1983 referred to above, the Haemophilia Society distributed to its members on 4 May 1983 a letter containing a statement by Professor Bloom. He commented that the number of AIDS cases in haemophilia patients was small, that he was unaware of any proven case in 'our own haemophilia population' and (incorrectly) that none had been reported from Germany.

<sup>113</sup> Ibid [DHF.001.4322]

<sup>114</sup> *Mail on Sunday*, 1 May 1983 [DHF.001.4320]

<sup>115</sup> Ibid [DHF.001.4323]

<sup>116</sup> *The Daily Mail*, 2 May 1983 [DHF.001.4328]

<sup>117</sup> *The Daily Express*, 2 May 1983 [DHF.001.4328]

**9.90** In an apparent attempt to reassure Society members, Professor Bloom wrote:

The cause of AIDS is quite unknown and it has not been proven to result from transmission of a specific infective agent in blood products .... Thus whilst it would be wrong to be complacent it would equally be counter-productive to alter our treatment programmes radically.<sup>118</sup>

**9.91** Mr David Watters, former General Secretary of the Haemophilia Society, told the Inquiry how the Society had come to send the letter. He explained that what had prompted the Society's letter was the assertion in the *Mail on Sunday* that the UK did not have to rely on the US for Factor VIII as there was an alternative source in Switzerland. He continued:

[T]hat simply was not true and it made it appear as if we had been allowing people to be treated with suspicious product, whereas there was a known safer source. And of course, the media on its high horse knows better than everyone else what is correct and good for society; in this case they got it quite horribly wrong.<sup>119</sup>

**9.92** Mr Watters further explained that the Society's letter was intended to reassure members that there were no known cases of AIDS in the haemophilia population. He felt that the Society had better information than the media and said: 'the *Mail on Sunday* had quite clearly diagnosed two entirely on its own'.<sup>120</sup>

**9.93** At this time, Mr Watters was receiving telephone calls day and night from people who were worried. He was happy with Professor Bloom's message, bearing in mind that '[p]eople with haemophilia were really between a rock and a hard place: do you discontinue treatment and run the risk of a fatal bleed or do you continue to treat and run a potential other infection risk?'<sup>121</sup>

**9.94** Everyone involved in the framing of the letter considered that reassurance was required. Mr Watters advised that members of the board who had access to faxes saw the letter and he was confident that it was also faxed to members of the medical advisory panel. Nobody expressed dissent from what was said in the letter.<sup>122</sup>

**9.95** The reassurance was, however, based on data that were incorrect and that could have been readily checked. The *Mail on Sunday* article specifically stated that the suspected UK case was in Cardiff where Professor Bloom was Director of the Haemophilia Centre. Based on reports from that centre, a bulletin from the CDSC, dated 6 May 1983, reported the case of AIDS in a 20 year old man with haemophilia in Cardiff. The patient had been ill with 'AIDS-related complex' (ARC) for three months.<sup>123</sup> The report stated that this was the first case of AIDS in a UK haemophilia patient known to the CDSC. Dr Winter thought it possible that Professor Bloom was a laboratory-based specialist, not a clinician, and that he did not know of the case.<sup>124</sup> Dr Winter did not think that a clinician would have made comments such as

<sup>118</sup> The Haemophilia Society – statement on AIDS [DHF.001.4474]. Preliminary Report, para 8.25

<sup>119</sup> Day 87, page 65

<sup>120</sup> Ibid page 69

<sup>121</sup> Ibid page 71

<sup>122</sup> Ibid pages 64–72

<sup>123</sup> CDSC report for week ending 6th May 1983 [PEN.015.0244]

<sup>124</sup> Day 16, page 41. However, Dr Cacchia, who had assisted Professor Bloom at Cardiff, said that Professor Bloom was a very 'hands-on' and 'person-centred' clinician as well as a leading academic, which tends to undermine Dr Winter's speculation. Day 83, page 8.

those made by Professor Bloom at the time.<sup>125</sup> Professor Ludlam questioned whether the Cardiff case was AIDS, but at the time the CDSC recognised this and another case, from Bristol, as cases of AIDS.<sup>126</sup>

**9.96** There were also, by this stage, early reports of infection in West Germany. The Council of Europe report of 28 April 1983 dealt with AIDS in two German haemophilia patients.<sup>127</sup> The report, perhaps prepared earlier in April, noted that there were no reports of cases following the transfusion of blood or blood products in the UK.<sup>128</sup> By May the situation was changing.<sup>129</sup> It is unclear how widely the deliberations of the Council would have been read. Dr Winter indicated that the deliberations of the Council of Europe were not perceived as relevant to haemophilia clinical practice.<sup>130</sup> He thought that the recommendations in the report had clearly been written by people who were not 'haemophilia people'.<sup>131</sup> Professor Lever had a similar view: the Council of Europe was not influential in his area of work.<sup>132</sup> As appears in the discussion of screening for HCV, however, transfusionists and virologists did take note of the views of the Council and its expert committees.<sup>133</sup> Whatever the degree of authority otherwise accorded to its statements, the report of infections in Germany was fact and further undermined Professor Bloom's letter. Later reports in December 1983 from the WHO conference in Geneva appear to indicate a significant acceleration in identification of infection between then and October, when 42 cases were reported from West Germany to the WHO.<sup>134</sup>

**9.97** In light of the Haemophilia Centre's report of the Cardiff case to the CDSC in time for the publication in the edition for the week ending 6 May 1983, it is difficult to understand the reference to lack of awareness of cases in 'our own haemophilia population'. The newspaper report had identified Cardiff as the location of the haemophilia patient who had been unwell with ARC for three months before the date of the published letter. Preparations must at least have been in hand by 4 May to report the case as a definitive case of AIDS for publication by the CDSC for the week ending 6 May. If publication by the CDSC was essential to the description of a case as 'definitive' or if the word 'proven' was being used because of the absence of identification of the causative pathogen, Professor Bloom's letter may have been literally accurate but then it would also have been disingenuous. If he did not in fact know of the case, questions would arise concerning arrangements for the dissemination of important and relevant information about patients within his centre.

**9.98** In the UK, the systems for reporting instances of AIDS, which were introduced in 1982, were not well developed by this stage. However, absolute accuracy apart, it is of concern that commentators, such as Professor Bloom in these instances, could publish that there were no reports of disease in the UK and two only in Germany respectively, when of necessity they must have been proceeding on information that was quite wrong in fact. In the case of Professor Bloom, he could not have failed to discover the true position if he

<sup>125</sup> Day 16, page 43

<sup>126</sup> Day 18, Pages 126–130. The 'Bristol' case is noted in paragraph 9.125 below. In May 1983, he was considered to be a 'mild' or prodromal (that is, exhibiting early symptoms) case of AIDS [SNF.001.7556]

<sup>127</sup> Committee of Experts on Blood Transfusion and Immunohaematology – 6th Meeting [DHF.001.4394] at 4397; Dr Winter – Day 16, pages 44–47

<sup>128</sup> Committee of Experts on Blood Transfusion and Immunohaematology – 6th Meeting [DHF.001.4394] at 4401

<sup>129</sup> Day 18, pages 131–132

<sup>130</sup> Day 16, page 48; DHSS Memo: 'Recommendations, Resolutions, etc by International Bodies' dated July 1983 [DHF.002.2148]

<sup>131</sup> Day 16, page 49

<sup>132</sup> Day 26, page 126

<sup>133</sup> See Chapter 31, *The Introduction of Screening of Donated Blood for Hepatitis C*

<sup>134</sup> Acquired Immunodeficiency Syndrome – An Assessment of the Present Situation in the World [SNF.001.2575]. According to the table, 33 cases were diagnosed in the FDR in 1983.

had sought information, even assuming that he could have headed the centre without being aware of such a critical matter affecting a patient there. In the result, the letter was misleading. It gave false reassurance to patients who read it.

### Official responses in the United Kingdom

**9.99** Dr Galbraith responded to the reports he had read. He wrote to Dr Ian Field, DHSS, in May 1983.<sup>135</sup> He commented that the Cardiff case had involved US Factor VIII concentrate and that the case fitted the recognised criteria for a diagnosis of AIDS. He referred to the three Spanish cases (see paragraphs 9.81–9.82) and recent reports from the USA, in particular the case of the multiply-transfused child (see paragraph 9.31). In his supporting paper he commented that the mortality rate of AIDS at that point exceeded 60% and was expected to reach 70%. As a public health doctor, he took a serious view of the threat to haemophilia patients in the UK.

**9.100** Media comment brought a further reaction. There was a special meeting of the Haemophilia Reference Centre Directors at St Thomas' Hospital on 13 May 1983.<sup>136</sup> Recent media publicity about AIDS was said to have caused considerable anxiety to haemophilia patients and their medical attendants as well as the DHSS, making it necessary for the Directors to consider what should be done with regard to the surveillance and reporting of suspected cases and the management of patients. It was noted that, up to that date, one haemophilia patient in the UK was suspected of suffering from AIDS and that, in London, there were reported to be 10 cases of confirmed AIDS in homosexual males. The minutes proceeded:

It was felt that there might be many individuals with evidence of impaired cell-mediated immunity but only a very small number of these might progress to a full-blown picture of the condition. It is important that such individuals are not classified as suffering from AIDS. It was accepted that because of our lack of knowledge of the nature of AIDS, decisions about diagnosis and reporting of suspected cases would prove difficult.<sup>137</sup>

**9.101** At this stage, the viral aetiology of AIDS (that is, knowledge that a virus caused the disease) had not been established by generally accepted evidence. In particular, Robert Gallo and his colleagues had yet to disclose the identification of HTLV-III as the transmissible agent, satisfying US specialists who had not been persuaded by the French research previously published by Luc Montagnier and others.<sup>138</sup> Narrowly defined reporting requirements risked suppressing the prevalence of infection with the (as yet unknown) agent of transmission, however.

### Reporting criteria

**9.102** It was decided that, for reporting purposes, CDC criteria would be used and the importance of opportunistic infection was stressed. A definitive diagnosis would be attached if the patient developed intractable disease. It was noted that many Haemophilia Directors had, up to that point, reserved NHS concentrates for children and mildly affected patients

<sup>135</sup> Dr Galbraith's letter: 'Action on Aids' dated May 1983 [MIS.001.0001], retyped as [MIS.001.0005]; Preliminary Report, para 8.24

<sup>136</sup> Minutes of Special Meeting of Haemophilia Reference Centre Directors on 13 May 1983 [DHF.001.4384]. Preliminary Report, paragraph 8.26

<sup>137</sup> *Ibid* [DHF.001.4384] at 4384–5

<sup>138</sup> As discussed later, the Institut Pasteur reported the discovery of LAV, a virus identical to HTLV-III, in May 1983, but that was not generally accepted at this stage. See also Chapter 29, *The Discovery of HIV and the Development of Screening Tests*.

and it was suggested that it would be 'circumspect' to continue with that policy. It was agreed that there was insufficient evidence to warrant the restriction of the use of imported concentrates in other patients in view of the immense benefits of therapy. It was noted that, once the condition was fully developed, it seemed irreversible so that there would be no clinical benefit to be gained from changing from one type of concentrate to another.

**9.103** The requirement for evidence of intractable disease added to the burden of proof of infection (as had happened previously when a requirement for clinically manifest disease was included in the definition of non-A, non-B Hepatitis infection – see Chapter 15, *Knowledge of Viral Hepatitis 2 – 1975-1985*). There was no requirement for notification of cases of impaired cell-mediated immunity. As a result, the data required for a comprehensive understanding of the epidemiology of the disease were incomplete.

**9.104** Meanwhile, media coverage continued. On 18 May 1983 *The Sun* published an article 'U.S. Gay Blood Plague Kills Three in Britain'.<sup>139</sup>

### *Developing knowledge*

**9.105** Apart from haemophilia clinicians, developing knowledge of AIDS was also of relevance to fractionation scientists (those concerned, that is, with the preparation of blood products). Dr Foster of the PFC attended the meeting of the World Federation of Hemophilia and International Society for Thrombosis and Haemostasis in Sweden in June 1983.<sup>140</sup> He also recorded data provided by Dr Evatt about the spread of AIDS in the USA and elsewhere.<sup>141</sup>

**9.106** The Sub-Committee on Biological Products of the CSM discussed AIDS on 13 July 1983.<sup>142</sup> Reported comments on AIDS provide a clear insight into the understanding of this important body about the epidemic in mid-1983. Transmissibility of the postulated transmissible agent was thought to be low. Risk was thought to be small, so small that it did not justify serious consideration of withdrawal of US commercial concentrates (as had been suggested by Dr Galbraith in his letter to Dr Field, DHSS).<sup>143</sup> These outcomes had been anticipated in a 'suggested agenda' for the meeting.<sup>144</sup> For the proposal to be considered unworthy of serious consideration, however, the perceived risk to the UK community must have been considered small indeed. Unfortunately, this was to prove an inaccurate assessment. It was also noted that both haemophilia doctors and their patients, who saw at first hand the benefits of Factor VIII over cryoprecipitate, did not wish US blood products withdrawn. The committee will have taken this into account. There were 2167 patients with haemophilia receiving treatment in the UK at the time.<sup>145</sup> In England and Wales a high proportion received imported concentrates, while in Scotland the proportion was much lower. Only a relatively small percentage of blood products used in Scotland in 1983 came from the USA.<sup>146</sup> Nevertheless, overall there was a high exposure to risk and a high incidence of infection emerged over time.

<sup>139</sup> *The Sun*, 18 May 1983 [DHF.001.4415]

<sup>140</sup> Preliminary Report, paragraphs 8.37 and 8.38; paragraph 9.56 above

<sup>141</sup> Memorandum [SNF.001.3712]

<sup>142</sup> Committee on Safety of Medicines – Sub-Committee on Biological Products – Minutes of the Meeting held on 13 July 1983 [MIS.001.0291]. The minute does not refer expressly to Dr Galbraith's letter; Preliminary Report, para 8.41

<sup>143</sup> Retyped letter [MIS.001.0005] Preliminary Report, para 8.24

<sup>144</sup> Suggested Agenda for Discussion on AIDS in Relation to Licensed Blood Products – CSM (B) July 13 1983 [DHF.001.4587]

<sup>145</sup> Preliminary Report, para 8.44

<sup>146</sup> *Ibid* para 8.42

**9.107** On 14 July 1983, in the House of Lords, Baroness Dudley asked how widespread AIDS was and what steps were being taken to prevent it spreading into the community.<sup>147</sup> Lord Glenarthur (then the Parliamentary Under-Secretary of State, DHSS) replied that 14 cases had been reported to the CDSC and two more were being investigated. There were approximately 60 cases within member states of the Council of Europe. When asked why the UK imported blood products from the USA, Lord Glenarthur said: ‘We have to import Factor VIII, which is an agent used in the cure for haemophiliacs. We shall need to continue to do that until we are self-sufficient ourselves’.

**9.108** At this stage, there was doubt at UK government level whether a link between blood transfusion and AIDS had been established. In the course of his answer to Baroness Dudley, Lord Glenarthur stated:

Although there is no conclusive evidence that AIDS is transmitted by blood or blood products, the department [DHSS] is considering the publication of a leaflet indicating the circumstances in which blood donations should be avoided.<sup>148</sup>

**9.109** ‘No conclusive evidence’, appears to have been a recurring form of words used with some frequency at this time. In a letter to the Association of Scientific, Technical and Managerial Staffs (ASTMS), undated but marked as received on 26 August 1983, Lord Glenarthur referred to the need to emphasise that ‘there is no conclusive evidence that AIDS is transmitted through blood products’.<sup>149</sup> The leaflet anticipated in Lord Glenarthur’s reply on 14 July was issued on 1 September 1983 for use throughout the United Kingdom.<sup>150</sup> A Press Release issued to accompany the leaflet stated: ‘there is no conclusive proof that the disease [AIDS] can be transmitted in blood or in blood products’.<sup>151</sup> On 14 November 1983, in answering a Parliamentary Question in the House of Commons by Edwina Currie MP, Kenneth Clarke MP, Minister of State for Health and Social Services, said: ‘There is no conclusive evidence that acquired immune deficiency syndrome (AIDS) is transmitted by blood products’.<sup>152</sup>

**9.110** In contrast, the leaflet issued on 1 September 1983 for distribution to blood donors included in the series of questions and answers the following: ‘Can AIDS be transmitted by transfusion of blood and blood products?’ with an answer which began: ‘Almost certainly yes ...’, explaining that the risk of transmission was higher to people with haemophilia than to recipients of ordinary blood transfusions.<sup>153</sup>

**9.111** The Haemophilia Society was concerned that there should be no attempt to suspend the importation of US commercial products in the absence of ‘definite evidence’ that that would be necessary. On 15 August 1983, the Coordinator of the Society wrote to a government official regarding a meeting arranged between representatives of the Society and Lord Glenarthur to take place on 8 September 1983.<sup>154</sup> Avoiding the banning

<sup>147</sup> Hansard, 14 July 1983, columns 893–894 [SGH.002.6720]

<sup>148</sup> Ibid [SGH.002.6720] at 6721

<sup>149</sup> Letter to ASTMS [DHF.001.4718]

<sup>150</sup> Leaflet – ‘AIDS and how it concerns blood donors’ [SGH.002.6675]

<sup>151</sup> Press notice [SNF.001.0416]. Compare a draft of this press release which continued to state that ‘there is no conclusive evidence that AIDS is transmitted through blood or blood products’ [SGH.002.6668] at 6672.

<sup>152</sup> Hansard extract [DHF.001.5064]

<sup>153</sup> Leaflet – ‘AIDS and how it concerns blood donors’ [SGH.002.6675] at 6676

<sup>154</sup> Letter from the coordinator of the Haemophilia Society [DHF.001.4691]. The identity of the recipient of the letter has been removed by redaction.

of importation of concentrates from the USA was one of the issues the Society wanted to discuss. An undated file copy of a letter from Lord Glenarthur to the society records points made at the meeting.<sup>155</sup> He commented that, in considering whether the importation of blood products from the USA should cease, it was deemed necessary to weigh the possible risks of infection with AIDS against the obvious risks arising from inadequate supplies of Factor VIII. He noted that the FDA in the USA had introduced regulations designed to exclude plasma donors presenting a high risk of AIDS but that there was still a considerable quantity of pre-March 1983 stock, both in the UK and in the USA awaiting export. The FDA had decided not to ban the use of this stock, since doing so would cause a crisis in supply, in both the UK and the USA.<sup>156</sup> Importation would, on this view, continue.

**9.112** By letter dated 13 December 1983, Lord Glenarthur wrote to John Maples MP, who had enquired about the government's assessment of risk in light of recent press reports. The letter stated that the cause of AIDS was as yet unknown and that there was no conclusive proof that the disease had been transmitted by US blood products.<sup>157</sup> It proceeded to repeat the information given to the Haemophilia Society that importation would continue, including stock collected before the regulations introduced by the FDA from March 1983.

**9.113** On 5 January 1984, another letter was sent by Lord Glenarthur to the ASTMS. The first full paragraph of the letter appears to indicate that the official view had become qualified (emphasis as in original):

It remains the case that there is no conclusive evidence of the transmission of AIDS through blood products, although the circumstantial evidence is strong.<sup>158</sup>

**9.114** The Department of Health papers also include a photocopy of an article from *The Sunday Times* of 25 March 1984 which records:

Doctors now have conclusive proof that the mysterious and generally fatal ailment known as AIDS has been passed to a hospital patient through a blood transfusion.<sup>159</sup>

**9.115** On what appears to be the reverse of this photocopy, someone has written:

We dropped "there is no conclusive proof that AIDS is transmitted through blood or blood products" from our standard line some time ago.<sup>160</sup>

**9.116** The evidence available suggests that the line was dropped between January and March 1984.

**9.117** It appears that, until the spring of 1984, a highly nuanced use of language had been adopted in communicating the government's position and the Inquiry sought to explore the situation. Within the papers released by the Department of Health, there was

<sup>155</sup> Lord Glenarthur's letter [DHF.001.4573]

<sup>156</sup> At the meeting of the Biological Sub Committee of the CSM on 13 July, it had been commented that concentrates from the USA to be used in the UK should be derived from plasma complying with those regulations, provided supply could be assured. See [DHF.002.8865] at 8866

<sup>157</sup> The Archer Inquiry Report, pages 51–52

<sup>158</sup> Lord Glenarthur's letter, 05 Jan 1984 [SGH.007.6160]

<sup>159</sup> 'New Aids alarm over blood link' – *The Sunday Times*, 25 March 1984 [DHF.001.5335]

<sup>160</sup> Hand-written note [DHF.001.5334]

a photocopy of an excerpt from *The Guardian* published on 19 November 1983 referring to the Bristol haemophilia patient who had died of AIDS (see paragraph 9.125 below). Along the foot of the photocopy, in a handwritten note which appears to have been dated 23 November, the following is written:

Have you seen [this]? On X [a section marked in the article about the Bristol patient] is it OK for me to continue to say "there is no conclusive proof that the disease has been transmitted by American blood products". PS Congratulations on your promotion.<sup>161</sup>

**9.118** In different handwriting, along the top, there is what appears to be a response:

Thanks. Yes it is OK.<sup>162</sup>

**9.119** In 2010, the Inquiry was advised by the Department of Health that the first note was written by a middle-ranking official and that the response was by Dr Diana Walford.<sup>163</sup>

**9.120** The Inquiry asked Dr Walford about the formulation and maintenance of the standard line. With particular reference to the question in November 1983 concerning whether it was OK to say that there was no conclusive evidence of a link between AIDS and blood products, Dr Walford replied that 'given the state of knowledge about AIDS and its causative agent at that time, this was the appropriate answer to the question as posed'.<sup>164</sup>

**9.121** Before testifying at this Inquiry, Dr Winter had provided evidence to the Archer Inquiry. He had said in his submission:

In November 1983, the Health Minister, Kenneth Clark [sic], announced in Parliament that "there was no evidence that AIDS is transmitted by blood products".<sup>165</sup>

**9.122** It was suggested to Dr Winter that his recollection of what Mr Clarke had said was incorrect. In relation to the words 'no conclusive evidence', Dr Winter commented:

What, if you like, I objected to is the clear sentiment. The sentiment is saying, "We have no good evidence that AIDS is due to blood products". I mean, all haemophilia clinicians by this stage clearly believed that commercial blood products could and were transmitting AIDS. So it would have been more appropriate if the Secretary of State had said something to that effect, rather than using that form of words, with its implication that there remained doubt. Technically he was correct but I don't think he realised how fortunate he was, in terms of that, really.<sup>166</sup>

**9.123** The Inquiry is sympathetic to Dr Winter's observations. It is not at all clear what evidence one requires beyond that required for 'near certainty' (the view of the association set out in the leaflet of 1 September 1983) to amount to 'conclusive proof' or 'conclusive

<sup>161</sup> *The Guardian*, 'US Blood Caused AIDS', *The Guardian*, 01 November 1983 [DHF.001.5006]

<sup>162</sup> Hand-written note [DHF.001.5006]

<sup>163</sup> Letter from DoH to the Inquiry, 14 October 2010 [PEN.015.0484]. At that time, Dr Walford was a senior medical civil servant and the medical member of the secretariat to the Advisory Committee on the National Blood Transfusion Service for England and Wales.

<sup>164</sup> Letter from Dr Walford [PEN.010.0079]

<sup>165</sup> Dr Winter's submission to the Archer Inquiry [PEN.015.0283]

<sup>166</sup> Day 16, page 88



evidence' of an association between blood and blood products and transmission of an infective agent in the public health area. The risk of misinterpretation, as evidenced by Dr Winter's comments, appears to have been real, though the Inquiry cannot know whether the use of the standard line did in fact mislead any individual or body. As matters stood, it was not until mid-1984 that there was general (though not even then universal) acceptance that AIDS was caused by parenteral transmission of HIV, as discussed in Chapter 11, *AIDS Aetiology*. As Dr Winter noted, the official position was 'technically' correct, but it risked contributing to a false sense of security. However, at this stage the incidence of AIDS in the UK remained low.

**9.124** Of the 14 cases of AIDS reported to the UK CDSC by 31 July 1983, six were cases of KS without PCP, five were cases of PCP without KS and three involved other opportunistic infections.<sup>167</sup> Five patients, all adult homosexual men, had died. One of the 14 patients, the youngest at 20, was a haemophilia patient.<sup>168</sup>

**9.125** On 10 September 1983, Dr Craske issued an update on the UKHCDO investigation of AIDS cases in patients with blood coagulation disorders.<sup>169</sup> 'The Cardiff patient – reported as a possible case of AIDS in the CDSC Bulletin for the week ending 6 May 1983 – remained in reasonable health.<sup>170</sup> 'The Bristol patient', a mildly affected haemophilia patient aged 57 and considered to be a mild or prodromal case of AIDS (signalling the onset of disease), had remained unwell through June and July and died in August. A post-mortem had revealed PCP. This was considered to be the first confirmed case of death from AIDS possibly associated with transfusion of blood products in the UK. The case clearly met the criteria decided on 13 May: the patient had developed intractable disease. The same cases were reported to the UK Haemophilia Centre Directors' Hepatitis Working Party on 14 September 1983.<sup>171</sup>

### *Haemophilia Reference Centre Directors' meeting*

**9.126** A meeting of the Haemophilia Reference Centre Directors was held on 19 September 1983.<sup>172</sup> Scotland was represented at this meeting by Professor Ludlam. The minutes of the meeting recorded that Dr Craske's paper updating the situation regarding AIDS in the UK was discussed at length.<sup>173</sup> Professor Bloom said that Dr Galbraith of the CDSC was somewhat concerned that he had not heard about the Bristol patient who had died of AIDS. Differing views were expressed about whether it was the responsibility of the centre directors themselves to report directly to the CDSC as well as to Dr Craske. It was agreed that reporting to the CDSC should be through Dr Craske after discussion with the doctor involved in the patient's management. It was also agreed that patients who had received the same batches of NHS or commercial Factor VIII as the Bristol patient should be followed-up. Dr Craske stressed the need for a properly conducted epidemiological study of AIDS in the haemophilia population. It was noted that Dr Peter Jones (Newcastle Haemophilia Centre) and Dr Forbes were both taking part in a forthcoming international study.

<sup>167</sup> 'Surveillance of the acquired immune deficiency syndrome in the United Kingdom, January 1982–July 1983, *British Medical Journal*, 1983; 287:407–408 [LIT.001.0232] at 0233; Preliminary Report, para 8.44

<sup>168</sup> This appears to be the same patient as was reported in the Bulletin of 6 May 1983.

<sup>169</sup> Haemophilia Centre Directors AIDS Investigation – Surveillance of AIDS Cases in Patients With Blood Coagulation Disorders [SNB.001.7556]. Preliminary Report, para 8.48

<sup>170</sup> CDSC report for week ending 6th May 1983 [PEN.015.0244]

<sup>171</sup> Minutes of the 12th Meeting of the UK Haemophilia Centre Directors' Hepatitis Working Party held at the Oxford Haemophilia Centre on 14 September 1983 [LOT.003.5434]

<sup>172</sup> Minutes of the Haemophilia Reference Centre Directors meeting [LOT.003.2862]

<sup>173</sup> *Ibid* [LOT.003.2862] at 2864

**9.127** Professor Bloom's update of the May AIDS circular prepared for the Haemophilia Society was approved by the Haemophilia Reference Centre Directors. It was released as a fact sheet, called 'Haemofact A.I.D.S. Release No 2', on 22 September 1983.<sup>174</sup> It reported that there had been one death recorded in a person with haemophilia (the Bristol patient) and that there remained one other suspected case in Cardiff. There had been no other cases relevant to haemophilia patients reported to the PHLS. In the summary, the leaflet stated that the Society had maintained close liaison with all relevant personnel and government departments to ensure the Society's views were known.

**9.128** A representative of the DHSS (probably Dr Diana Walford, the only representative of the Department in attendance) drafted a note of the Haemophilia Reference Centre Directors' meeting. She wrote that the relatives of the man who died in Bristol had taken legal advice and were keen to sue the manufacturers (Alpha and Immuno) of the commercial concentrate which he received in 1981. The author commented: 'If they go ahead, this could put the cat among the pigeons'.<sup>175</sup>

**9.129** The two confirmed cases were reported on 27 September 1983 to the UK Working Party on Transfusion Associated Hepatitis. The current position on AIDS was reviewed by Dr Craske.<sup>176</sup> He reported 20 AIDS cases in the UK, including the two haemophilia patients. In discussion, Dr Howard Thomas of the Royal Free Hospital, London, questioned the diagnoses, especially in the case of the Bristol patient. There was renewed concern among the Directors about responsibility for reporting suspected cases of AIDS. The report of the UKHCDO Hepatitis Working Party (under the chairmanship of Dr Craske) for 1982–83 was published on 28 September 1983.<sup>177</sup> It stated that, up to that time, 16 cases of the syndrome which fitted the criteria used by the CDC and were associated with the transfusion of Factor VIII concentrate had been reported in the USA. Five cases had been reported from Europe. This included a suspect case notified recently in the UK, notified shortly before publication. The report did not disclose the total number of UK cases within the European total. Having regard to the information provided on 27 September, the report was already out of date.

**9.130** The varying descriptions of the patients and their signs and symptoms cause some uncertainty as to the precise numbers of haemophilia patients affected by AIDS at this stage. It appears highly likely, however, that there had been two only who had reached the stage of developing intractable disease, as stipulated by the CDC criteria, and that one of the patients had died in August 1983.

### *Medical Research Council Working Party on AIDS*

**9.131** On 10 October 1983, the Medical Research Council (MRC) Working Party on AIDS met.<sup>178</sup> The position on AIDS was reviewed. The manifestations of AIDS were noted to vary according to both host and environmental factors. The underlying difficulties in assessing the extent of the disease at this time are reflected in some of the discussion reported:

The pattern emerging in early UK cases seemed different in some respects from the American experience .... The laboratory markers for disease were

<sup>174</sup> Fact Sheet [DHF.001.4767]

<sup>175</sup> Redacted memorandum [DHF.001.4759]

<sup>176</sup> Note of Meeting of UK Working Party on Transfusion Associated Hepatitis – Tuesday 27 September 1983 [SNF.001.1039] Preliminary Report, para 8.50

<sup>177</sup> UK Haemophilia Hepatitis Working Party – Annual Report for the Year 1982–3 [SNF.001.0948]. This is labelled Appendix C. AIDS is mentioned in Appendix C(i) page 4

<sup>178</sup> Minute of Medical Research Council meeting [SNF.001.3759]

well established for AIDS itself but their relevance in screening and in a possible precursor state was not established. The problems of definition and interpretation of these so called precursor syndromes were outlined by several members.<sup>179</sup>

**9.132** The special features arising in relation to haemophilia were discussed. There were said to be varying and considerable periods of incubation (one to four years). It was noted that:

The possibility that AIDS as currently defined was the tip of an iceberg in terms of the range of clinical or subclinical responses to infection with a putative AIDS agent was mentioned; it was recognised that the existence of milder forms would be hard to establish without a marker for such an agent.<sup>180</sup>

**9.133** In reviewing available information on epidemiology, it was noted that in the USA the pattern of the number of cases doubling every six months appeared to be continuing. The UK figure (now standing at 24 cases) indicated that there had been a recent increase almost conforming to a six-month doubling time. It appears from the report of the discussion that, at least among the members of this group, there was an apprehension that the current definition of AIDS for reporting purposes was failing to produce data reflecting the full extent of the problem.<sup>181</sup>

#### *Further meetings*

**9.134** On 17 October 1983, at a meeting of the Advisory Committee of the National Blood Transfusion Service, Dr Walford, DHSS, said that there had been 24 cases of AIDS reported in the UK, two of whom were haemophilia patients and one of whom had died, and that comparison with 'reported incidence in the UK [*sic* – US<sup>182</sup>] haemophilia population' suggested that the UK could anticipate between two to four deaths from the disease among people with haemophilia from the disease.<sup>183</sup> Unfortunately this was to prove to be a considerable underestimate but it may have reflected her understanding of experience in the USA to that date. There was by that stage, in the official view as represented by Dr Walford, 'no conclusive proof of a link between AIDS and blood products' that might have instructed a different assessment of the risk.

**9.135** At the 14th meeting of the UK Haemophilia Centre Directors on the same day, 17 October 1983, Dr Craske presented his paper on AIDS.<sup>184</sup> He outlined his proposals for investigating the UK cases of AIDS in haemophilia patients and proposed follow-up for three years of patients who had received 'suspect batches of concentrate.'

<sup>179</sup> Ibid [SNF.001.3759] at 3760

<sup>180</sup> Ibid [SNF.001.3759] at 3760

<sup>181</sup> Ibid [SNF.001.3759] at 3761

<sup>182</sup> Dr Walford's comment would make better sense if the comparison had been with the reported incidence of AIDS in the 'US' haemophilia population. WHO intelligence at the end of 1983 reported 19 US cases of AIDS in haemophilia patients with no other known risk factor [SNF.001.2575] at 2577, a rate of about 0.09% of the US haemophilia population, with a high mortality. This data would have indicated a very low number for AIDS deaths in the UK haemophilia population of 2167 at 1983 of fewer than two.

<sup>183</sup> Minutes of the Eighth Meeting of the Advisory Committee on the National Blood Transfusion Service Held on 17 October 1983 [SGH.001.8446] at 8449. Dr Walford had attended the meeting of the MRC Working Party on AIDS as a Departmental Observer [SNF.001.3759]

<sup>184</sup> Minutes of the 14<sup>th</sup> UK Haemophilia Centre Directors meeting [SNB.001.7517]

**9.136** Dr Robert Perry of the PFC prepared a note of the meeting in which he listed the numbers and categories of people with AIDS in the USA.<sup>185</sup> He then wrote in relation to the USA:

Crude interpretation of these figures provides the following risk statistics.

Transfusion – 1 in 500,000 at risk

Haemophiliacs – 1.2 in 1000 at risk

Conclusion – Serious disease in haemophiliacs a low possibility??<sup>186</sup>

**9.137** For haemophilia patients the risk factor reflected the information that there had been 15 cases with AIDS in the USA reported at that time. Dr Perry noted the UK situation, as reported, to be that there were 22 patients who met the NIH criteria, 10 of whom had died, and two who were haemophilia patients. Again, comparison with US experience, as understood at the time, would have suggested that very few UK haemophilia patients were at risk of death from AIDS.

**9.138** *The Guardian* of 19 November 1983 reported that the Bristol patient who had died of AIDS in August almost certainly caught the disease from contaminated supplies of imported Factor VIII,<sup>187</sup> quoting from a letter by Bristol clinicians published in *The Lancet* of that date.<sup>188</sup> The haemophilia patient, otherwise fit, had undergone surgery in December 1981 and had received intensive treatment with Factor VIII of US origin. Over 12 days he received 48,253 international units of freeze-dried Factor VIII, his first exposure to commercial concentrate having previously received NHS cryoprecipitate and concentrate manufactured at the Blood Products Laboratory (BPL – the manufacturer of NHS blood products in England and Wales), Elstree, over 10 years at an average rate of 5000 units per annum. His deteriorating condition was traced from the emergence of signs and symptoms early in 1982 until his death. The letter stated:

The diagnosis of AIDS is essentially clinical but our patient met the Centers for Disease Control's criteria in that, without any known cause for immunodeficiency, he had *P. carinii* pneumonia.

**9.139** The patient had become unwell a few weeks after receiving the treatment. The writers thought it highly probable that the development of AIDS was related to his treatment.

**9.140** Dr McClelland and Mr John Watt (Director of the PFC) represented the SNBTS at a WHO conference held in Geneva between 22 and 25 November 1983.<sup>189</sup> The draft report of the conference was circulated on 14 December 1983<sup>190</sup> and contained European data up to October 1983.<sup>191</sup> By 20 October, 268 cases of AIDS had been reported to the European Regional Office of the WHO.<sup>192</sup> These included 24 from the UK (17 diagnosed in 1983) and 42 from the Federal Republic of Germany, as already noted (but none from the GDR, the Soviet part of the country). Reported from France were 94 cases (47 in 1983)

<sup>185</sup> Note of the 14<sup>th</sup> UK Haemophilia Centre Directors meeting [SNB.001.7531]. From surrounding documents, it appears that this was prepared by Dr Perry.

<sup>186</sup> Ibid [SNB.001.7531] at 7533

<sup>187</sup> 'US blood caused AIDS', *The Guardian*, 01.11.1983 [DHF.001.5006]

<sup>188</sup> Daly and Scott, 'Fatal AIDS in a haemophiliac in the UK', *The Lancet*, 19 November 1983 [LIT.001.0413]

<sup>189</sup> WHO Meeting on Acquired Immune Deficiency Syndrome Emergencies – Geneva 22 – 25 November 1983 – List of Participants [SNB.002.0306]. See Preliminary Report paragraph 8.65 for a more extensive discussion of this conference.

<sup>190</sup> Acquired Immunodeficiency Syndrome – An Assessment of the Present Situation in the World [SNF.001.2575]; Covering letter dated 14 December 1983 [SNF.001.2574]

<sup>191</sup> Acquired Immunodeficiency Syndrome – An Assessment of the Present Situation in the World [SNF.001.2575] at 2609, Table 3

<sup>192</sup> Ibid [SNF.001.2575] at 2609, Table 3

and, from Belgium, 38 cases (24 in 1983). For Europe, four per cent of cases were said to be in people with haemophilia.<sup>193</sup> Coagulation factor concentrates had been implicated. Dr McClelland prepared an initial report on the meeting dated 5 December 1983 for the Scottish Regional Transfusion Directors.<sup>194</sup> The directors met on 8 December and discussed AIDS.<sup>195</sup> Dr McClelland reported that the WHO had received a report of two cases of AIDS in haemophilia patients in the UK. The number of reported cases remained low at this stage.

**9.141** It is apparent that, apart from the general concerns noted by the MRC Working Party on AIDS on 10 October 1983, there was still little anxiety about the position in Scotland at this point. However, media comment was soon to follow. An article by Dr Galbraith in *The Lancet* of 10 December 1983 noted two new UK cases, bringing the total to 26, which included the two haemophilia patients previously recorded.<sup>196</sup> This was taken up in *The Guardian* of 9 December 1983, in which Andrew Veitch, medical correspondent, commented on the emerging pattern, and also noted that the DHSS had reported two new deaths, bringing the total to 12.<sup>197</sup> The comment was balanced and well informed but, in the wider political context, it provided a focus for increasing concern, though the numbers of British haemophilia patients reported as having symptoms remained small at the time. He reported the additional cases and, in the case of haemophilia patients, wrote:

The victims include two haemophiliacs, one of whom died, who are thought to have contracted the disease from contaminated supplies of Factor VIII, the blood clotting agent, imported from the US.

The risk of haemophiliacs developing the disease are put into perspective today by Dr Peter Jones, director of the Newcastle upon Tyne haemophilia centre.

He calculates, in a leading article in the *British Medical Journal*,<sup>198</sup> that the incidence of Aids among haemophiliacs here and in US is about 0.8 per thousands.

....

Fears among British specialists that Aids arrived from the US two years ago and may reach epidemic proportions next year, are born [*sic*] out today by a report from doctors at West Germany's federal Aids working group headquarters in Berlin.

So far 44 cases have been registered and 14 have died, they write in the *Lancet*. Clusters of cases have been identified in Munich, Frankfurt and Berlin.

They warn: 'These data indicate ... that the epidemic is now spreading within the German homosexual community and may increase exponentially. The incubation period of Aids infection suggests that the increase will parallel that observed in 1981-82 in the US, but with a time lag of 1 ½ - 2 years.'

<sup>193</sup> Ibid [SNF.001.2575] at 2578

<sup>194</sup> Initial Report for Scottish Regional Transfusion Directors Meeting on 8 December 1983 [SNF.001.0552]

<sup>195</sup> Minutes of Directors Meeting Held on Thursday 8 December 1983 [SNF.001.0178]

<sup>196</sup> McEvoy and Galbraith, 'Haemophilia and AIDS in the UK', *The Lancet*, 10 December 1983 [LIT.001.0580]

<sup>197</sup> *The Guardian*, 9.12.1983 [SGF.001.0944] Clearly Mr Veitch had advance sight of *The Lancet* letter as the letter to which he referred was, in fact, published the following day, 10 December.

<sup>198</sup> Jones, 'Acquired immunodeficiency syndrome, hepatitis, and haemophilia', *British Medical Journal*, 10 December 1983 [LIT.001.0243]. Again, Mr Veitch appears to have had advance sight of this publication in writing his report.

**9.142** Dr Jones' calculation was no doubt intended to indicate that the incidence of AIDS among haemophilia patients was low (though broadly consistent with other contemporaneous data) but equating the UK risk with the risk in the USA was unlikely to be comforting to those who had believed that the disease was a phenomenon particularly associated with the USA. Nevertheless, although the trends were beginning to be well established in the USA, it remained the position that, at the end of 1983 and into 1984, AIDS was still not seen by clinicians and officials in this country as presenting a major threat to haemophilia patients in the UK.

**9.143** A meeting arranged by the NIBSC to examine the infectious hazards of blood and blood products, with particular reference to hepatitis and AIDS, was held on 9 February 1984.<sup>199</sup> The SNBTS was represented by Professor John Cash and Dr McClelland. Dr Thomas reported that the most recent information indicated that two UK patients and nine other European patients with haemophilia had contracted AIDS. A recent report from the CDC had also identified 31 people in the USA who had been recipients of a blood transfusion and who had subsequently contracted AIDS.<sup>200</sup> Dr Craske reported on the two UK haemophilia patients who had contracted AIDS, one of whom had died.<sup>201</sup> Concentrates had been received by 231 other patients from one or more of the nine batches used in the case of the two infected patients. These other patients were traced but none had developed AIDS by that point.<sup>202</sup>

**9.144** A report by doctors at the Glasgow Western Infirmary of what appears to have been the first reported case of AIDS in Scotland was published on 11 February 1984.<sup>203</sup> The report, accepted for publication on 3 October 1983, concerned a man who had returned to the UK after working in east Africa for many years and who fulfilled the criteria for AIDS. The signs and symptoms of disease found were said to suggest a disorder of cell-mediated immunity but gave no insight into its cause. The discussion focused on the efficiency of serological testing.

### *European survey*

**9.145** On 30 June 1984 *The Lancet* published an article by Professor Bloom of Cardiff giving the results of his survey of European haemophilia centres.<sup>204</sup> Together with previous data, the survey pointed to 11 cases of AIDS in 13,147 treated haemophilia patients (0.08%). Commenting on his survey of AIDS in Europe at the end of 1983 and early 1984, Professor Bloom wrote:

A relation of AIDS and the other reported disorders to transfusion of imported blood products was not established .... [T]he role of American concentrates in the causation of AIDS in European haemophiliacs must be regarded as unproven .... In view of the immense benefits that haemophiliacs have derived from treatment physicians are naturally reluctant to abandon these agents, with

<sup>199</sup> Draft Minutes of Meeting on the Infectious Hazards of Blood Products NIBSC, 9 February 1984 [SNB.004.8628]; Preliminary Report, para 8.75

<sup>200</sup> Draft Minutes of Meeting on the Infectious Hazards of Blood Products NIBSC, 9 February 1984 [SNB.004.8628]

<sup>201</sup> Daly and Scott, 'Fatal AIDS in a haemophiliac in the UK', *The Lancet*, 19 November 1983 [LIT.001.0413]

<sup>202</sup> Meeting on the Infectious Hazards of Blood Products NIBSC, 9 February 1984 [SNB.004.8628] at 8630

<sup>203</sup> Shiach et al, 'Pyrexia of undetermined origin, diarrhoea, and primary cerebral lymphoma associated with acquired immunodeficiency', *British Medical Journal*, 1984; 288:449-450 [LIT.001.0219]; Preliminary Report, para 8.76

<sup>204</sup> Bloom, '[AIDS] and other possible immunological disorders in European haemophiliacs', *The Lancet*, 1984; 1452-55 [LIT.001.0409]; Preliminary Report, para 8.87

their hypothetical dangers, in the absence of alternative concentrates which have been proven safer. This attitude may change as information accrues, and haemophilia treatment needs to be monitored world-wide.<sup>205</sup>

**9.146** He stated that no haemophilia patient with AIDS definitely related to transfusion of blood products was reported from West Germany where very large amounts of US Factor VIII concentrates had been used for many years.<sup>206</sup>

**9.147** Reports of cases outside the USA continued to be published. An example, which later came to have relevance in Scotland as part of a comparative study, was a letter in *The Lancet* of 7 July 1984 by Dr Mads Melbye and others dealing with a group of Danish haemophilia patients who had been treated with US Factor VIII concentrate.<sup>207</sup> Of the 22, among the first outside the USA to be tested, 14 were anti-HTLV-III positive.<sup>208</sup>

**9.148** Until this point, reporting in the UK continued to be limited to cases of overt AIDS and AIDS-related diseases. That was to change in the second half of the year for reasons (discussed in Chapter 10, *Knowledge of the Geographical Spread and Prevalence of HIV/AIDS 2*) relating to the discovery of LAV/HTLV-III and the consequent ability, shown by Melbye above, to test for the presence of antibodies to the virus, although those discoveries did not have an impact on reporting until the autumn of 1984. As discussed in Chapter 11, *AIDS Aetiology*, the cause of AIDS remained controversial into 1984. With important exceptions, there was little attention paid to the first of the discoveries, the isolation of a Lymphadenopathy Associated Virus (LAV) published in May 1983 by Montagnier and Barré-Sinoussi of the Institut Pasteur in France.

## Summary

**9.149** By July 1984 the following was known:

- AIDS first affected individuals in the USA in 1978 and in the UK in 1979.
- The first recorded cases of seroconversion in Scotland occurred in 1982.
- The first reports of AIDS in the USA were published in June 1981, indicating that the disease might be associated with a significant prodromal period before overt signs and symptoms became apparent.
- Throughout the period covered in this chapter, the disease was considered to be very largely a US problem.
- An early association of AIDS exclusively with sexual behaviour was undermined by emerging reports of cases not associated with such behaviour.
- Knowledge of AIDS among medical practitioners in the UK generally was patchy throughout this period, with few clinicians having direct experience of the disease. Published material was of specialist rather than general interest.

<sup>205</sup> Ibid [LIT.001.0409] at 0412 (See, for example, Professor Bloom's comments.)

<sup>206</sup> Ibid [LIT.001.0409] at 0412

<sup>207</sup> Melbye 'High prevalence of Lymphadenopathy Virus (LAV) in European haemophiliacs', *The Lancet*, 1984; 40–41 [LIT.001.0423]; Preliminary Report, para 8.90

<sup>208</sup> Interestingly, when the research was published in December, it was said that 59% of the Danish patients were infected. 59% of 22 would be 13, not 14.

- Incomplete reporting of instances of AIDS, in the UK and throughout Europe, but especially in Germany, supported a misapprehension in the UK, prevalent until autumn 1983, that blood products imported from the USA were not likely to be associated with transmission of infection to blood disorder patients.
- The epidemic was well established in the USA by July of 1984 both generally and in relation to blood disorder patients.
- Until mid-1984, diagnosis of AIDS in UK patients receiving blood transfusions or blood, blood component or blood product therapy depended on clinical evidence of intractable disease, particularly opportunistic infection such as PCP.
- It was known that the development of opportunistic infection was preceded by cell-mediated immune deficiency, over a period that might be variable but remained significant. However, immune deficiencies, of whatever order of magnitude, were not thought to be diagnostic of a condition likely to progress to AIDS except in very few cases.
- It remained a common view among most commentators in the UK until July 1984 that the cause of AIDS was unknown and that it had not been established that it resulted from transmission of a specific agent in blood products.
- Some scientists, such as fractionation specialists, thought that AIDS was caused by a transmissible agent that could be found in blood and blood products.
- It was believed among haemophilia clinicians that there would be few cases of AIDS among UK blood disorder and transfusion patients.
- Throughout this period, blood disorder therapy continued to include the use of imported commercial factor concentrates from the USA.



## CHAPTER 10

### KNOWLEDGE OF THE GEOGRAPHICAL SPREAD AND PREVALENCE OF HIV/AIDS 2

#### Introduction

**10.1** Until mid-1984, official reports of AIDS cases in the UK, as set out in the last chapter, were of 26 infected individuals, of all populations at risk, of whom two were haemophilia patients. One of the haemophilia patients had died. The diagnosis of AIDS depended on the identification of intractable AIDS-defining disease, at least moderately predictive of a defect in cell-mediated immunity, occurring in a person with no known cause for diminished resistance to that disease ('the CDC criteria').<sup>1</sup> The diseases included Kaposi's sarcoma (KS) and *Pneumocystis carinii* pneumonia (PCP), but covered a wider range for reporting purposes.<sup>2</sup> Evidence of impaired cell-mediated immunity was not reportable; it was not considered sufficient for classification of a case of AIDS. The lack of a requirement for reporting impaired cell-mediated immunity was due particularly to the belief that only a very small number of those so affected might progress to full-blown AIDS. Perceptions of the risk of progression to an AIDS-defining disease changed slowly over a period of two to three years.

**10.2** Meantime, scientific research increased awareness of the prevalence of HIV infection in the UK and quickly demonstrated that the populations at significant risk of progressing to life-threatening disease were, in numerical terms, considerably greater than had previously been appreciated. The major developments happened in late 1984 and 1985. The science is discussed in Chapter 29, *The Discovery of HIV and Development of Screening Tests*. The present chapter is concerned with developing knowledge of the epidemiology and natural history of HIV/AIDS from mid-1984 but principally in the second half of the 1980s.

#### United Kingdom research towards testing for HTLV-III/LAV

##### *Development of the Weiss/Tedder research assay*

**10.3** In early 1984, Professor Robin Weiss of the Chester Beatty Laboratories<sup>3</sup> and Professor Richard Tedder of the Middlesex Hospital Medical School<sup>4</sup> were engaged in research aimed at developing an assay for the detection of HTLV-III/LAV-1 in human blood.<sup>5</sup> They had available, for research purposes only, HTLV-III isolate provided in February 1984 by Mikulas Popovic and Robert Gallo of the National Cancer Institute, Bethesda, and LAV-1 provided in May by Luc Montagnier of the Institut Pasteur, Paris. Their studies showed that the two viruses, later re-designated HIV, were indistinguishable.<sup>6</sup> For the purposes of this chapter, the relevant part of their research related to the study of the prevalence of antibodies to HTLV-III in UK subjects using the Gallo material. They collected sera from 2000 individuals from a wide range of populations, including AIDS patients with clinically diagnosed KS or PCP; patients with PGL (persistent generalised lymphadenopathy: enlarged lymph nodes, a condition that occurs frequently in the latent period of HIV infection); sexual contacts of

<sup>1</sup> *MMWR*, 24 September 1982; 31(37): 507-8 [LIT.001.0540]

<sup>2</sup> See, for example, [DHF.002.3521], a form for reporting patients with coagulation defects who met the UK Haemophilia Centre Directors Hepatitis Working Party survey criteria for AIDS.

<sup>3</sup> Professor Weiss is currently Emeritus Professor of Viral Oncology at UCL Medical School.

<sup>4</sup> Professor Tedder is currently Professor of Medical Virology at UCL Medical School.

<sup>5</sup> See Chapter 29, *The Discovery of HIV and Developments Screening Tests*

<sup>6</sup> Cheingsong-Popov et al, 'Prevalence of antibody to human t-lymphotropic virus type iii in aids and aids-risk patients in Britain', *The Lancet*, 1 September 1984 [LIT.001.0417] at 0419

AIDS patients; homosexual patients positive for Hepatitis B or syphilis and symptom-free cohorts of homosexual volunteers; heterosexual subjects recruited from genito-urinary medicine clinics; intravenous drug users (IVDUs) screened for Hepatitis B; haemophilia patients undergoing regular replacement therapy with clotting factor concentrates; and 1000 randomly selected blood donors. Sera from haemophilia patients had been collected at the Oxford Haemophilia Centre from 1982 onwards and were provided by Dr Charles Rizza, the Director of the centre. Sera from IVDUs were collected in 1983 and 1984. Sera from the other groups had been collected between June 1983 and July 1984. As will be seen in Chapter 29, *The Discovery of HIV and Development of Screening Tests*, the research programme was an extension of earlier research into other retroviruses which expanded to include LAV/HTLV-III. The chronology is important in understanding the relationship between their work and research by others in the field. What they found and the timing of the publication of their findings are the current issues.

**10.4** The results of their research were published on 1 September 1984 by Dr Rachanee Cheingsong-Popov, Professor Weiss, Professor Tedder and others.<sup>7</sup> They commented that there had previously been reported only limited studies of antibody prevalence in groups at risk for AIDS. All of the reports cited were published in 1984. That limitation was consistent with the previous lack of an effective assay and the focus on intractable disease as the prerequisite of an AIDS diagnosis. Attention began to shift from diagnosis of AIDS on that basis to testing for anti-HTLV-III in the course of the year and this landmark paper made a major contribution to the change. The researchers found a striking prevalence of seropositivity<sup>8</sup> among members of the risk groups, including a high prevalence among haemophilia patients who had received pooled clotting factor products (34%). The results for the risk groups studied fitted a pattern that strongly suggested an agent transmissible by sexual or blood contact. The opinion remained tentative, however, and views of the prognosis for those infected were qualified. The article stated:

Even if HTLV-III is causally related to AIDS and PGL, as is strongly suggested by the evidence, we should not assume that these disorders will develop in all patients infected with this retrovirus. Symptomless seroconversion or seroconversion accompanied by mild symptoms is often seen for many infections, including retroviruses. Although it is too early to draw firm conclusions, it seems possible that overt disease will not develop in at least some, and perhaps the majority, of seropositive subjects. On the other hand, the long latent period and a possible role for co-factors in determining the expression of disease make such a suggestion tentative.<sup>9</sup>

**10.5** They commented that the risks had to be set against the relatively low incidence of disease in the haemophilia risk group (roughly 1:1000 as reported at that time) and, further, that the likelihood was that infection resulted from commercial rather than NHS concentrates. There was said to be a relatively low risk at that time of acquiring HTLV-III or AIDS from blood transfusion in the UK.

<sup>7</sup> Ibid [LIT.001.0417] at 0419

<sup>8</sup> That is, showing a significant level of HIV antibodies indicating infection with HIV.

<sup>9</sup> Cheingsong-Popov et al, 'Prevalence of antibody to human t-lymphotropic virus type iii in aids and aids-risk patients in Britain' *The Lancet*, 1 September 1984 [LIT.001.0417] at 0419

### Research in Glasgow

**10.6** At about the same time, a similar view was being formulated in Glasgow. In October 1983, Dr Karin Froebel and colleagues had argued against a disease vector specific to blood products from the USA after studying changes in T-cell ratios indicating cell-mediated immune dysfunction in Scottish haemophilia patients exposed to both Scottish (NHS) and commercial (US) Factor VIII concentrates.<sup>10</sup> On 29 October 1984, however, Dr Froebel wrote to Dr Robert Perry at the Scottish National Blood Transfusion Service (SNBTS), stating that, after checking records, she and her colleagues now thought that seropositivity for HTLV-III was in fact strongly associated with the patients having received commercial concentrate, mostly before 1981.<sup>11</sup> Dr Perry wrote to her on 15 November 1984 offering to cooperate in HTLV-III studies and asking for information.<sup>12</sup> With her reply,<sup>13</sup> Dr Froebel sent an abstract of a proposed paper. The full text of the paper in draft, entitled 'Evidence for Transmission of HTLV-III to European Haemophiliacs via US Imported Factor VIII Concentrate', had been prepared by a group including herself and Dr Gallo and a colleague from the US National Cancer Institute.<sup>14</sup> It was based on a comparative study of evidence of transmission of HTLV-III to haemophilia patients in Denmark and Scotland and presented a picture of confidence in locally-manufactured products, concluding that the data indicated that European haemophilia patients exposed to HTLV-III had been so exposed via infected imported Factor VIII concentrate from the USA.

**10.7** Initial comment on the study had been published in a letter to *The Lancet* on 7 July 1984.<sup>15</sup> The final paper was published in *The Lancet* on 22 December 1984.<sup>16</sup> Dr Gallo was among the accredited authors and the Cheingsong-Popov article was cited. The relevant conclusion was that:

Our findings suggest that HTLV-III was distributed through haemophiliac populations by factor VIII concentrate made from US donor material.<sup>17</sup>

**10.8** By the date of publication, the validity of the comments about the safety of local products had already been undermined, so far as Scotland was concerned, by the discovery of HIV infection in 16 Edinburgh haemophilia patients discussed in detail below. The comments remained at least partially correct in a UK context.

**10.9** This marked the end of a period of underestimation of the risk of HTLV-III transmission in Scotland. Evolving events were soon to dispel finally the belief that the blood supplies of the UK and the domestic blood products of the NHS were free from HTLV-III infection. Meantime, however, the Cheingsong-Popov paper received wide publicity and perpetuated the belief that the risks were associated primarily with imported products. Andrew Veitch, medical correspondent, wrote in *The Guardian* of 31 August 1984:

<sup>10</sup> Froebel et al, 'Immunological abnormalities in haemophilia: are they caused by American factor VIII concentrate?' *British Medical Journal*, 1983;287:1091 [LIT.001.0215]

<sup>11</sup> Letter from Dr Froebel to Dr Perry dated 29 October 1984 [SNB.004.8734]

<sup>12</sup> Letter from Dr Perry to Dr Froebel dated 15 November 1984 [SNB.004.8739]

<sup>13</sup> Letter from Dr Froebel to Dr Perry dated 05 December 1984 [SNB.004.8777]

<sup>14</sup> Draft paper 'Evidence for Transmission of HTLV-III to European Haemophiliacs via US Imported Factor VIII Concentrate' [SNB.004.8779]

<sup>15</sup> Melbye, M et al 'High prevalence of lymphadenopathy virus (LAV) in European haemophiliacs' *The Lancet*, 1984; 324:40-41(40-41) [LIT.001.0423]

<sup>16</sup> Melbye et al 'HTLV-III seropositivity in European haemophiliacs exposed to Factor VIII concentrate imported from the USA' *The Lancet*, 1984; 324:1444-1446 [LIT.001.1702]

<sup>17</sup> Ibid [LIT.001.1702] at 1704

### Study confirms fears on spread of Aids

Fears that the Aids virus is widespread among homosexuals are confirmed today by the biggest British investigation into the disease so far.

The investigators – teams of doctors from seven centres – also found traces of the virus in a third of haemophiliacs given the blood clotting agent, Factor 8: American Factor 8 is strongly implicated.

But, the doctors stress, it seems possible that some of those infected – perhaps even the majority – may not develop the disease.

The number of Aids victims in Britain has risen from 13 in June 1983 to 51 in June this year. By yesterday the Department of Health had confirmed 61 cases, 32 of whom have died. The majority are London homosexuals.

The doctors tested 2000 people for antibodies to the Aids virus – the tell-tale sign that they had been infected. The results are published in *The Lancet* today.

They found the antibodies in 89 per cent of patients with the Aids-related disease, persistent generalised lymphadenopathy (PGL). It has previously been shown that hundreds of homosexuals are suffering from PGL. The symptoms include swollen glands, night sweats, and general malaise.

Antibodies were also found in 59 per cent of homosexuals with mild symptoms; 42 per cent of homosexuals who were sexual contacts of Aids or PGL sufferers; and in 17 per cent of homosexuals who were supposedly healthy or were being routinely screened for hepatitis.

The doctors say their results confirm that the virus, called HTLV-III and discovered earlier this year, is the cause of Aids and PGL. They found antibodies to it in 30 of their 31 Aids patients; the exception had an [un]usually benign form of the illness.<sup>18</sup>

**10.10** The findings had been placed squarely in the public domain. The natural history of HIV infection was still not fully understood and the relative safety of domestic blood supplies was given emphasis.

### *The Weiss/Tedder research assay and early testing in the United Kingdom*

**10.11** Change was, however, imminent. The Weiss/Tedder research assay for HTLV-III, as reported by Dr Cheingsong-Popov and colleagues, was more widely used in the autumn. Haemophilia clinicians provided archived samples of serum from their haemophilia patients for testing and a high prevalence of HTLV-III infection was observed. For example, Dr Peter Kernoff at the Royal Free Hospital in London submitted stored samples of sera from his haemophilia patients to Professor Tedder in October 1984. More than a hundred samples tested positive. Dr Kernoff then had a further series of tests of samples carried out on stored blood samples to determine when his patients had become infected. Almost all of the patients were infected between 1980 and 1982. As no antibody was found in any sample from before 1979, it appeared that HIV had not entered the blood supply before

---

<sup>18</sup> 'Study confirms fears on spread of AIDS', *The Guardian* 31.8.84 [SGF.001.0930]

that date. If Scotland had been dependent on imported products to the extent England and Wales had been, it is likely that the incidence of HIV infection in Scotland would have been of the same order as that in England and Wales.<sup>19</sup>

**10.12** In submitting stored samples for testing, Dr Kernoff was following the general practice of the day.<sup>20</sup> His actions reflected growing apprehension among haemophilia clinicians that factor concentrate therapy might have caused widespread infection within the haemophilia population. Dr Mark Winter said that at that time a haemophilia clinician who had stored samples would submit them for testing without consulting the patients and that samples were stored in case they might be needed for such a purpose.<sup>21</sup> The patient would, however, have been consulted if a fresh sample was required.<sup>22</sup> It is understood that Dr Kernoff did not consult the patients before submitting the samples to Professor Tedder.<sup>23</sup> Dr Winter did not have stored samples.<sup>24</sup> He had to invite his patients to come specially and to explain why he wanted additional blood. Dr Winter obtained and sent 31 samples from his own haemophilia centre at Kent and Canterbury Hospital to Professor Tedder for testing. On 26 October 1984, he received the results: 30 were positive for HIV.<sup>25</sup>

**10.13** On 23 October 1984 Dr John Craske of the Public Health Laboratory Service (PHLS), Withington Hospital, Manchester, circulated a letter to haemophilia clinicians.<sup>26</sup> He advised that a batch of Factor VIII concentrate from the Blood Products Laboratory (BPL), the manufacturer of NHS concentrates in England, had been found to be infected with HTLV-III. He warned of the possible risk of infection with HTLV-III and subsequent development of AIDS. The letter stated that only a proportion of those transfused with an infected batch were likely to contract HTLV-III infection. It commented:

So far 21 patients are known to me who have clinical features of AIDS or the AIDS related complex. It is likely that the proportion of patients who contract HTLV-3 infection who contract AIDS will be of the order of 1/100 – 1/500.<sup>27</sup>

**10.14** The long-term prognosis for patients with HTLV-III infection was said to be unknown.

**10.15** By the end of October 1984, among haemophilia clinicians in the UK generally, there was growing awareness that HTLV-III infection could be, and had been, contracted from Factor VIII concentrate and that transmission could be associated with domestic as well as imported products. Between the end of October and the end of the year, further intelligence emerged in Scotland.<sup>28</sup>

<sup>19</sup> Dr Winter – Day 16, pages 101–6. As noted in paragraph 9.10 of Chapter 9, *Knowledge of the Geographical Spread and Prevalence Of HIV/AIDS 1*, the most up-to-date data available to the Inquiry indicate that for the UK, excluding Scotland, 1310 patients with bleeding disorders tested positive for HIV by April 2012. Scotland has roughly 10% of the UK haemophilia population but only 60 patients treated in Scotland tested positive. See also Chapter 3, *Statistics*.

<sup>20</sup> For more detailed discussion of the ethical issues surrounding the testing of stored samples, please see Chapters 32 and 33.

<sup>21</sup> Day 16, pages 169–70

<sup>22</sup> Day 16, pages 156–7

<sup>23</sup> Day 7, pages 82–85; Evidence to Lord Archer <http://www.archercbbp.com/hearing.php>

<sup>24</sup> Day 16, page 157

<sup>25</sup> Day 16, page 157–160. See also his evidence to the Archer Inquiry, Day 7, page 86 <http://www.archercbbp.com/hearing.php>

<sup>26</sup> Letter [SNF.001.4020]

<sup>27</sup> Ibid [SNF.001.4020] at 4021. Compare Dr Craske's letter to Dr Ludlam dated 30 November 1984 referred to at paragraph 10.31.

<sup>28</sup> See Chapter 11, *HIV/AIDS Aetiology*, at paragraphs 11.59–11.61

### **'The Edinburgh Cohort': the initial disclosure**

**10.16** Any residual complacency in Scotland was shattered by the discovery that a group of Edinburgh patients ('the Edinburgh Cohort') who had received Factor VIII concentrate therapy manufactured at the Protein Fractionation Centre (PFC) in Edinburgh, some exclusively and some almost exclusively, had developed antibodies to HTLV-III during 1984. In the immediate aftermath of the discovery it was thought that the infections must be attributed to products manufactured at the PFC (the Scottish equivalent of the BPL in England).<sup>29</sup> Evidence available to the Inquiry relating to the events surrounding the discovery was at times inconsistent and a little confused. The news clearly had a disturbing effect on those who first heard it and witnesses' recollections reflected the degree of turmoil that affected the SNBTS and haemophilia circles when the information emerged.

**10.17** Dr Brian McClelland, Director of the Edinburgh and East of Scotland Blood Transfusion Service, gave an account of events in his written statement to the Inquiry. Professor Christopher Ludlam, Director of the Edinburgh Haemophilia Centre, telephoned him at home on the evening of Friday 26 October 1984 to inform him that six patients with haemophilia under his (Professor Ludlam's) care had developed antibodies to HTLV-III. The tests had been performed in a research laboratory by Professor Tedder.<sup>30</sup> The date, and the number of patients affected, gave rise to discussion in the course of the oral hearings of the Inquiry.

**10.18** There had been a meeting of the PFC heads of department on the morning of 26 October 1984.<sup>31</sup> The minutes of the meeting indicate that Dr Perry was concerned that the PFC, of which he was Director,<sup>32</sup> might be asked, in the future, what plans had been made to reduce AIDS infection in blood products. He proposed, and it was agreed, that it would be useful to collate all information and data on heat-treated products and that further meetings should be arranged to discuss this matter.<sup>33</sup>

**10.19** The Inquiry explored the possibility that Dr Perry and his colleagues had already been informed of the HTLV-III transmissions in Edinburgh by this stage.<sup>34</sup> On the written and oral evidence available, it is unlikely that they had.<sup>35</sup> The picture that emerged, however, was of a state of some confusion among this group as information (not always consistent or comprehensive) was exchanged and people began to respond to the events as they evolved.

**10.20** Dr Bruce Cuthbertson, SNBTS, said that he remembered that it was definitely Dr McClelland who phoned him and told him that there had been evidence of infection in three Edinburgh haemophilia patients. He also remembered clearly a meeting with Dr McClelland and Dr Perry approximately a week to 10 days later where they went through the analysis that Dr McClelland had done with Professor Ludlam which showed which batches of Factor VIII had been received by the 16 infected patients identified by that time.<sup>36</sup>

<sup>29</sup> Letter from Dr McClelland to Dr Cash dated 15 November 1984 re analysis of PFC Factor VIII batches [SNF.001.3624]

<sup>30</sup> Dr McClelland's Witness Statement [PEN.011.0062] at 0063

<sup>31</sup> Minutes of a Meeting of Heads of Department/Section Managers held on Friday 26 October 1984 [SNB.010.3479]. Dr Perry told the Inquiry that the heads of department meetings were held regularly on Friday mornings at this time: Day 42, pages 52–3.

<sup>32</sup> Dr Perry had been Quality Control Inspector at the PFC from 1981–1984. He was appointed Acting Director in 1984 and the role was made substantive the following year, 1985. See Day 11, pages 93–4.

<sup>33</sup> Minutes of a Meeting of Heads of Department/Section Managers held on Friday 26 October 1984 [SNB.010.3479] at 3481

<sup>34</sup> Schedule to Witness Statement requests on Topic B3, Heat Treatment to 1985 [PEN.012.1531] at 1538

<sup>35</sup> See, for example, Dr Perry – Day 45, page 106; Dr Perry's Witness Statement [PEN.012.1759] at 1777

<sup>36</sup> Day 46, page 76

**10.21** Dr Foster's evidence was that he first learned of the infections in late October 1984, when he overheard a telephone conversation in Dr Cuthbertson's office.<sup>37</sup> The call was, he thought initially, from Dr McClelland, but it might have been from Dr Frank Boulton, Consultant in Haematology and Blood Transfusion at the Royal Infirmary of Edinburgh (RIE). Dr Cuthbertson said that Dr Foster had told him about the call over the years but that he could not himself remember the event. However, he said of Dr Foster:

It's certainly true that he was in an adjacent office and I'm sure when the information came from Dr McClelland, that my voice would have risen by several octaves.<sup>38</sup>

**10.22** Steps were immediately taken to identify the batch of concentrate which was responsible for the infection of Professor Ludlam's patients. Professor Ludlam and Dr McClelland gave evidence about this period. On 29 or 30 October Professor Ludlam established from examination of transfusion records that three of the initial group of patients who had developed antibodies had received material from batch 023110090.<sup>39</sup> On 2 November 1984 Professor Ludlam received further data from Professor Tedder which indicated that in total 15 or 16 patients who had received that batch had tested positive for the HIV antibody. Three other patients were added on further analysis. Fourteen out of 32 patients who had received material from the batch remained uninfected. On 3 November 1984 Dr McClelland and Dr Frank Boulton contacted all Scottish and Northern Ireland Transfusion Centres and arranged for batch 023110090 to be recalled.<sup>40</sup>

**10.23** It was to be mid-November before a written account was prepared within the SNBTS and, by then, a certain amount of clarification of the history of events had evidently occurred. However, the group of HIV-infected haemophilia patients that was to become known as 'the Edinburgh Cohort' had been discovered at the end of October.

**10.24** Dr Perry stressed that it had never been established conclusively that batch 023110090 was infective but, at the time, the SNBTS proceeded on the basis that it was 'a justifiable, though unproven, assumption'<sup>41</sup> that the batch was responsible for the infections. He explained that the decision to recall was an example of an application of 'the precautionary principle'. His understanding of that principle was that, where there was evidence available to a manufacturer that a medical risk associated with a particular product may exist, it was incumbent upon him and the supplier to take action to mitigate that risk.<sup>42</sup>

**10.25** On 15 November 1984, Dr McClelland wrote to Professor John Cash, Medical Director of the SNBTS:

I have had several discussions with Dr Christopher Ludlam following the discovery that some recipients of PFC Factor VIII have developed antibodies to HTLVIII during 1984 ....

---

<sup>37</sup> Dr Foster's Witness Statement [PEN.012.1438] at 1472

<sup>38</sup> Day 46, page 78

<sup>39</sup> Day 35, pages 97–102 and Day 40, pages 82–89; Edinburgh Haemophilia and Thrombosis Centre – Appendix to witness statement from Professor Ludlam [PEN.012.0351] at 0354; Note of a Meeting between Professor Ludlam and the Penrose Inquiry legal team [PEN.012.0774] at 0784

<sup>40</sup> 'Events Leading up to the Recall of Factor VIII Batch 023110090' [SNB.006.5996]

<sup>41</sup> 'Actions surrounding FVIII Batch 023110090' [PEN.016.1258] at 1263

<sup>42</sup> Day 38, pages 13–14

As I reported to the Scottish RTDS last week, it appeared that there are, so far, 16 patients in whom seroconversion is known to have occurred during 1984 and who have received exclusively PFC factor VIII, or (in one case only) commercial factor VIII several years ago which can be discounted from the present problem.

Initial analysis by Dr Ludlam and Dr Tedder showed that one batch of product had been received by all but one of the 16 patients and therefore was highly suspect. This batch (023110090) has been withdrawn.<sup>43</sup>

**10.26** The batch assumed to have been implicated had been identified and action had been taken. After examination of the records, it was concluded that no other recent batch stood out as being 'distinctively strongly implicated' and there was therefore thought to be no obvious basis on which to advise a selective withdrawal of any other material.

## Reactions to developing knowledge in late 1984

### *Official reactions*

**10.27** Following on the media comment by Andrew Veitch and others<sup>44</sup> and the discovery of the Edinburgh Cohort, the incidence of disease in the Scottish population moved into the political arena. In a parliamentary answer on 28 November 1984 relating to the incidence of AIDS in Scotland, it was announced that there were three confirmed cases by 26 November.<sup>45</sup>

**10.28** On 29 November 1984, the SNBTS and Haemophilia Centre Directors met specially to discuss the implications of the recent findings of HTLV-III infection in Scottish haemophilia patients, measures being taken by the SNBTS to prevent the spread of AIDS by blood products and the media attention associated with these developments.<sup>46</sup> All relevant agencies in Scotland were clearly informed of the incidence of infection as understood at that time.

**10.29** At that meeting, outbreaks in three centres were discussed. Professor Ludlam discussed the Edinburgh Cohort and Professor Charles Forbes described the findings of the study of patients at the Glasgow Royal Infirmary and Danish patients.<sup>47</sup> Dr Brenda Gibson reported the anxiety felt by parents of children with haemophilia: five out of 10 children treated at the Royal Hospital for Sick Children, Yorkhill, Glasgow, where imported Factor VIII concentrate had been widely used, were HTLV-III antibody positive.

**10.30** At a meeting of the SNBTS Directors on 11 December 1984, Dr McClelland reported that he had attended a meeting of the National Blood Transfusion Service Working Group on AIDS which had taken place on 27 November 1984.<sup>48</sup> He reported that Dr Marcella Contreras had run a trial of a New York Blood Center questionnaire in the West London Donor Centre, offering donors the chance to elect for their blood to be used for research if they belonged to a risk group. A small number had agreed to do so. All of the declared homosexuals followed up were HTLV-III antibody-negative on testing.

<sup>43</sup> Letter from Dr McClelland to Dr Cash dated 15 November 1984 re. analysis of PFC Factor VIII batches [SNF.001.3624]; reported in *The Scotsman* 22.12.84 [SGH.002.6484]; Preliminary Report, para 8.102

<sup>44</sup> See Chapter 9, *Knowledge of the Geographical Spread and Prevalence of HIV/AIDS 1*, paragraph 11.41.

<sup>45</sup> Hansard 28 November 1984, column 494 [SNF.001.3313]

<sup>46</sup> Note of Meeting of Haemophilia Directors and SNBTS Representatives on 29 November 1984 [SNB.001.5256]; Preliminary Report, paragraphs 8.104 to 8.107

<sup>47</sup> See paragraph 10.6 above

<sup>48</sup> Minute of meeting [SGF.001.0137] at 0139. See Dr McClelland's Note on meeting of Advisory Group on AIDS, 27 November 1984 [PEN.012.1938]



**10.31** On 30 November 1984, Dr Craske wrote to Dr Ludlam providing materials for investigation of the cases of infection in Edinburgh patients. He stated that certain ‘facts’ might help Dr Ludlam appreciate the position. In summary, these included:

- (i) Only a proportion of the patients transfused with an infected batch were likely to contract HTLV-III infection.
- (ii) Some patients who had received commercial factor VIII since 1 January 1980 would already have contracted HTLV-III infection from other infected batches.
- (iii) The proportion of patients infected with HTLV-III who would eventually contract AIDS was unknown but, as serum from 34% of symptomless haemophilia patients was positive for HTLV-III antibody (the Cheingsong-Popov finding), it was thought likely that a significant proportion of patients would remain in good health. He narrated that by that date 21 patients had been reported to him as having the clinical features of AIDS (four patients) or the AIDS-related complex (17 patients). He said that it was likely that the proportion of patients with HTLV-III infection who developed AIDS would be of the order of 1/100–1/500.
- (iv) The long term prognosis for patients with HTLV-III infection was said to be unknown. The incubation period of AIDS, based on projection of the epidemic curve at the CDC, was from nine months to six years, with a mean of four years.
- (v) There was evidence that HTLV-III infection could be transmitted by sexual contact. Therefore some sexual partners of recipients of Factor VIII contaminated with HTLV-III might be at risk.
- (vi) Those patients who were likely to transmit infection, or who were likely to contract AIDS, could not yet be distinguished by means of laboratory tests.<sup>49</sup>

**10.32** Some of these statements proved to be wrong.<sup>50</sup> It was not likely that a significant proportion of patients would remain in good health and it was not likely that the proportion of patients who contracted HTLV-III infection and went on to develop AIDS would be of the order of 1/100–1/500. Over a short period at the end of the year results of tests on sera were rapidly changing perceptions. Dr Craske’s letter set out clearly one set of perceptions about the disease at this time and reflected some of the ‘known unknowns’ as then understood.

**10.33** The UK Haemophilia Reference Centre Directors met on 10 December 1984.<sup>51</sup> By this time, some 800 UK haemophilia patients had been tested for the antibody: the prevalence in haemophilia patients overall was about 35%, but 75% in patients with severe haemophilia.<sup>52</sup> Professor Ludlam is reported to have ‘confirmed that in Scotland, some patients who were previously antibody +ve are now -ve.’<sup>53</sup> Haemophilia Directors wanted to test all of their patients.

<sup>49</sup> Summarised from a letter from Dr Craske to Dr Ludlam dated 30 November 1984 re: Suspect Batches of Edinburgh Factor VIII and Factor IX [LOT.003.4331] at 4332

<sup>50</sup> Dr Winter – Day 16, page 116

<sup>51</sup> Meeting of the Haemophilia Reference Centre Directors – 10 December 1984 [DHF.003.0898]; Notes of the Haemophilia Reference Centre Directors Meeting Blood Products Laboratory Elstree, 10 December 1984 [SNF.001.3850]. The Haemophilia Reference Centre Directors was a committee of UKHCDO and Drs Ludlam, Cash and Forbes were in attendance. More detail of events from this point until the end of 1984 are set out in the Preliminary Report at paragraphs 8.116–8.119

<sup>52</sup> Meeting of the Haemophilia Reference Centre Directors – 10 December 1984 [DHF.003.0898]

<sup>53</sup> Notes of the Haemophilia Reference Centre Directors Meeting Blood Products Laboratory Elstree, 10 December 1984 [SNF.001.3850] at 3853. From later discussion of infection in the Edinburgh Cohort, the record appears to be wrong: some patients who had been negative before receiving the implicated batch were subsequently found to be positive. Some were found to be negative before and after receiving the implicated batch.

**10.34** It was thought that there was a clear need for research to determine prevalence in the UK. A report of the meeting noted a view that inconsistencies in the results of the tests revealed that a study of the haemophilia population would provide invaluable material to increase knowledge of the disease. There was a wide-ranging discussion on a number of important issues but few conclusions were drawn by the haemophilia clinicians present. The prevalence of infection was far from clear and, furthermore, the likelihood of developing AIDS for those who were HTLV-III positive was unknown.

**10.35** On 14 December 1984, the United Kingdom Haemophilia Centre Doctors Organisation (UKHCDO) produced an 'AIDS Advisory Document.'<sup>54</sup> The background information provided included data on infection, as understood by the UKHCDO. In the USA, where there had been over 6000 cases of AIDS, 52 haemophilia patients had been infected. It was said that in the UK there had been 102 cases of AIDS with three reported haemophilia patient cases and 'no doubt other cases ... developing.'

### *Press reports*

**10.36** In the media there was more reporting. A *Daily Express* article dated 21 December 1984 stated:

56 are given AIDS killer blood: Alert as homosexual admits being a donor.

Blood which has been infected with the killer AIDS virus has been given to 56 people, it was revealed yesterday.

Fifteen of the recipients are Scots. Another 32, including a pregnant woman, are from England, and nine others are from Wales.

Most are haemophiliacs but none has yet contracted the disease – although it has an incubation period of up to four years.

Shocked experts at the Blood Transfusion Service made the discovery when the patients mysteriously developed antibodies to the AIDS virus, which is normally transmitted by homosexuals.

Then horrified doctors at a Bournemouth hospital discovered that a young homosexual who is seriously ill with AIDS had been a regular blood donor all over England.

His blood was used for transfusions to patients in the Midlands and the North, but mainly in the South and in Wales. The contaminated blood given to Scots patients is not thought to come from the same source. 'We are still trying to identify the donor' said a Scottish Office spokesman ....

The AIDS virus was discovered among the 15 Scots patients when recently developed tests showed up traces of antibody to the disease in their blood.

Dr Frank Boulton, deputy head of the Edinburgh Blood Transfusion Service said: 'Previously, the only way that AIDS was diagnosed was by the illness itself. But the tests have not been around long enough for us to know what degree of immunity the presence of antibodies indicates.'<sup>55</sup>

---

<sup>54</sup> AIDS advisory document [SGF.001.2388]; Preliminary Report, para 8.117

<sup>55</sup> '56 are given AIDS killer blood', *The Daily Express*, 21.12.84: [SGF.001.0904]

**10.37** In *The Scotsman* of 22 December 1984, William Paul wrote:

AIDS 'barrier' proves illusory

With the benefit of hindsight, it is now possible for doctors to reflect on the inevitability of AIDS ... gaining a foothold in Scotland.

The disease has largely established itself in Europe and in England since originating in the U.S. and Dr Brian McClelland, director of the Edinburgh and South-East Scotland Blood Transfusion Service, admitted yesterday that it would not have been realistic to expect Scotland to be by-passed.

Even so, Scotland's self-sufficiency in blood and blood products was seen as a significant barrier and the medical profession must have experienced a sense of disappointment when routine tests on haemophiliacs at Edinburgh Royal Infirmary recently uncovered the fact that 15, or possibly 16, of them had contracted the HTLV 3 virus which can cause AIDS.

The virus was transmitted in injections of the blood-clotting agent Factor 8, used by most haemophiliacs to control their condition, which had been prepared from a particular batch of plasma, now identified and withdrawn. Its source was a blood donation given somewhere in the East of Scotland about 12 months ago.

Government scientists are now working to trace the donor but it is by no means certain that they will be successful as plasma is made up from many thousands of individual blood donations.

The balance of probability, according to Dr McClelland, is that the donor of the contaminated blood was a practising homosexual male because that is the section of the population considered to be most at risk from the disease ....

Dr McClelland prefers to think that the contaminated blood must have been donated unwittingly, but cannot rule out the possibility that the donor deliberately went ahead knowing himself to be a member of the at-risk groups ....

'If we had to be 100 per cent certain of the purity of all the blood we turn out we would have to cease operations', Dr McClelland said.

'But the risk to people from not having blood available would be far greater than the risk of AIDS being transmitted for the foreseeable future. The chances of getting AIDS virus from a transfusion are put at a million to one.'

The haemophiliacs in Edinburgh who have been told their blood has produced antibodies to fight the AIDS virus are all described as clinically very well. The odds against them actually developing symptoms of the disease proper ... are said to be 2000 to one.<sup>56</sup>

---

<sup>56</sup> 'AIDS "barrier" proves illusory', *The Scotsman*, 22.12.84 [SGH.002.6484]

**10.38** The quoted risk of 2000:1 against developing the disease proper was clearly very wrong indeed and, even at that time, was more optimistic than other estimates. The source of some of the information in these media reports is unclear. However, accuracy apart, the extent and tone of media comment reflected growing public concern about the spread of the epidemic.

**10.39** In and after 1985, there was intense interest in the Edinburgh Cohort. The patients comprised in the group were studied by clinicians and scientists seeking more information about HIV and AIDS. Several of the articles published about this group of people emphasised the value from a research point of view of being able to study the disease in a group assumed to have had a common source of infection.<sup>57</sup> Several of the articles are referred to in the Preliminary Report at paragraphs 8.205–8.214. It will be appropriate to return to some of these in the context of other developments.

### 1984–1985

#### *HIV in the United Kingdom: a matter of public health*

**10.40** With the discovery of the Edinburgh Cohort, the risk of transmission of HIV by SNBTS factor concentrate, despite the exclusive use of Scottish blood donations in its manufacture, was demonstrated and there was no longer room for differentiating Scottish patients from others at risk, so far as exposure to the epidemic by means of blood, blood components or blood products was concerned. Advice and comment took on a more general character thereafter.

**10.41** An editorial in *The Lancet* of 22 December 1984 (the issue in which the article discussed at paragraph 10.7, above, was also published) contained discussion of 'Blood transfusion, haemophilia and AIDS'.<sup>58</sup> It noted that 52 haemophilia-associated cases of AIDS had been reported in the USA and three in the UK. The overall prevalence of AIDS in treated US haemophilia patients was about twice that in Europe but it was thought that in countries that used Factor VIII concentrate from the USA the number was likely to increase. This obvious inference had previously been resisted but it is difficult to understand how a product manufactured by a given pharmaceutical company for general distribution could have a higher rate of infectivity in its country of origin, the USA, than in importing countries abroad. The prevalence of HTLV-III infection in homosexuals and others seemed to be increasing rapidly in countries outside the USA. It was observed that contamination of local blood products could only be a matter of time. The editorial discussed the options for treatment of blood disorders against this background.

**10.42** There was growing concern about public health. A Ministerial answer by Kenneth Clarke, MP, then Minister of State for Health, to a Parliamentary Question on 21 January 1985 reflects the position of the government at the time:

We are considering the public health implications of AIDS and what further steps might be taken to control it. We have established an expert advisory group<sup>59</sup> to advise the health departments in the United Kingdom, whose members will include experts on all aspects of the disease. Their advice will be valuable in assisting the formulation of a strategy for prevention and control.

<sup>57</sup> See, for example, Preliminary Report, para 8.205

<sup>58</sup> 'Blood Transfusion, Haemophilia, and AIDS', *The Lancet*, 1984; 324:1433–35 [LIT.001.0446]. See Preliminary Report para 8.119 for further details.

<sup>59</sup> The members of the expert advisory group are listed at [SNF.001.3323]

There is at present no vaccine against AIDS or specific treatment, but general preventive measures and health education have a major part to play in controlling the disease ....

Internationally, we are in touch with the Centers for Disease Control in the United States and the World Health Organisation AIDS Reference Centre in Paris, which have considerable data on the disease. Research in this country is proceeding through five projects funded by the Government through the Medical Research Council.<sup>60</sup>

**10.43** He answered further questions (i) to the effect that AIDS was not a notifiable disease under the Public Health (Control of Disease) Act 1984; (ii) relating to monitoring arrangements; and (iii) relating to the intention to make the disease notifiable and the practical implications of that:

Interim guidelines drawn up by the Advisory Committee on Dangerous Pathogens<sup>61</sup> on the safe handling of AIDS patients have recently been published jointly by our Department and the Health and Safety Commission. These set out the measures which should be taken to protect clinical and laboratory staff who come into contact with patients suffering from AIDS or with specimens taken from them. We are taking steps to reduce the risk of the spread of AIDS through blood transfusion and the use of blood products. We are strengthening our efforts to dissuade those in AIDS high-risk groups from donating blood, and our revised leaflet 'AIDS Important New Information for Blood Donors' will be distributed individually to all donors. We are also considering the need to screen blood donations for the HTLV III antibody. Supplies of heat-treated factor VIII for haemophiliacs will shortly be made available to the NHS from the Central Blood Laboratories Authority.<sup>62</sup>

### *Reaction in Scotland*

**10.44** In Scotland, steps had already been taken to protect staff at the PFC. On 31 December 1984 Dr Perry had issued a memorandum setting out the current understanding of AIDS risk and encouraging the use of safe working practices.<sup>63</sup> There was an understandable emphasis on staff safety but some of the information provided in the memorandum gives an insight into the impact of media comment and the understanding within the PFC at the time: the memorandum distinguished transfusion from factor concentrate therapy; and it noted that there had been no cases of AIDS in Scotland or Northern Ireland associated with transfusions of blood or blood products from the SNBTS and that some haemophilia patients had HTLV-III antibodies, evidence of exposure to the AIDS virus, but that none had symptoms of AIDS. It narrated that the patients who had been exposed to the AIDS virus all received some vials from the suspect batch and that some had also received material from a number of other batches. It was stated that the fact that these patients had evidence of exposure to HTLV-III did not necessarily mean that they would go on to develop AIDS. Employees were encouraged to work safely but they were reassured that at that time there had been no cases (worldwide) of AIDS in any centres manufacturing blood products despite the fact that the spread of AIDS in the USA was some two to three years ahead of Europe.

<sup>60</sup> Written Parliamentary Answer, 21 January 1985, columns 345–348 [DHF.001.9150]

<sup>61</sup> Acquired Immune Deficiency Syndrome (AIDS) – Interim Guidelines [DHF.001.6071]

<sup>62</sup> Written Parliamentary Answer, 21 January 1985, columns 345–348 [DHF.001.9150]

<sup>63</sup> Memorandum from Dr Perry to All Staff dated 31 December 1984 re AIDS [SNB.004.8843]

**10.45** Dr Perry distributed a second memorandum to all PFC staff, dated 31 January 1985, discussing further the transfusion risks associated with blood components.<sup>64</sup> Red cells and platelets had been used normally by Regional Transfusion Centres (RTCs) and there was no evidence to date to indicate that the recipients of these products had developed HTLV-III antibodies. He provided information on attempts to identify donors who had contributed to the batch implicated in the infection of the Edinburgh Cohort and to quarantine all plasma from those individuals who had been identified and who subsequently gave donations. The memorandum narrated:

The decision to quarantine this plasma was taken to safeguard both product and staff safety in the belief that additional evidence and further investigation of repeat donations would identify the infective donation(s) and permit the remaining donations to be entered into process. As you know, a suitable test is not yet available for large scale application to individual donations with the result that it is not possible at the present time or in the foreseeable future to establish the relative infectivity of plasma pools or product batches. On this basis, the quarantined plasma was released for process. You will also be aware of the fact that plasma from these donors has inevitably entered process on previous occasions. While this does not necessarily provide comfort or reassurance, one must conclude that, at this stage, it is impossible to judge that some plasma is 'safer' than others or that one pool of plasma represents a higher risk than others either from a patient or staff safety point of view.<sup>65</sup>

**10.46** On 4 February 1985, the Scottish Home and Health Department (SHHD) distributed the advice of the Advisory Committee on Dangerous Pathogens in the form of 'Interim Guidelines on AIDS' (dated December 1984).<sup>66</sup> Their interim character was emphasised but the guidelines provide a useful summary of contemporaneous knowledge of the disease and its clinical course.<sup>67</sup> It was noted that HTLV-III and LAV had been recovered from patients with AIDS. It was said that the two agents (in fact, it would later be discovered that they were the same) had also been isolated from patients with PGL, haemophilia patients and apparently healthy male homosexuals. The prevalence of infection in AIDS patients, haemophilia patients who had received pooled clotting factors and others was tabulated. Eighty-eight cases had been reported between *The Lancet* report of 12 December 1981 and October 1984 and 37 individuals had died. One patient had been diagnosed retrospectively as having been infected in 1979. The cases were grouped according to their prime recognisable condition:

Kaposi's sarcoma (KS)	30
Pneumocystis carinii pneumonia (PCP)	32
KS plus PCP	5
Other opportunistic infections	20
Cerebral lymphoma	1 <sup>68</sup>

<sup>64</sup> Memorandum from Dr Perry to All Staff dated 31 January 1985 re AIDS [SNF.001.3715]

<sup>65</sup> Ibid, [SNF.001.3715]. This conclusion led to the release of plasma for processing.

<sup>66</sup> Interim Guidelines [DHF.001.6071]

<sup>67</sup> The interim guidance was accompanied by a letter: an example is [SGH.001.0360]

<sup>68</sup> Interim guidelines [DHF.001.6071] at 6077

**10.47** Of the 88 cases, over 75% were male homosexuals while the remainder were patients with direct or indirect contact with central Africa, recipients of pooled clotting factors and a small group with no recognised risk factor. The Interim Guidelines commented:

If the trend in the UK follows that seen in the USA we can expect an exponential increase in the number of cases of clinical AIDS diagnosed. Furthermore the serological studies ... seem to indicate that whereas the most severe outcome of infection with HTLV III is certainly AIDS, it cannot be assumed that all infections with this virus will necessarily lead to this disease, although the possibility cannot be ruled out.<sup>69</sup>

**10.48** There was now a realistic official assessment of the probability of a growing epidemic in the UK. On 16 January 1985, the Department for Health and Social Security (DHSS), jointly with the Health and Safety Executive, issued a press release: 'AIDS guidelines for clinical and laboratory staff'.<sup>70</sup> The press release noted the publication of the Interim Guidelines and stated that a review of the measures recommended would be undertaken within the next 12 months to take into account any new knowledge or understanding of AIDS.

**10.49** On 25 February 1985 Mr John MacKay, Under-Secretary of State for Scotland, told Parliament that there had been four cases of AIDS reported in Scotland.<sup>71</sup> One patient had died in 1982 and one in 1984. In addition a patient ordinarily resident in England had died in Scotland in 1984.

**10.50** Over the next few months there was an explosion of published material. Typical examples are referred to in the Preliminary Report.<sup>72</sup>

### *Official statements*

**10.51** Official statements were distributed. On 1 April 1985, the Chief Medical Officer (CMO) for Scotland issued a circular letter to Chief Administrative Medical Officers and community medicine specialists,<sup>73</sup> together with a leaflet entitled 'Some Facts about AIDS'<sup>74</sup> which was then available for distribution. It was produced by the Health Education Council and reprinted for the Scottish Health Education Group. This was followed, on 17 May 1985, by a letter from the Deputy Chief Medical Officer (DCMO) to all doctors.<sup>75</sup> The papers sent with the letter contained a further summary of the state of knowledge of the UK government at the time entitled 'AIDS – general information for doctors', dated May 1985, and a paper dated 22 February 1985 prepared by the Communicable Disease Surveillance Centre in London giving a detailed account of the epidemiology of the condition.<sup>76</sup>

<sup>69</sup> Ibid, [DHF.001.6071] at 6077

<sup>70</sup> Press release: 'AIDS guidelines for clinical and laboratory staff' [SNB.001.0124]

<sup>71</sup> Written Parliamentary Answer [DHF.001.9389]

<sup>72</sup> See, for example: Madhok 'HTLV III antibody in sequential plasma samples: from haemophiliacs 1974-1984' *The Lancet*, 1985; 325:524-525 [LIT.001.1673]; See also the Preliminary Report, paragraphs 8.146 and 8.147

<sup>73</sup> Letter from the CMO dated 1 April 1985 [SNB.004.9328]

<sup>74</sup> Leaflet 'Some Facts About AIDS' [SNB.004.9329]

<sup>75</sup> Letter from the DCMO dated 17 May 1985 [SGH.004.6581]

<sup>76</sup> 'AIDS – general information for doctors' [SGH.004.6582]; CDSC Epidemiology Paper [SNB.004.9642]

**10.52** The paper dated 22 February 1985 and prepared by the Communicable Disease Surveillance Centre stated:

[T]here is a wide spectrum of clinical states associated with HTLV3 infection ranging from healthy antibody-negative persons to patients with fully developed AIDS. It seems probable that only a very few of the infected persons become ill ....

....

Tests for antibodies to HTLV3 have been developed but these are not tests for AIDS and are difficult to interpret.<sup>77</sup>

**10.53** The paper 'AIDS – general information for doctors' reiterated the established criteria for reporting AIDS, following the US CDC definition,<sup>78</sup> and noted that they had been accepted by other countries and by the World Health Organization (WHO). It stated that, by the end of February 1985, 132 cases of AIDS had been reported within the UK and that there had been 58 deaths. Data indicated that three haemophilia patients were included and that there were no cases of infected blood transfusion recipients. The covering 'Dear doctor' letter from the DCMO gave more up-to-date data: there were four cases of AIDS registered 'to date' in Scotland and 159 cases in the UK. Doctors who had patients with AIDS under their care were invited to assist in the maintenance of a register by reporting in strict confidence to the Communicable Diseases (Scotland) Unit in Glasgow.

**10.54** Further observations in the UK government's general information for doctors included:

The risk of infection as a result of blood transfusion is extremely low. Infection with HTLV-III has occurred as a result of treatment with Factor VIII and Factor IX. Heat treated Factor VIII is now available and in use and is likely to eliminate the risk of transmission.<sup>79</sup>

And:

HTLV-III infection is already widespread in certain groups at risk (e.g. in homosexuals with multiple sexual partners and in haemophiliacs). Estimates vary as to what percentage of infected individuals will ultimately develop AIDS, but it may be in the order of 10 per cent.<sup>80</sup>

**10.55** The prevailing view, as published, remained that HTLV-III infection was unlikely to progress to AIDS in the majority of cases but that the risk to haemophilia patients, and a lesser risk to transfusion patients generally, was recognised. There appears to have been a conscious effort to avoid panic reactions while providing doctors generally with information and advice about AIDS and HTLV-III infection that was not otherwise available in textbooks at that stage.

**10.56** Some experts thought that there were aspects of AIDS that were not adequately monitored in the UK. The Preliminary Report set out details of arguments advanced by Professor Julian Peto, Professor of Epidemiology at the Institute for Cancer Research, in

---

<sup>77</sup> CDSC Epidemiology Paper [SNB.004.9642] at 9643

<sup>78</sup> See paragraph 10.1 above.

<sup>79</sup> 'AIDS – general information for doctors' [SGH.004.6582] at 6586

<sup>80</sup> *Ibid.*, [SGH.004.6582] at 6589



a letter dated 20 May 1985 circulated to members of the Medical Research Council.<sup>81</sup> He thought that AIDS might already be 'catastrophic' for haemophilia patients and for homosexual men in London. His attached paper<sup>82</sup> was a plea for further research but it presented a more pessimistic projection of future progression of the disease than the official government position. Professor Peto suggested that many and possibly the majority of seropositive individuals might eventually die of AIDS. Even the fact that AIDS was always, or almost always, fatal was still not universally appreciated at this time as only half the individuals diagnosed with the disease had so far died. It was thought by Professor Peto that only a minority, if any, of the general population might be capable of mounting an effective immune response to initial infection and it seemed to him likely that the chronic infection that ensued constituted a permanent infective carrier state.

### *The Edinburgh Cohort revisited*

**10.57** On 23 May 1985, Professor Ludlam sent Dr Perry a copy of the final draft of the RIE study of the Edinburgh Cohort,<sup>83</sup> later published in *The Lancet* on 3 August 1985.<sup>84</sup> The introduction to the published paper reported as background that the virus HTLV-III/LAV was the most likely cause of AIDS and that tests carried out on stored serum samples from haemophilia patients showed that HTLV-III antibodies were first detectable in the USA in 1978 and in the UK no later than 1979. The summary stated:

Fifteen haemophiliac patients acquired antibodies to [HTLV-III] during 1984. One batch of factor VIII concentrate given to all these patients is presumed to be the cause of the seroconversion. A further eighteen patients who received the same batch did not seroconvert .... Ten other patients received a batch of factor IX concentrate from the same donor plasma; none of these patients seroconverted.

**10.58** The article further commented in its introduction:

In contrast to haemophiliacs elsewhere in the UK, almost all patients attending the Edinburgh Haemophilia Centre have received factor VIII and IX concentrates prepared exclusively from locally collected plasma by the Scottish National Blood Transfusion Service (SNBTS). Until recently there were no reported cases of AIDS in Scotland and it therefore seemed possible that our patients might not be exposed to HTLV-III ...

As part of the continuing assessment of our haemophiliacs, we have now observed that sixteen of our patients acquired anti-HTLVIII during 1984; all but one of these patients had received a common batch of SNBTS factor VIII concentrate.

**10.59** The study discussed 34 patients with Haemophilia A and eight patients with Haemophilia B. It reported their treatment histories and noted that samples dated up to early 1984 were all negative on testing for anti-HTLV-III. None of the infected patients was known to have risk factors for developing antibodies to HTLV-III other than replacement therapy.

<sup>81</sup> Preliminary Report, para 8.153; Professor Peto's Letter [DHF.002.5498]

<sup>82</sup> Professor Peto's paper [DHF.002.5499]

<sup>83</sup> Letter from Dr Ludlam to Dr Perry [SNF.001.3271]; Final Draft of Paper [SNF.001.3272]

<sup>84</sup> Ludlam, C *et al* 'HTLV-III infection in seronegative haemophiliacs after transfusion of factor VIII' *The Lancet*, 1985; 326:233-236 [LIT.001.1669] Preliminary Report, para 8.154

**10.60** The paper set out the results in some technical detail. In summary, the discussion noted:

- The prevalence of anti-HTLV-III in Scotland among haemophilia patients at the beginning of 1984 was relatively low and where it occurred could be attributed to occasional use of commercial blood products. In contrast, in some places prevalence had risen to over 90%.
- One specific batch had probably caused the infection in the Edinburgh Cohort: a definitive investigation would have to await a reliable test of infectivity. All but one of the 16 patients with Haemophilia A who had developed anti-HTLV-III had received the batch between March and May 1984.
- The risk of developing HTLV-III was a function of the recipient's helper/suppressor cell ratio,<sup>85</sup> the number of transfused vials of presumed infected Factor VIII and the total annual consumption of Factor VIII.
- If the study were otherwise correct in its conclusions, half of the patients who received the single suspect batch did and half did not develop antibodies to HTLV-III.
- Patients who received Factor IX prepared from the same pool were known. None demonstrated seroconversion when tested up to four months after infusion.

**10.61** The presumed infective batch was manufactured in November 1983 from plasma collected in the autumn of the same year. Following the reports of product infectivity, attempts were made to identify the specific donation(s) which led to the product being infective but these were unsuccessful. The paper noted that the PFC had developed a programme to study possible methods of eliminating the transmission of viral infections by blood factor concentrates. The expertise developed had been put immediately into effect, following the finding of HTLV-III antibodies in Scottish patients.

### *The reality of risk for recipients of blood and blood products*

**10.62** The AIDS Information and Advisory Group at the Glasgow Royal Infirmary (GRI) met on 31 May 1985.<sup>86</sup> In common with others, they recognised the need for further research. In the west of Scotland, 16% of haemophilia patients were HTLV-III antibody positive.<sup>87</sup> All had, in retrospect, seroconverted between 1981 and 1983. The minutes of the meeting noted that the Regional Reference Laboratory was using the 'Abbott' kit,<sup>88</sup> confirmed by immunofluorescence testing, for HTLV-III antibody testing, with reference to Dr Tedder in London in the event of inconsistent results. Dr Robert Crawford, a Consultant at the West of Scotland Blood Transfusion Service, reported that the national HTLV-III test evaluation was progressing. The aim was to test all blood donations at major regional blood transfusion centres, with the particular aim of protecting the higher-risk pooled products, rather than the low-risk single-donor products, from infected donations. It was stated that arrangements should be made to counsel blood donors found to be HTLV-III antibody positive.

<sup>85</sup> Helper/suppressor ratios are discussed in Chapter 11, *HIV/AIDS Aetiology*, paragraph 11.86

<sup>86</sup> Minutes of AIDS Information and Advisory Group, 31 May 1985 [SNB.004.9656]; Preliminary Report, para 8.155

<sup>87</sup> By 1991 the rate of infection in treated haemophilia patients in Edinburgh was said to be 25%: Cuthbert et al, 'Immunological studies in HIV seronegative haemophiliacs' *British Journal of Haematology*, 1991; 80:364–9 [PEN.012.0405]

<sup>88</sup> The testing kit developed by Abbott Diagnostics in the USA.

**10.63** The focus was changing away from discussing whether there actually was a risk of transmission of infection: interest was now focused on the response to the reality of the risk for recipients of blood and blood products and the need for care of donors and patients. Inactivating virus contamination by heat-treatment was promoted as part of the response and Dr Crawford reported that the second generation of heat-treated Factor VIII concentrate was being clinically evaluated. Heat-treated Factor IX concentrate was still under development and had not been released for clinical evaluation at that stage.

**10.64** Government agencies continued to collect data. On 20 September 1985 a note to the Private Secretary of John MacKay, Under Secretary of State for Scotland, and copied to the offices of the Secretary of State, the CMO and other senior officials, provided data on the incidence of AIDS to the end of August.<sup>89</sup> There were said to be 206 cases in the UK, of which 114 individuals had died. The figures for Scotland were six cases and two deaths. Comparative figures to the end of February had been 132 cases in the UK, of which 58 had died, with Scotland having four cases and two deaths.

**10.65** On 26 September 1985, a press release was issued by the DHSS<sup>90</sup> and, in turn, a press release was drafted by the SHHD.<sup>91</sup> The SHHD press release was entitled 'Countering the Spread of AIDS in Scotland' and stated that, to that date, six people in Scotland had developed AIDS, of which two had died. The UK total was 206 cases of AIDS, of which 114 had died.

#### *The prevalence of HTLV-III antibody in haemophilia patients in the UK*

**10.66** There was by now growing interest in the prevalence of HTLV-III antibody in haemophilia patients in the UK.<sup>92</sup> The need for research had been anticipated and was now in hand. Dr Rizza and Miss Rosemary Spooner of the Oxford Haemophilia Centre contacted the 109 haemophilia centres in the UK requesting information on the antibody status of their patients and on 27 September 1985, the results were circulated.<sup>93</sup> Eighty-one centres provided data. Of the remaining 28, four replied that they could not cooperate because of confidentiality issues and three said that they would try to provide information later. The survey was destined to be less than comprehensive.

**10.67** At the time there were 4918 Haemophilia A patients, 896 Haemophilia B patients and 1725 von Willebrand's disease patients on the national haemophilia register. Of the 2970 Haemophilia A, Haemophilia B and von Willebrand's disease patients treated in the UK in 1984, 2525 had been tested.<sup>94</sup> The range of results as reported for those groups was as follows:

<sup>89</sup> Note to Mr MacKay and others [SGF.001.0831]

<sup>90</sup> DHSS Press Release: 'the fight against AIDS – more government money' [DHF.001.7916]; Preliminary Report, para 8.136

<sup>91</sup> SHHD Press Release [SGH.002.7072]

<sup>92</sup> Preliminary Report, para 8.164

<sup>93</sup> Interim Report on Survey of HTLVIII Antibody in Haemophiliacs in UK [SNB.001.7593]

<sup>94</sup> A total of 2570 patients were tested including carriers of Haemophilia A and B and other groups. Data from these cohorts (45) are not represented above.

**Table 10.1: UK Haemophilia AIDS Survey**

	Patients treated in 1984	Patients Tested for HTLV-III	% of Treated Patients Tested	Number HTLV-III Positive	% of Tested Patients Positive
Haemophilia A	2277	1994	88	873	44
Haemophilia B	391	316	81	20	6
von Willebrand's	302	215	71	11	5
<b>Total</b>	<b>2970</b>	<b>2525</b>	<b>85</b>	<b>904</b>	<b>36</b>

**10.68** In the case of severely affected Haemophilia A patients (defined for this purpose as having less than 2% Factor VIII)<sup>95</sup> the proportion testing positive for HTLV-III rose to 59%. The average proportion testing positive in the three groups combined was 36%.

**10.69** The age profile for severely affected haemophilia patients with HTLV-III antibodies (expressed as a percentage of the total numbers tested) was:

**Table 10.2: age profile for severely affected haemophilia patients with HTLV-III antibodies**

Age	0 - 5	5 - 9	10 - 14	15 - 19	20 - 29	30 - 39	40 - 49	50 - 59	60 - 69	70 +
Haem A	6	32	68	65	68	65	61	51	34	20
Haem B	0	0	0	9	15	3	6	14	20	0

**10.70** The highest percentages according to age groups were in those aged 10–14 years and those aged 20–29.

**10.71** On the basis of the data collected, and assuming that those patients not yet tested were at the same risk as those already tested, the authors of the report predicted that if all children with Haemophilia A up to the age of 19 (865 children) were to be tested, 320 patients (37%) might be expected to be HTLV-III positive.<sup>96</sup>

**10.72** Tables prepared by Dr Craske dated 1 October 1985 gave data on cases of AIDS-related diseases reported to the Oxford Haemophilia Centre.<sup>97</sup> A total of 67 cases in patients with Haemophilia A or von Willebrand's disease had been reported along with three cases in patients with Haemophilia B.

<sup>95</sup> See Chapter 2, *Patients at Risk*, paragraph 2.26 for discussion of the categorisation of haemophilia into 'mild', 'moderate' and 'severe' categories.

<sup>96</sup> Interim Report on Survey of HTLVIII Antibody in Haemophiliacs in UK [SNB.001.7593] at 7596

<sup>97</sup> Haemophilia AIDS Group – Cases of AIDS Related Diseases Notified to Oxford 1 October 1985 – Table 1 [SNF.001.1106]

**10.73** The diseases reported were:

**Table 10.3: Cases of AIDS-related diseases, October 1985**

Syndrome	Haemophilia A		Haemophilia B	
	Total	Deaths	Total	Deaths
AIDS: <i>Pneumocystis carinii</i> pneumonia	7	6		
AIDS: opportunistic infections	3	2	1	1
'AIDS Related Complex' (the patient who died committed suicide)	15	1		
Other syndromes	3		1	
Thrombocytopenia	20	1		
Persistent Generalised Lymphadenopathy	12		1	
Glandular fever-like syndrome	7			

**10.74** Seventy-five family contacts were also tested and four partners were found to be anti-HTLV-III positive.<sup>98</sup>

**10.75** On 28 November 1985, an internal DHSS memorandum was sent to the Chief Medical Officer for England and Wales.<sup>99</sup> It commented on some hearsay evidence that haemophilia patients were seroconverting to become anti-HTLV-III positive despite being given heat-treated Factor VIII. This became an issue for discussion in 1986. If true, it would have indicated that the epidemic was less likely to be contained by the existing production technology employed in the manufacture of blood products for therapeutic use.

## 1986

### *Further information on prevalence*

**10.76** Additional information on prevalence was gathered. On 7 February 1986 there was a meeting to discuss the virological aspects of the safety of blood products at the National Institute of Biological Standards and Control (NIBSC).<sup>100</sup> At the meeting, Professor Forbes raised the issue of seroconversion after treatment with heat-treated concentrates, with particular reference to three specific patients.<sup>101</sup> The question was to attract attention for some time and cast some doubt on the effectiveness of the PFC's heat-treatment of Factor VIII concentrate. It was dealt with in official correspondence in February and March.<sup>102</sup> So far as concerns the spread of the epidemic, it was eventually shown to be a false trail. A general consensus was reached that the seroconversions of the three patients were related to previous treatment with untreated material of either commercial or NHS origin.

**10.77** The survey data now covered 2609 UK patients from 81 haemophilia centres. Of Haemophilia A patients, 46% were positive for HTLV-III antibody. For Haemophilia B patients and von Willebrand's disease patients the figures were 6% and 5% respectively.

<sup>98</sup> Ibid, [SNF.001.1106] at 1107

<sup>99</sup> Memo to CMO [DHF.001.8523]

<sup>100</sup> Minutes of a meeting on the Virological Aspects of the Safety of Blood Products, held at the NIBSC on February 7th, 1986 [SNB.005.1495]; Preliminary Report, para 8.168

<sup>101</sup> Ibid [SNB.005.1495] at 1501. This was the issue raised with the CMO, England and Wales, on 28 November 1985, noted above.

<sup>102</sup> Dr Perry's letter [SNB.004.7776]; Dr Forbes' letter [SNB.004.7732]; Preliminary Report, para 8.171

**10.78** The source of infection in patients with coagulation defects continued to be debated. In discussion at the meeting on 7 February, Professor Tedder reported that, tests of stored samples dating from 1978 to 1984 showed that seropositivity rose rapidly from 33% in 1980 to 64% in 1982 in the case of patients who had received commercial concentrates. In the case of patients who had received NHS concentrates, samples were seronegative until 1982. Between 1983 and 1984 seropositivity rose from 1% to 11%. These rates were considerably higher than those indicated by the data on AIDS cases reported on CDC criteria down to 1984 which were discussed in Chapter 9, *Knowledge of the Geographical Spread and Prevalence of HIV/AIDS 1*. The Director of the NIBSC, Geoffrey Schild, asked if anyone knew the reasons for the low incidence of clinical AIDS (around 1%) in seropositive haemophilia patients. Dr Craske and Professor Forbes said that the true incidence of AIDS was probably much higher, due to a tendency to suppress reporting.<sup>103</sup> It has to be remembered, however, that until Professor Tedder's tests were applied data were collected only on cases meeting the CDC definition of AIDS. Under-reporting of AIDS may have been a factor but, with the benefit of hindsight, long periods of asymptomatic infection with HIV must also have contributed to the difference as the CDC criteria required the presence of intractable AIDS-associated disease for a case to be 'confirmed' as one of AIDS. The natural history of the disease was still not understood.

**10.79** At a meeting of the SNBTS Directors on 25 March 1986, it was reported that the transfusion service was concentrating on following up patients who had received donations known to have been contaminated by HTLV-III.<sup>104</sup> Professor Tedder intended to study the epidemiology of infected donors and all recipients of implicated blood and blood products, retrospectively for five years. It is not clear that these studies progressed or produced meaningful results but they reflected growing appreciation of the need for better understanding of the natural history of the disease.

**10.80** At successive conferences, new data on HIV prevalence were reported with reference to different cohorts and with inconsistent and irreconcilable results.

**10.81** At a conference on AIDS held in Newcastle between 11 and 13 February 1986 and sponsored by the Haemophilia Society, Professor Tedder commented that the small number of seroconversions following the use of heat-treated Factor VIII concentrates was due to 'a long delay in the latent phase'. On this view, transmission of infection as a result of treatment had occurred but diagnoses had been made only after the change of treatment regime to include heat-treated products. The natural history of HIV infection was becoming more clearly understood and AIDS was said to present a significant problem for the future.<sup>105</sup> There were estimated to be about 20,000 positive individuals in the UK, spread among four groups. Dr Foster's report summarised the information available<sup>106</sup> as follows:

<sup>103</sup> Minutes of a Meeting on the Virological Aspects of the Safety of Blood Products, held at the NIBSC on February 7th, 1986 [SNB.005.1495] at 1502

<sup>104</sup> Minutes of a Directors Meeting Held in the HQ Unit on 25 March 1986 [SNF.001.0135] at 0138-9; Preliminary Report, para 8.173

<sup>105</sup> Report of AIDS Conference, 11-13 February 1986 [SNF.001.4215] at 4216; Preliminary Report, para 8.169

<sup>106</sup> Ibid, [SNF.001.4215] at 4218

**Table 10.4: UK Situation by February 1986**

Group	Total Number	% Antibody Positive	Trend
Haemophiliacs	4000	25%	Down
Blood recipients	1,000,000	0.006%	Down
IV drug users	20,000	5%	Up
Gay people	500,000	3%	Up

**10.82** The percentage of antibody positive haemophilia patients was significantly lower than that reported by Dr Rizza and Miss Spooner above.

**10.83** Dr Peter Jones, Director of the Newcastle Haemophilia Centre, also spoke specifically about the incidence in patients with haemophilia: he estimated, extrapolating from the limited data available, that 1200 UK haemophilia patients would already have seroconverted. In relation to treatment, he said that of those who had been treated with cryoprecipitate only, 1% tested positive for the virus; of those treated with NHS concentrate only, 10% were positive; and of those treated with commercial concentrate only, 45% had tested positive. His basic data were not consistent with the data collected by Dr Rizza and Miss Spooner but referred to a cohort of similar size and with less variance than the data reported by Dr Foster.<sup>107</sup>

**10.84** At the 19th Congress of the International Society of Blood Transfusion in Sydney between 11 and 16 May 1986, the association of AIDS with the use of blood products was discussed.<sup>108</sup> Participants reported their experiences. There were differences both internationally and within and among regions.

**10.85** Professor Arthur Bloom reported that 43 out of 153 haemophilia patients in Cardiff (28%) had seroconverted, compared with the rate for the UK as a whole, which he said was 44%. He said that the incidence of transfusion-associated AIDS in Australia was 10 times greater than in the UK. He also commented on the timescale of seroconversions of Haemophilia A and B patients. The time from exposure to seroconversion ranged from six days to one year and the mean timescale for developing 'full blown' AIDS was three years. He suggested that haemophilia patients might be 'lagging behind' other high-risk groups in developing AIDS.<sup>109</sup>

**10.86** Dr Jones reported experience among people with haemophilia in Newcastle. There were eight confirmed cases of clinical AIDS and four awaiting confirmation, an incidence of eight to ten per cent.<sup>110</sup> In the report, written by Dr Foster, Dr Jones is said to have claimed that the degree and type of treatment in Newcastle was no different to many other centres and he was unable to postulate any reason why haemophilia patients in Newcastle should have been affected so differently. Other reports on infection among haemophilia patients, from the USA, Australia and France, gave comparative data. Dr Bruce Evatt, CDC, reported on the incidence of seropositivity in the USA. As already noted<sup>111</sup> prevalence values were 74% in people with Haemophilia A and 35% in people with Haemophilia B, with 15%

<sup>107</sup> Report of AIDS Conference, 11-13 February 1986 [SNF.001.4215] at 4220. Dr Jones had data from 2025 patients compared to the 2525 reviewed by the Oxford study.

<sup>108</sup> Dr Foster's report of the Congress [SNB.008.6547]

<sup>109</sup> Ibid [SNB.008.6547] at 6548-49

<sup>110</sup> Ibid [SNB.008.6547]

<sup>111</sup> Chapter 9, *Knowledge of the Geographical Spread and Prevalence of HIV/AIDS 1*, at paragraph 9.65.

of 'haemophilia wives' also seropositive and with the seroconversion rate still increasing. A 12-month French study reported by Professor Jean-Pierre Allain showed 58% seroconversion in the patients included. Dr Roger Garsia from Australia found 45% seroconversions among the 161 patients studied. The Congress also discussed the incidence of seroconversion in non-haemophilia patients following treatment with blood products.<sup>112</sup>

**10.87** This was a wide-ranging conference in which doctors from around the world shared their experiences of the epidemic. It exposed the prevalence of AIDS and HIV antibody positivity over a number of countries. The advantage of heat treatment of products was a major topic. According to Dr Garsia, there had been no cases of seroconversion in Australia since the introduction of heat-treated products. Others, however, spoke of experiences of seroconversion following use of heated products. The Congress appears to have been exploratory in nature, with each participant contributing to the general understanding of the wider AIDS epidemic.

### *The European context*

**10.88** Between 28 and 31 May 1986, the Committee of Experts on Blood Transfusion and Immunohaematology met at Berne.<sup>113</sup> Much of the background material in the report was repeated in the Advisory Committee on Dangerous Pathogens (ACDP) guidelines issued in June and is dealt with in that context below.<sup>114</sup> The factual material set out the wider European understanding of the position at the time. It was observed that, prior to the screening of donated blood, many haemophilia patients had become infected, as had a few recipients of transfusions. It was said that these routes of infection had now been closed by a combination of measures – publicity to deter those in high-risk groups from donating blood, heat-treating blood products to inactivate any virus they might contain and testing all blood donations for antibody and discarding any that were found to be positive.

**10.89** The report tabulated data on: AIDS cases and deaths up to various dates in 1985 and 1986; screening of blood donations; information to and counselling of donors and follow-up of patients receiving blood from antibody-positive donors; cases of positive tests for the virus and of AIDS in patients with haemophilia; and treatment of haemophilia.<sup>115</sup> The information provided on UK non-haemophilia patients up to March 1986 was that there had been 342 cases of people infected with AIDS, of whom 172 had died. The data relating to Haemophilia A and B patients were derived from the Oxford study discussed above with some updating. The total population remained the same: 4918 people with Haemophilia A and 896 people with Haemophilia B. The position for UK haemophilia patients was set out as:<sup>116</sup>

<sup>112</sup> Dr Foster's report of the Congress [SNB.008.6547] at 6549-50 and 6554

<sup>113</sup> Extract from the Report of the Committee of Experts on Blood Transfusion and Immunohaematology – Berne 28-31 May 1986 [SNB.004.8127]; Preliminary Report, para 8.180

<sup>114</sup> Advisory Committee on Dangerous Pathogens (ACDP) – Revised Guidelines on LAV-HTLV III – The Causative Agent of AIDS and Related Conditions [DHF.002.1456]

<sup>115</sup> Extract from the Report of the Committee of Experts on Blood Transfusion and Immunohaematology, Berne, 28-31 May 1986 [SNB.004.8127]

<sup>116</sup> *Ibid* [SNB.004.8127] at 8136



**Table 10.5: Data on AIDS cases and deaths by 1986**

	Number of patients	Number treated	Anti-HTLV tested	Positive	%	Number with AIDS/ARC <sup>117</sup>
Haem A	4918	2277	2025	896	44	18/20
Haem B	896	391	324	20	6	3/0

**10.90** The percentages of patients testing positive had not changed and the numbers with AIDS or ARC remained broadly the same.

**10.91** By way of comparison, it was reported that:

The positive rate for anti-HTLV 3/LAV in patients suffering from Haemophilia A varied considerably from 4% in Belgium and 8% in Norway to over 90% in Malta and the USA. The usual level of positivity was between 35 and 60%. The low rate of positivity in Belgium and Norway could probably be attributed to the almost exclusive use of cryoprecipitates prepared from local donors.<sup>118</sup>

**10.92** It was further reported that, with a few exceptions, the positive anti-HTLV-III/LAV rate for patients with Haemophilia A was greater than that for Haemophilia B and that the incidence of AIDS and AIDS-related complex was also higher in Haemophilia A in most instances. Dr Albert Farrugia (Malta) suggested that the 95% incidence of anti-HTLV-III/LAV antibodies in Haemophilia A patients in Malta had almost certainly arisen because these patients had been exclusively treated with imported Factor VIII concentrate, whilst patients with Haemophilia B had been treated with Factor IX concentrate obtained from European voluntary donors.<sup>119</sup>

**10.93** In June 1986, the ACDP issued 'Revised Guidelines' on LAV/HTLV-III.<sup>120</sup> It was reported that the number of cases of AIDS (in Europe) continued to double every 6 to 12 months. Detailed figures were provided for reported cases and estimated rates per million of population in 21 European countries including the UK.<sup>121</sup>

**10.94** Rates of infection in those European countries supplying figures ranged from 1.0 per million of population (Greece) to 11.9 (Belgium).<sup>122</sup> The figure for the UK was 4.0 per million. Globally, it was stated:

In certain parts of Africa where LAV/HTLV III has probably been present longer than in the USA, small surveys have detected evidence of infection in as much as a fifth of the sexually active population and in some parts of the USA it now seems that a majority of male homosexuals are infected. It is not assumed that this will necessarily happen in the UK but it has to be recorded that such levels of infection have been observed elsewhere.<sup>123</sup>

<sup>117</sup> AIDS related complex

<sup>118</sup> Extract from the Report of the Committee of Experts on Blood Transfusion and Immunohaematology, Berne, 28-31 May 1986 [SNB.004.8127] at 8144

<sup>119</sup> Ibid [SNB.004.8127] at 8144

<sup>120</sup> Advisory Committee on Dangerous Pathogens (ACDP) – Revised Guidelines on LAV-HTLV III – The Causative Agent of AIDS [DHF.002.1456]

<sup>121</sup> Ibid [DHF.002.1456] at 1464-5

<sup>122</sup> Advisory Committee on Dangerous Pathogens (ACDP) – Revised Guidelines on LAV-HTLV III – The Causative Agent of AIDS [DHF.002.1456] at 1465. NB Several reported 0% infection rates (Czechoslovakia, Hungary, Iceland, Poland, USSR).

<sup>123</sup> Ibid [DHF.002.1456] at 1464-65

**10.95** The general hazard and risk statement commented:

[T]here are very serious consequences for a proportion of those infected, although not all will necessarily develop AIDS, which to date has invariably been a fatal disease. For this reason the intrinsic hazard of infection should not be under-estimated.<sup>124</sup>

**10.96** By this stage, the likelihood of patients having developed antibodies to HIV from blood products produced prior to the introduction of heat-treatment was understood to be high, in severely affected Haemophilia A patients in particular. It was also appreciated that AIDS was a fatal illness, although the risk of progression to AIDS was still underestimated. The natural history of untreated HIV infection was still not well understood.

***United Kingdom data updated***

**10.97** On 10 September 1986, Dr Craske issued an update on a retrospective study of HIV-related illness.<sup>125</sup> The data were incomplete: a second HIV antibody survey was in hand. By the date of the report, returns to the Oxford Centre in 1985 had identified eight batches of NHS Factor VIII and two of Factor IX that had been associated with either an anti-HIV positive donor or a donor who later developed HIV-related illness. Evidence of transmission had been identified in five of the Factor VIII batches, two were possibly associated with transmission, and there was no information on the remaining batch. There was evidence of transmission in one batch of Factor IX and information was awaited on the other batch. Quantification aside, the association between NHS factor products and the transmission of infection was clear.

**10.98** The report narrated:

The total number of patients reported to Oxford with HIV related illness by 22.4.86 was 109. This was 12.9% of the total antibody positive patients identified in the Survey in August 1985 (896) .... The number of AIDS cases reported of which 15 have died is 23. Eighteen cases are known to the Communicable Disease Surveillance Centre .... Two of these had not been notified to Oxford so that the total may come to 25.<sup>126</sup>

**10.99** The comparative number of patients with AIDS or AIDS-related conditions in the August 1985 survey had been 38. In September 1986, 109 cases were listed under three categories: (i) 'AIDS', comprising PCP (15), opportunistic infection (8) and AIDS related complex (20); (ii) 'unclassified' comprising abdominal lymphoma (1) and (iii) 'other syndromes,' comprising thrombocytopenia (28), purpura (5), PGL (30) acute glandular fever (10) and encephalopathy (2).<sup>127</sup>

**10.100** The paper stated that a significant number of HIV-infected persons would continue to develop AIDS-related illness over a period of years, despite the efficacy of heat-treated Factor VIII and Factor IX in preventing further patients being infected.<sup>128</sup> The

<sup>124</sup> Ibid [DHF.002.1456] at 1468; Preliminary Report, para 8.186

<sup>125</sup> Update on HIV Related Illness – September 1986 [SNF.001.1114]; Preliminary Report, para 8.189

<sup>126</sup> Update on HIV Related Illness – September 1986 [SNF.001.1114]. This appears to relate to Haemophilia A patients only: 896, the figure used in calculation, was the number of such patients who were antibody positive as at March 1986. The change of terminology within the papers from AIDS-related to HIV-related does not appear material in view of the specification of diseases given.

<sup>127</sup> Update on HIV Related Illness – September 1986 [SNF.001.1114] at 1116

<sup>128</sup> Ibid [SNF.001.1114] at 1115

small proportion of Haemophilia B patients so far infected with HIV was said to be partly accounted for by a lower contamination rate of Factor IX concentrate as compared with Factor VIII. This was said to be confirmed by independent observations of the Edinburgh Cohort.<sup>129</sup>

**10.101** Dr Craske advised that further study was necessary. He proposed that the next step in research should be to identify patients who were HIV-positive post-exposure and to increase the cohort for study to at least 30 or 40 patients. These patients would be followed up every six months in their usual review clinic. He emphasised that only limited additional investigations would be necessary. Dr Craske was still encountering obstacles. He wrote:

For the past 6 months there has been a lot of natural concern regarding the confidentiality of data reported to the National Survey at Oxford. Arising from this there was a noticeable drop in the rate of case reporting early this year. This had increased again in recent months, but I think it is still important to emphasise that reporting is necessary to enable us to obtain information on the size of the problem; to establish the efficiency of preventative measures e.g. safety of heat treated factor VIII, and to identify new patterns of the disease associated in the HIV infection.<sup>130</sup>

**10.102** On 3 October 1986, Dr Rizza and Miss Spooner of the Oxford Haemophilia Centre distributed a further report on the incidence of anti-HIV in people with haemophilia in the UK.<sup>131</sup> In this survey, 84 out of a total of 109 haemophilia centres made returns. Confidentiality remained an issue. Thirteen centres which contributed data in 1985 failed to do so in 1986 and 14 centres which had not made returns in 1985 did return data in 1986. The report noted that this had to be borne in mind in comparing data. 40.48% of 2228 Haemophilia A patients, 6.74% of 386 Haemophilia B patients and 2.75% of 327 von Willebrand's disease patients were anti-HIV positive. Individuals present in both the 1985 and 1986 returns were 1707 Haemophilia A, 283 Haemophilia B and 161 von Willebrand's disease patients. The analysis of results by age group and severity of blood disorder showed a broadly similar pattern to the 1985 survey.

**10.103** However, this was not intended to be a sample survey; rather, it was an attempt at a total survey of the whole haemophilia population. Piecemeal returns, with significant gaps, necessarily undermined the reliability of the exercise and the resulting information distributed to UKHCDO members cannot be treated as presenting a complete and valid picture of the prevalence of infection.

**10.104** In Scotland, data on registered blood donors were shared by all regions. At a meeting of SNBTS Directors on 9 October 1986 the current status of HIV antibody-positive donations reported since screening was started was: Inverness one; Aberdeen none; Dundee three; Edinburgh eight; Glasgow two; Belfast two.<sup>132</sup> The next meeting of the SNBTS Directors was on 17 December. The current status of HIV antibody-positive donations reported at that meeting was: Inverness, one; Aberdeen, none; Dundee, three; Edinburgh, nine; Glasgow, six; and Belfast, two.<sup>133</sup>

<sup>129</sup> Ibid [SNF.001.1114] at 1118

<sup>130</sup> Update on HIV Related Illness – September 1986 [SNF.001.1114]; Preliminary Report, para 8.190

<sup>131</sup> Provisional Report on 1986 Survey of Anti-HIV in Haemophiliacs in UK [SNB.001.7684]

<sup>132</sup> Minutes of a Directors Meeting held on 9 October 1986 [SGF.001.0268] at 0269; Preliminary Report, para 8.191

<sup>133</sup> Minutes of Directors Meeting held on 17 December 1986 [SGF.001.0189] at 0190

**1987**

**10.105** The minutes of the meeting of SNBTS Directors held on 3 March 1987 noted that one further donor in Edinburgh had been found to be positive.<sup>134</sup>

**10.106** On 22 June 1987, the Scottish Office issued a press release.<sup>135</sup> The latest AIDS figures for Scotland up to the end of May 1987 reported a total of 20 AIDS cases, with 12 deaths; this included two haemophilia patients who had both died. The figure also included one recipient of whole blood and one recipient of a blood product,<sup>136</sup> both of whom had died. (The equivalent figures for the UK were 791 reported AIDS cases with 444 deaths; these included 31 haemophilia patients of whom 25 had died; one haemophilia patient, who was also an intravenous drug user, who had died; and six recipients of blood by transfusion in the UK, all of whom had died.)

**10.107** When the UK Haemophilia Centre Directors met in London on 25 September 1987, AIDS had become the leading cause of death in UK haemophilia patients.<sup>137</sup> A third national survey of anti-HIV among haemophilia patients was under way. Three new patients had been reported as being seropositive in 1987. Amongst 314 sexual partners of anti-HIV seropositive haemophilia patients who had been treated, 18 (5.7%) had been found to be positive. Dr Craske commented that this compared with rates of up to 15% in the USA.

**10.108** In October 1987, a table in the journal *International Plasma News* showed the percentages of HIV seroconversion among haemophilia patients in eight European geographical areas and in Canada. Scotland had the lowest percentage, at 15%; the 'UK' figure (presumably England and Wales) was 46%; Canada and Spain were 69%. For Sweden, Italy, France, West Germany and Denmark, the values ranged from 31% to 60% and averaged 50%.<sup>138</sup>

**10.109** At the end of the year there was renewed discussion on the association between the use of heat-treated Factor VIII concentrate and HIV seroconversions in 'naïve' (otherwise 'virgin' or 'previously untreated') haemophilia patients. On 21 December 1987, following a telephone conversation with Dr Dale Lawrence of the CDC, Professor Bloom circulated information to haemophilia directors about experience in Canada.<sup>139</sup> There had been six initial seroconversions in the period from spring to summer 1987. The products used included dry-heated material developed by Cutter (heated at 68°C for 72 hours) and Armour (heated at 60°C for 30 hours) and possibly others. Canadian research implicated the manufacture of the Armour product and Travenol and production and distribution had been stopped.<sup>140</sup> Armour Factor VIII had been implicated in transmission in the USA and West Germany. The company had withdrawn its product in the USA. Professor Bloom noted that the CDC was convening an emergency meeting of manufacturers and haemophilia doctors in Atlanta on 11 January 1988. He commented that BPL's product (dry heated at 80°C for 72 hours) was 'in the air', and was to be discussed, with all of

<sup>134</sup> Minutes of a Directors Meeting held on 3 March 1987 [SGH.001.6653] at 6655

<sup>135</sup> Press Release: 'Latest AIDS figures for Scotland' [SNB.004.8475]

<sup>136</sup> Presumably a non-haemophilia patient.

<sup>137</sup> Minutes of the 19th Meeting on the UK Haemophilia Centre Directors – 25th September 1987 [SNB.001.7768] at 7771; Preliminary Report, para 8.197

<sup>138</sup> *International Plasma News* October 1987 [SNB.005.9298]; Preliminary Report, para 8.198

<sup>139</sup> Letter dated 21 December 1987 [SNB.006.4583]

<sup>140</sup> *Ibid* [SNB.006.4583] at 4584; Preliminary Report, paragraphs 8.198–8.200

the information, in the February meetings of the UKHCDO.<sup>141</sup> Product specification, and particularly heat-treating protocols, was entering into the discussion of factors influencing the development of the epidemic.

### 1988 and beyond

**10.110** In and after 1988, intelligence on the prevalence of HIV in the UK and the risks of progression to AIDS continued to be published and Parliament was updated on the developing position. For example, in a Parliamentary answer on 21 December 1989, it was stated that there had been 76 HIV-positive haemophilia patients and 12 non-haemophiliac HIV-positive recipients of blood or blood products in Scotland.<sup>142</sup> By the end of February 1990, the total number of haemophilia patients with AIDS in the UK who had died was 118.<sup>143</sup> In 1990 there was a report on patients with haemophilia in Edinburgh who had acquired HIV from commercial concentrates.<sup>144</sup> There was highly technical Scottish research into factors possibly indicating that an individual was at increased risk of swiftly progressing to full-blown AIDS.<sup>145</sup> The Edinburgh Cohort provided a particular focus for research and comment.

### The Edinburgh Cohort: developing knowledge

**10.111** At the time of the recall of batch 023110090, no chemical or biological test was carried out to ascertain whether it was infective. Dr Perry doubted whether there was a test available that could have been used. He said that those assays 'simply didn't exist'<sup>146</sup> and that the test used by Professor Tedder was not validated for patient samples, let alone as part of a pharmaceutical evaluation process.<sup>147</sup> The first testing on batch 023110090 by SNBTS was performed in 1985 using a commercial assay. This was a first-generation antibody test and the result was negative. This early version of the test was, however, unable to pick up low levels of antibodies in samples tested.<sup>148</sup>

**10.112** Between 1985 and 1986 further tests were carried out in a number of laboratories including the NIBSC. The tests then available would have been Enzyme-Linked Immunosorbent Assay (ELISA) tests,<sup>149</sup> all of which were looking for antibodies. None of the tests carried out gave any chemical or biochemical indicator that the batch contained an infectious virus or that it contained antibodies to a virus.<sup>150</sup> No test that was carried out indicated the presence of antibody to the virus until very much later.

**10.113** Dr Perry explained that after HIV screening was introduced in October 1985, all donors found positive were studied and their previous donations were traced and library samples, where available, of their donations were tested. These investigations established that none of those donations had been used to make up batch 023110090.<sup>151</sup>

<sup>141</sup> Letter dated 21 December 1987 [SNB.006.4583]

<sup>142</sup> Hansard, 21 December 1989, columns 379–380 [SGF.001.1248]

<sup>143</sup> Hansard, 18 April 1990, column 876 [SGF.001.1202]

<sup>144</sup> Zhang, LQ *et al* 'Detection, quantification and sequencing of HIV-1 from the plasma of seropositive individuals and from factor VIII concentrates' *AIDS*, 1991; 5:675–81 [LIT.001.0516]; Preliminary Report, para 8.213

<sup>145</sup> Simmonds, P *et al*, 'Determinants of HIV disease progression: six-year longitudinal study in the Edinburgh haemophilia/HIV cohort' *The Lancet*, 1991, 338:1159–1163, [LIT.001.0279]; Preliminary Report, para 8.214

<sup>146</sup> Day 38, page 17

<sup>147</sup> Day 38, page 18

<sup>148</sup> Day 38, pages 16–18

<sup>149</sup> ELISA tests use an enzyme to detect antibodies in a sample and include various reagents which give a colour reaction. Dr Dow – Day 4, pages 85–6; Professor Weiss – Day 48, pages 161–2

<sup>150</sup> Day 38, pages 19–20

<sup>151</sup> 'Actions surrounding FVIII Batch 023110090' [PEN.016.1258] at 1265–6

## Publications

**10.114** An article in the *British Medical Journal (BMJ)* of 27 February 1988 set out results obtained from testing serum from the Cohort.<sup>152</sup> The narrative recorded that there were 18 patients affected and that 'infection was acquired from a single batch of Factor VIII during a short period starting in March 1984'. It was also suggested that:

[T]he low prevalence of HIV 1 infection in Scotland in 1983, when blood for the batch was collected, makes it probable that the batch was contaminated by a single donation.<sup>153</sup>

**10.115** It was reported that 32 patients had been transfused. Eighteen of those patients had undergone seroconversion.<sup>154</sup> Eight patients had developed symptoms before March 1987 ('the unwell group') and the other 10 remained asymptomatic in mid-1987. The symptoms included PGL, AIDS Related Complex (ARC) and AIDS. The authors tentatively suggested that there was a relationship between the amount of Factor VIII transfused and time to seroconversion. It was said that much of the variability in the course of infection was clearly the result of differences in susceptibility of the patients to infection.<sup>155</sup>

**10.116** The progression of disease in the Edinburgh Cohort received further attention in a paper written in 1988 by Professor Ludlam and colleagues.<sup>156</sup> The study period ran from early 1987 to mid-1988. By the end of that period two patients had died and only seven patients remained wholly asymptomatic. It was concluded that the amount of Factor VIII transfused did not influence clinical progression or the ability of doctors to isolate HIV from a patient's serum. It was also pointed out that:

Compared with other cohorts, the rate of morbidity and mortality in this cohort is relatively high with half the HIV seropositive patients having developed serious clinical complications within 4 years .... Thus in clinical terms, the implicated viral strain appears to be particularly virulent.<sup>157</sup>

**10.117** In an article published in *The Lancet* in 1988 by Dr C Michael Steel and others (including Professor Ludlam), the factual understanding of the source of infection at that time was set out:

It was ... established that a single batch of locally produced factor VIII had been contaminated with [HIV].... That batch was used by 32 previously seronegative patients between March and May, 1984.<sup>158</sup>

<sup>152</sup> Simmonds et al, 'HIV antigen and antibody detection: variable responses to infection in the Edinburgh haemophiliac cohort', *British Medical Journal*, 1988; 296:593-8 [LIT.001.0305]; Preliminary Report, paragraphs 8.206 and 8.207

<sup>153</sup> Simmonds et al, 'HIV antigen and antibody detection: variable responses to infection in the Edinburgh haemophiliac cohort', *British Medical Journal*, 1988; 296:593-8 [LIT.001.0305] at 0306

<sup>154</sup> Cuthbert, RJG et al 'Five year prospective study of HIV infection in the Edinburgh haemophiliac cohort' *BMJ*, 1990; 301:956-61 at 957, [LIT.001.0291]. As late as 1991, Dr Cuthbertson of the PFC was referring to there having been 16 seroconversions. Preliminary Report, para 8.221. Originally, 16 were reported but three further seroconversions were observed during follow-up between October and December 1984, with one of the original 16 being discounted as not having been infected by the implicated batch.

<sup>155</sup> Simmonds et al, 'HIV antigen and antibody detection: variable responses to infection in the Edinburgh haemophiliac cohort', *British Medical Journal*, 1988; 296:593-8 [LIT.001.0305]

<sup>156</sup> Cuthbert et al, 'Human immunodeficiency virus detection: correlation with clinical progression in the Edinburgh haemophiliac cohort' *British Journal of Haematology*, 1989; 72: 387-90 [LIT.001.0581]; Preliminary Report, para 8.211

<sup>157</sup> Ibid, [LIT.001.0581] at 0584. A possible link with a particular genetic feature in some of the affected individuals was explored in Steel et al, 'HLA haplotype A1 B8 DR3 as a risk factor for HIV-related disease' *The Lancet*, 1988; 1185-8, [LIT.001.0895], this was corroborated in later American and Australian studies. Kaslow et al, 'A1, Cw7, B8, DR3 HLA antigen combination associated with rapid decline of T-helper lymphocytes in HIV-1 infection' *The Lancet* 1990; 335: 927-30 [LIT.001.3825]

<sup>158</sup> CM Steel et al, 'HLA haplotype A1 B8 DR3 as a risk factor for HIV-related disease' *The Lancet*, 1988; 1185-8 [LIT.001.0895]

**10.118** By this stage, sophisticated methods of analysis of the evolutionary relationships among groups of organisms, such as HIV, had been developed. Typically presented as 'phylogenetic trees', the findings on analysis enabled the definition of genetic relationships among samples from several sources. In 1988, Professor Peter Simmonds and associates reported on phylogenetic analyses of two regions of the *env* gene, a component of the 'viral envelope' of HIV, in the Edinburgh Cohort. Sequences from most of the patients studied were grouped together on phylogenetic trees with common origins.<sup>159</sup>

**10.119** The study dealt with nine patients, eight of whom were members of the Cohort. Six were grouped closely on analysis and it was inferred that they were infected with HIV sequences from a single donor. It was suggested that three of the nine, including two members of the Cohort, may have been infected independently of the others at about the same time. The conclusion that one common batch of concentrate was implicated in the infection of the Cohort, reached previously on analysis of the transfusion records, was weakened. At that stage, however, 10 members of the Cohort had not been included in the study.

**10.120** A further study reflecting results obtained from examination of the Edinburgh Cohort was published in the *BMJ* in 1990.<sup>160</sup> The study did not identify any immunological variable or clinical characteristic which distinguished the patients who seroconverted from those who did not. It reported that, within the Edinburgh Cohort, the cumulative incidence of serious HIV-related disease was 55.5% at five years. A third member of the Cohort, a patient born in 1948, had died (in 1989).

**10.121** The understanding of the Cohort changed further with the publication in 1995 by Edward Holmes and others of further virological findings.<sup>161</sup> The study was aimed at clarifying the number and origins of the batches of Factor VIII involved in the HIV infection of the Edinburgh haemophilia patient population. It would be inappropriate in this report to enter into a detailed technical discussion of the studies carried out but some of the conclusions are material. With two exceptions, the patients studied were formed part of a single phylogenetic tree and fell into a single group. The patients were identified only by number. Patients 74 and 82 were the two patients distinguished in the 1988 study as possibly having been infected independently. In this 1995 study, patient 74 could not be separated from the main group with any confidence but there was good evidence that patient 82 was not a member of the main Cohort because his data suggested a close relationship with a patient, patient 80, who had never been exposed to batch 023110090 of the PFC's NY Factor VIII product and now appeared to have been infected by a different batch which patient 82 had also received. The similar viruses found in patients 82 and 80 must have been derived from a Factor VIII batch that they were known to have shared. Taking the results of their several studies together, the authors commented:

The most striking finding was that there are several distinct HIV variants circulating in Edinburgh. The haemophiliac patients appear to be divided into a number of distinct groups whose members were infected by at least two batches of contaminated factor VIII. This is particularly surprising since most of

<sup>159</sup> Balfe et al, 'Concurrent Evolution of Human Immunodeficiency Virus Type 1 in Patients Infected from the Same Source: Rate of Sequence Change and Low Frequency of Inactivating Mutations' *Journal of Virology*, 1990; 64:6221-6233 [PEN.012.1403]

<sup>160</sup> Cuthbert et al, 'Five year prospective study of HIV infection in the Edinburgh haemophilic cohort', *British Medical Journal*, 1990; 301:956-961 [LIT.001.0291]; Preliminary Report, para 8.2.12

<sup>161</sup> Holmes, EC et al 'The Molecular Epidemiology of Human Immunodeficiency Virus Type 1 in Edinburgh' *The Journal of Infectious Diseases* 1995; 171:45-53 [PEN.012.1679]

these patients seroconverted at about the same time (spring 1984) and were originally thought to have been infected after exposure to a single common batch.<sup>162</sup>

**10.122** After discussing the specific findings relating to patient 74, the paper stated:

Thus, there appear to have been 2 or 3 HIV-infected donors contributing to the local plasma pool at the time these batches were prepared (1983). This shows that there was substantial viral diversity during the early stages of the HIV epidemic in Scotland...<sup>163</sup>

**10.123** The same study discussed infected heterosexual and IVDU patients whose data had been analysed, and concluded:

The fact that the heterosexual and IVDU groups are some distance from the haemophiliac groups on all the phylogenetic trees shows that the HIV infections in these populations were independent and refutes suggestions the haemophiliacs could have been infected from the IVDU community.<sup>164</sup>

**10.124** Two potential sources of infection had been excluded. Further inferences were avoided. It appears from this work that the original conclusion, that there was a single donor source of infection transmitted to haemophilia patients by Factor VIII concentrates, was wrong.

### ***SNBTS investigations***

**10.125** On 25 January 1991, Dr Cuthbertson, then Quality Assurance Manager at the PFC, wrote to Professor Cash enclosing a final report, 'HIV Seroconversions related to SNBTS FVIII'.<sup>165</sup> This was an update of an earlier, interim report of 28 June 1986.<sup>166</sup> It reflected the information available to the PFC. The infection of 16 patients in Edinburgh was referred to, as was the infection of two patients in the West of Scotland, one of whom had seroconverted between 5 October 1984 and 25 October 1985. It was not possible to draw definitive conclusions as to the batches by which all these patients had been infected; batch 023110090 remained the main candidate for 15 of the 18 seroconversions but the other candidate batch(es) had not been identified.

**10.126** The report contained the following detail:

16 Haemophiliacs in the South-East of Scotland were found to have seroconverted to HIV at some stage during 1984. Fifteen of the 16 haemophiliacs received a common batch (023110090) and it has been concluded that this batch was infective.

Follow-up of West of Scotland haemophiliacs has revealed two patients receiving SNBTS FVIII who seroconverted in 1984 and 1985 respectively.

---

<sup>162</sup> Holmes et al, 'The molecular epidemiology of human immunodeficiency virus type 1 in Edinburgh' *The Journal of Infectious Diseases* 1995; 171:45–53 [PEN.012.1679] at 1685

<sup>163</sup> Ibid [PEN.012.1679] at 1686

<sup>164</sup> Ibid [PEN.012.1679] at 1686

<sup>165</sup> Letter from Dr Cuthbertson to Professor Cash, 25 January 1991 [SNF.001.3564]; Report 'HIV Seroconversions Related to SNBTS FVIII' [SNB.001.1243]

<sup>166</sup> Interim Report [SNB.008.6427]



PATIENT 1

Incomplete details available as no written report ever received from reporting clinician (Dr Maddock [*sic* – Madhok], GRI).

Sample 1.7.82 Negative

Sample 12.12.83 Positive.

PATIENT 2

Seroconverted between 5.10.84 and 25.10.85. At least five years since previous Commercial FVIII

The batches of product received by the ... seroconverters are summarised in Table 1. The following should be noted:

- a. Neither of the West of Scotland patients received the batch (023110090) implicated in the South-East Scotland seroconversions.
- b. No batch is common to the two West of Scotland seroconversions.
- c. If SNBTS FVIII was responsible for each of the 18 seroconversions, then at least three infective batches must have been issued.<sup>167</sup>

**10.127** It is possible that there were four, not three, sources of infection. One of the South-East Scotland patients did not receive batch 023110090: there had to have been at least two sources of infection in that area. Two patients were infected in the West of Scotland but neither had received batch 023110090 and they did not receive batches in common with others. A manuscript note on a copy of Dr Cuthbertson's report recovered by the Inquiry questioned whether cryoprecipitate was a source. Cryoprecipitate was a potential alternative cause of limited spread infection in the West of Scotland where it was a popular therapeutic material. The probability of a single infection from a pooled product must be relatively low and must get lower as one multiplies examples. It is not possible for the Inquiry to identify definitively the source of infection in all cases. The discussion in the quoted report is in many respects inconclusive. It was noted at the end of Dr Cuthbertson's report that polymerase chain-reaction (PCR) studies were being carried out which might define more precisely the implicated batches but that the position remained uncertain, apart from in the Edinburgh Cohort.

**10.128** The final position on numerical data on the incidence of HIV infection and AIDS in those affected by blood, blood components and blood products, so far as uncovered by the Inquiry, is set out in Chapter 3, *Statistics*. For present purposes, it is sufficient to note that the final numbers consistently exceed the earlier estimates.

**10.129** At the date of the Inquiry's hearings, it appears that 15 of the 18 members of the Edinburgh Cohort had died.

### The Edinburgh Cohort: 2008 testing

#### *The history of batch 023110090*

**10.130** The history of batch 023110090 was investigated in great detail by the Inquiry. Although perhaps somewhat tangential to the progress of the AIDS epidemic in the period under discussion, it illustrates many of the difficulties confronting scientists at the time in conducting research into the association of AIDS with blood product therapy. In

<sup>167</sup> Report 'HIV Seroconversions Related to SNBTS FVIII' [SNB.001.1243]

addition there is some advantage in setting out the Inquiry's findings in the context of the foregoing discussion of the impact of the infected product on patients.

**10.131** Further investigations into the history of the infection of the Edinburgh Cohort took place in 2008. The preparation of batch 023110090 was studied in some detail and Dr Perry explained that the batch had a conventional history. Collection took place between June and October 1983, with plasma collected from each of the RTCs in Scotland. A total of 940 kilograms of plasma was collected from about 4000 donations. The plasma weight delivered to the PFC would have been recorded by each RTC.<sup>168</sup>

**10.132** At the PFC the plasma was first divided into intermediates or 'fractions', which were then stored frozen. When required they were taken out of inventory and entered into a specific batch manufacturing process, at which point a batch number was allocated. A record was kept to allow a trace back from the batch number of a product to the fraction.<sup>169</sup>

**10.133** Dr Perry explained that there were two forms of plasma record.<sup>170</sup> Boxes of 12 donations were bound together in groups of four for storage purposes and each group of four boxes was given a new identifier called a 'cold storage number'. The cold storage numbers for each group of four boxes were recorded in the batch record; these records were kept down to the box number. Each box had bar-coded labels. There was a clear link between the boxes and the donations from the RTC. Although the PFC could not itself identify individual donations, the RTCs had records which identified which plasma donations had gone into an individual box. From the record, 95 cold storage units were used to manufacture batch 023110090.<sup>171</sup>

**10.134** The batch record shows that the manufacturing process started on 7 November 1983 and produced 1070 vials of Factor VIII.<sup>172</sup> The batch record shows the number of vials placed at issue and entered into stock.<sup>173</sup> The product was cleared for issue on 10 February 1984 and the product clearance sheet showed when the batch was released for issue.<sup>174</sup> It was recorded that 1020 vials were sent to the South East of Scotland RTC and that fifty vials were supplied to the North East RTC in Aberdeen where they were held for the treatment of patients with haemophilia. A batch history sheet recorded the final quality release of the batch.<sup>175</sup> This document was used for stock control by PFC.<sup>176</sup>

### *Tracing the donations to batch 023110090*

**10.135** As the recording system was designed, the batch record allowed the SNBTS to trace the donations which had made up any particular batch. The cold storage numbers gave key references for the individual plasma boxes. The box number identified the RTC which supplied the box and the RTCs had records from which to identify the individual donations. From the individual donations it was then possible to identify the specific donors.<sup>177</sup>

<sup>168</sup> Day 38, pages 53–58

<sup>169</sup> Day 38, pages 46–47

<sup>170</sup> 'Actions surrounding FVIII Batch 023110090' [PEN.016.1258] at 1264 and Day 38, page 51

<sup>171</sup> Day 38, pages 50–2; 'Actions surrounding FVIII Batch 023110090' [PEN.016.1258] at 1264

<sup>172</sup> Batch Record [PEN.012.1339]; 'Actions surrounding FVIII Batch 023110090' [PEN.016.1258] at 1263

<sup>173</sup> Finished Product Documentation [PEN.012.1339] at 1373

<sup>174</sup> Product Clearance Sheet [PEN.012.1339] at 1340

<sup>175</sup> Batch Issue History sheet [PEN.012.1375]

<sup>176</sup> Dr Perry – Day 38, page 43–44; 'Actions surrounding FVIII Batch 023110090' [PEN.016.1258] at 1264

<sup>177</sup> Day 38, pages 58–59; 'Actions surrounding FVIII Batch 023110090' [PEN.016.1258] at 1263–4

**10.136** It was a deliberate policy to disable the PFC from identifying specific donors from its own records. This maintained a separation between the 'greater clinical environment' at the RTCs and the PFC, which was a pharmaceutical manufacturing plant.<sup>178</sup> Following a meeting on 6 November 1984, it was decided that repeat donations from the donors contributing to the implicated batch should be followed up.<sup>179</sup> That was done but none of the subsequent donations were found to be HIV-positive. Dr Perry did not know how many repeat or returning donors there were.<sup>180</sup>

**10.137** Subsequently, consideration was given to trying to test the donors of all 4000 donations.<sup>181</sup> Donation samples were available from about 50% of these donors. Having taken advice from Professor Tedder that 99.5% of the donors would be required for the exercise to be meaningful, this was not followed through and the proposal was not pursued.<sup>182</sup> Dr Perry referred to correspondence with Dr Tedder.<sup>183</sup> It was considered impossible to find the source of the donation in this way. Dr Perry accepted that as return donors came back the pool of potentially infective donors began to shrink. A chronology prepared by the SNBTS also set out the documents relevant to each event.<sup>184</sup>

### *2008 testing*

**10.138** Dr Perry explained that, by 2008, he personally was satisfied that batch 023110090 was the batch responsible for infecting most of Professor Ludlam's patients. He explained that after the present Inquiry was announced, the SNBTS anticipated that the question of the implicated batch would be investigated and they decided to look at the matter again. It turned out that the majority of the remaining vials of Factor VIII belonging to batch 090 had been destroyed in 1988. However a single vial was discovered in the laboratory of Professor Simmonds and it was sent for testing. The vial had been stored in uncontrolled conditions and there was concern that the contents would have deteriorated and that any virus would have degraded so that it was not detectable.<sup>185</sup>

**10.139** The samples were sent to the NIBSC on the authority of Professor Ian Franklin who was the National and Medical and Scientific Director of the SNBTS in 2008. The testing was done at the the NIBSC to extremely high standards. The vial was first tested by nucleic acid amplification (NAT) technology for the Hepatitis C virus (HCV), a PCR test for the presence of virus. Tests for HCV would provide a positive control if the assay was working. The SNBTS knew that products in 1983–84 and 1985 were likely to contain HCV, so if the test had come back negative for HCV this would have cast doubt over a negative result for the HIV test: it would have raised the inference that the product in the vial had degraded so much over the years that any virus originally in the vial had disappeared.

**10.140** In the event, the sample was positive for HCV RNA. The sample was negative, however, in a duplicate test for HIV-1 RNA by NAT, a standard commercial assay. The conclusion was that no HIV RNA could be found in the vial using that test.

<sup>178</sup> Day 38, page 59

<sup>179</sup> Letter from Dr Perry to Dr Brooks, 12 November 1984 [PEN.012.1378]

<sup>180</sup> Day 38, page 61

<sup>181</sup> Letter from Dr McClelland to Dr Tedder, 28 November 1984 [PEN.012.1423]; 'Actions surrounding FVIII Batch 023110090' [PEN.016.1258] at 1266

<sup>182</sup> Dr Perry – Day 38, page 63

<sup>183</sup> Letter from Dr Tedder to Dr McClelland, 20 December 1984 [PEN.012.1424]

<sup>184</sup> 'Actions surrounding FVIII Batch 023110090' [PEN.016.1258] at 1270

<sup>185</sup> *Ibid* [PEN.016.1258] at 1263 and 1266; Day 38 pages 21–23

**10.141** Further 'in-house' tests were then done, with the result that there was evidence for the detection of HIV-1 RNA sequences at very low levels.<sup>186</sup> The in-house tests were very specialist, essentially research assays developed by expert virologists at the NIBSC. Dr Perry explained that the results suggested that the sample might contain a fragment of HIV RNA but that one could not be absolutely sure. The results were inconclusive because the research assay had not been subjected to the rigorous analysis needed for a routine test. However, it provided an indicative result of a fragment of RNA of HIV.<sup>187</sup>

**10.142** The NIBSC also carried out a combination test for antigen and antibody. This result was quite clear: the sample was reactive; HIV had been detected in the sample. As it was a 'combination test', it was not clear whether the sample was reactive for the antigen or the antibody and the precise meaning of the result was that there was either HIV antibody or HIV antigen in the sample.<sup>188</sup>

**10.143** Other tests using ELISAs came back negative and the Western Blot test was indeterminate. Dr Perry explained that these tests in 2008 were the first chemical and biological evidence that were in line with the epidemiological evidence from the patients in 1985.<sup>189</sup>

**10.144** The level of technological sophistication that has now enabled scientists to form these views about the infectivity of batch 023110090 had not been achieved at any time during the course of the AIDS epidemic among recipients of blood, blood components or blood products. The risk that the product presented to haemophilia patients could not have been identified at the time it was administered or investigated by chemical or biological assays after the infections were first diagnosed.

## Discussion

**10.145** This chapter has sought to trace evidence of the growing awareness among relevant practitioners, and in particular haemophilia clinicians, of the incidence and characteristics of HIV infection and AIDS-related diseases during the critical period up to and covering the introduction of effective technology for the treatment of factor concentrates, looking at the position in the world in general but with specific reference to the UK.

### *The Edinburgh Cohort*

**10.146** Particular attention has been paid to the Edinburgh Cohort. The discovery of HTLV-III infection in that group was not an isolated event: it happened in the context of the testing of samples from Haemophilia Centres throughout the UK using the Tedder/Weiss assay. However, the infection of the Cohort was distinguished by its scale; its concentrated impact on one regional centre; the fact that infection in the Scottish domestic product was unexpected; and in the extent and intensity of the investigation that followed. The immediate confusion following the discovery has been described. The last point is most instructive of contemporaneous understanding of the implications for manufacturers, transfusionists and haemophilia clinicians alike.

---

<sup>186</sup> 'Actions surrounding FVIII Batch 023110090' [PEN.016.1258] at 1283

<sup>187</sup> Day 38, pages 27–28

<sup>188</sup> Day 38, page 33

<sup>189</sup> Day 38, pages 28–29

**10.147** The timescale for withdrawal of batch 023110090 was short. From the records, Professor Ludlam ascertained on 29 or 30 October 1984 that the three original recipients of SNBTS concentrate had received material from that batch. The additional information from Professor Tedder was received on 2 November. Dr McClelland and Dr Boulton arranged for the withdrawal of the batch on 3 November. That was clearly the correct course of action.

**10.148** At the end of 1984, when the scale of infection in the Cohort was established, none of those involved in the SNBTS and in the haemophilia clinical service had the technological means to identify infective donations, or to assess the infectivity of blood products, or to find explanations for the course of events that unfolded. That continued to be the position.

**10.149** Dr Perry's view that it was a 'justifiable, though unproven assumption' that batch 023110090 was implicated was valid on the information available. It left open two alternatives, however: it remained possible, on the one hand, that the batch would prove not to be infective and it remained possible, on the other, that other batches were infective.

**10.150** The second of these possibilities raises the more significant questions. Unless investigations were to establish that all of the patients who were infected had received batch 023110090 and that none of those found to be infected had received SNBTS material from any other batch, it would have been logically indefensible to conclude that only the single batch was infected. By May 1985 it was known that one of Professor Ludlam's infected patients had not received material from batch 023110090. Source donations could not be identified and it was not possible by that route to limit the potential range of infected batches. Further, cases of infection were being identified at the same time in other parts of Scotland, and in particular in the Glasgow and West of Scotland Region.

**10.151** Technology was not sufficiently developed at the time of the recall of batch 023110090 to test it for infectivity. Initial testing in 1985 and 1986 found no chemical or biochemical indicator that the batch contained an infectious virus or that it contained antibodies to a virus. The SNBTS staff were not surprised by the negative test in 1985 because they knew that the tests were relatively insensitive and also thought that, if the infection derived from one donation, it would have been diluted by 4000 other donations. In addition, they did not know at the time how the HIV antibody partitioned during the fractionation process.<sup>190</sup>

**10.152** The testing of serum from patients reported in the *BMJ* in February 1988 led to the conclusion that 18 patients had acquired infection from a single batch and that the batch was probably contaminated by a single donation. At that stage there was some technological support for the inferences being drawn. Further scientific support was provided by Professor Simmonds and his associates in 1988. Whatever objections on strictly logical grounds might be taken to the initial inference that there was a common source of infection, there was now apparent scientific proof of the inference drawn from the information available at that time.

---

<sup>190</sup> Dr Perry – Day 38, pages 40–41

**10.153** It was to be 1995, however, before scientific evidence was published that there were two infective batches and contributions to the local plasma pool at the time by two or three HIV-infected donors. It was 2008 before something approaching scientific proof was available of at least anti-HIV in the sole remaining sample of batch 023110090. Dr Perry explained that, in his view, putting the 2008 test results together with the epidemiological evidence, batch 023110090 was 'probably infectious'. It would always fall short of absolute proof but he thought that there was a very strong probability that batch 023110090 was the correct batch to have identified as being responsible for the transmissions. As for the putative second infective batch, the possibility that this existed was only raised in 1995. By that point it was not possible to take the matter forward, the materials (including samples of any implicated batches) having long since been used or discarded.

**10.154** Details of HIV infection in the Edinburgh Cohort were widely reported. On the other hand, infections in some other affected groups were not. Dr Cuthbertson's final report of 25 January 1991 dealt with two infected West of Scotland patients only. As shown in Chapter 3, *Statistics*, the actual final picture would be seen to be quite different.

#### *Wider surveillance*

**10.155** Throughout the UK, there were deficiencies in the reporting of instances of infection. The picture that emerges from the account of Dr Craske's surveys reflects inconsistent and incomplete disclosure of relevant information by significant numbers of Haemophilia Centres and frustrating attempts to analyse the problems related to patients and their illnesses which led to the publication of partial information when, within the relatively small group of Centres involved, comprehensive sources of information were available. The wish to protect patients' confidential personal data is understandable, as is the belief that any level of disclosure would threaten confidentiality and with it the patient-doctor relationship. The stigma surrounding HIV infection was indiscriminate and damaging. The accounts of patients and their families in Chapters 4 and 5 are eloquent of the concerns felt by clinicians at the time. However, the outcome was unfortunate in the respect that, at the time, more comprehensive data might have influenced the approach to management of infected patients and accelerated the appreciation at government level of the risks presented.

**10.156** The Communicable Diseases Report Review, no 8, of 17 July 1992 stated:

The surveillance of the spread of HIV infection in the United Kingdom relies on the voluntary reporting of AIDS cases and HIV infected individuals, and on large-scale unlinked anonymous seroprevalence surveys. The distribution of currently reported cases by region and exposure category reflects the pattern of infection some years ago, because of the long incubation period of AIDS. New reports of HIV infected individuals identified through voluntary testing reflect current transmission patterns more closely but also depend on the numbers tested in each exposure category. Unlinked anonymous testing provides seroprevalence estimates for sentinel groups in the population but is limited by the extent to which epidemiological information can be related to the sera tested, and by the composition of groups that can be sampled. Moreover, serial seroprevalence data can only provide an indirect estimate of the incidence of new infections.

To extend national surveillance, a collaborative study was set up in 1986 by the PHLS to record relevant epidemiological information for both HIV antibody positive and negative individuals tested voluntarily in selected laboratories in England. The main objectives of the study are to enhance interpretation of data from HIV antibody positive reports, by providing information on the numbers tested according to exposure category; to provide an indication of seroprevalence in groups not sampled or categorised in the unlinked anonymous testing programme, and to provide direct estimates of incidence in selected high risk groups.<sup>191</sup>

**10.157** Eighteen laboratories in England were selected. The results obtained were tabulated:

**Table 10.6: Prevalence of HIV antibody by exposure category: October 1986–September 1991**

Exposure category	Males		Females	
	Number tested	Tested positive (%)	Number tested	Tested positive (%)
<b>Sexual intercourse</b>				
Homosexual/bisexual	17,685	1582 (8.9)	514	–
Heterosexual				
lived in/visited Africa	1970	134 (6.8)	1037	109 (10.5)
lived in/visited Americas	358	4 (1.1)	197	4 (2.0)
HIV positive partner	321	14 (4.4)	634	43 (6.8)
high risk partner	1798	10 (0.6)	5317	32 (0.6)
moderate risk partner	3427	5 (0.1)	3692	2 (0.1)
many partners	11,527	21 (0.2)	14,682	10 (0.07)
<b>Injecting drug use</b>	7031	184 (2.6)	3017	75 (2.5)
<b>Blood</b>				
Blood factor (eg, for haemophilia)	1022	60 (5.9)	141	–
Blood/tissue transfer (eg, transfusion)	1147	8 (0.7)	1483	9 (0.6)
<b>Mother to infant</b>	98	15 (15.3)	83	9 (10.8)
<b>Other</b>				
Multiple exposure categories	2059	92 (4.5)	745	18 (2.4)
Unspecified contact with HIV positive or at-risk person	2796	16 (0.6)	3320	12 (0.4)
Household Contact/nursing/needlestick/bite	440	–	405	–
<b>No reported risk</b>	46,331	15 (0.03)	28,039	8 (0.02)
Total	98,010	2160 (2.2)	63,306	331 (0.5)

**10.158** The table probably provides a reasonably reliable basis for comparison of the balance of infection among the groups sampled. Given its selective nature, however, it cannot present a picture of the incidence of disease generally. So far as transmission to NHS patients is concerned, it shows a very small rate of transmission by blood and tissue, as would have been expected after the introduction of anti-HIV testing. As noted above, the Oxford report of 3 October 1986 showed that 40.48% of 2228 Haemophilia A patients, 6.74% of 386 Haemophilia B patients and 2.75% of 327 von Willebrand's disease patients, almost all tested before heat-treatment of concentrates and screening of donors was commenced, were anti-HIV positive. It would be expected that the number

<sup>191</sup> CDR Review, no 8, 17 July 1992 [LIT.001.4789]

of additional cases of infection identified after October 1986 would be much lower, again because of testing. Sixty additional cases from 1022 males tested would reflect that, though it is not clear when they were infected and the true number of additional infections may be lower still.<sup>192</sup>

**10.159** However, it is not possible, on the basis of these figures, to express any confident view of the scale of the epidemic in England and Wales and therefore of the scale of the problem in the UK as whole. Only general impressions of the scale and development of the epidemic can be suggested.

**10.160** There is inevitably a lack of certainty about the end of the epidemic so far as NHS patients are concerned – in terms of the date when HIV was last transmitted to a blood disorder patient by replacement therapy or to a patient receiving blood or blood components in the course of medical or surgical procedures. Factor VIII concentrates issued from January 1985 were heat-treated to inactivate HIV and heat-treated Factor IX was routinely issued from October that year. Meantime, routine anti-HIV screening of blood donations had been introduced on 14 October 1985. It is not possible to exclude completely the possibility that there might have been transmission of HIV to NHS patients after these procedures were in place.<sup>193</sup> Human error might have occurred, resulting in the clinical use in or after January 1985 of Factor VIII that had not been heat-treated but had remained in stock. There is the same transitional risk with Factor IX around October 1985 and unscreened blood or components might have been used after 14 October 1985. However, it seems reasonable to take these three events as marking the end of the period of risk for most patients.

**10.161** The numbers of patients infected with HIV were not determined until later. Final numbers, so far as ascertained by the Inquiry, are discussed in Chapter 3, *Statistics*.

## Summary

- Throughout the period when HIV transmission was a significant threat to recipients of blood, blood components and blood products, data on the numbers of individuals infected were incomplete and generally underestimated the extent of the developing epidemic.
- Adoption of the CDC test for AIDS, the identification of intractable AIDS-defining disease, without a requirement to report significant evidence of impaired cell-mediated immunity, inevitably had an impact on the understanding of the developing epidemic until late 1984 when testing for anti-HTLV-III became available.
- As a result, government and NHS agencies did not have accurate information on the scale of the epidemic as a guide to policy generally and in particular as a guide to management of blood disorder patients.
- In retrospect it is clear that the voluntary reporting system did not secure comprehensive reporting of the numbers of patients infected.

<sup>192</sup> Since the earlier surveys were incomplete, it cannot be concluded that all of the 60 cases were new infections after October 1986: they may equally have been omitted from the earlier data because they were registered at Haemophilia Centres which refused to provide data.

<sup>193</sup> One case is noted in the Preliminary Report at paragraph 8.194



- Neither the UKHCDO nor any other professional group had authority to require disclosure of the anonymised data which were needed properly to measure the emerging pattern of infection in blood disorder patients.
- There were no rules of conduct prescribed by any government agency with responsibility for the administration of the National Health Service that required such disclosure.
- This is an area in which the apparently unquestionable independence and autonomy of the medical consultant seriously inhibited the collection and analysis of information essential to a full understanding of these emerging diseases and their implications for the patient population.
- As a result, the extent of the AIDS epidemic in recipients of blood, blood components and blood products in the UK generally has only become apparent following extensive retrospective analysis.



## CHAPTER 11

### HIV/AIDS AETIOLOGY

#### Introduction

**11.1** This chapter discusses the aetiology of AIDS: the cause or causes of the Acquired Immune Deficiency Syndrome that exposed individuals to disproportionate risk of opportunistic infection, cancers and other diseases of the AIDS complex, as disclosed in public debate, professional literature and the written and oral evidence provided to the Inquiry.

#### *Inter-disciplinary research in the 1980s*

**11.2** Medical and scientific understanding of the epidemiology of AIDS, as set out in Chapters 9 and 10, *Knowledge of the Geographic Spread and Prevalence of HIV/AIDS 1 & 2*, provided the context for discussion of the cause or causes of the disease as well as the modes of transmission of infection. It is necessary, however, to repeat a note of caution at the outset. Multi-disciplinary research and cooperation were less well-developed features of medical and scientific practice in the 1980s compared to contemporary practice. There was a lack of coordination of the research of groups working on similar problems but focusing on their own specialist interests. So, virologists and infectious diseases specialists might take one view of emerging evidence of disease while haematologists and haemophilia clinicians might take different views. Fractionators – those involved in the manufacture of blood products – responded quickly to the Barré-Sinoussi article in *Science* on 20 May 1983 (the seminal publication by the Montagnier group at the Institut Pasteur in Paris announcing the isolation of a putative AIDS-causing virus, discussed at paragraph 11.90, below).<sup>1</sup> Their approach was influenced by their apprehension that their products were already transmitting non-A, non-B Hepatitis. Professor Ian Hann, Director of the West of Scotland Paediatric Haemophilia Centre, Yorkhill, Glasgow, between 1983 and 1987, thought that one of the beneficial lessons of the HIV era was the need for multi-disciplinary teams,<sup>2</sup> but in the early 1980s that did not generally happen. As a consequence, what might have been known to one discipline about an emerging syndrome cannot be assumed to have been known to another and, in particular, what was published (still, at this stage, largely in paper form) in even a prestigious publication of specialist interest to one professional discipline cannot be assumed to have been read by specialists in other areas. The material years of the early 1980s were before the advent of electronic literature searches now considered routine.

**11.3** In modern practice, the degree of insularity that appears to have existed would be considered inappropriate. With the benefit of hindsight, practice in the 1980s might be the subject of adverse comment but it is difficult to re-create the medical environment without imposing on it changes in attitude and developments in practice that would only be achieved later, often in the light of experience with HIV/AIDS and the Hepatitis C virus. The reality is that one cannot assume homogeneous dissemination of information or a common understanding of that information among the disparate groups of scientists and clinicians who became interested in AIDS in the early 1980s. It is particularly important

---

<sup>1</sup> Barré-Sinoussi et al, 'Isolation of a T-Lymphotropic Retrovirus from a Patient at Risk for Acquired Immune Deficiency Syndrome (AIDS)', *Science*, 20 May 1983 [LIT.001.0058]

<sup>2</sup> Day 21, page 57

to bear in mind the possibility that a fact well known to and understood by an infectious diseases specialist, for example, might have been wholly unknown to, or if known misunderstood by, a haemophilia specialist, even though each might have had an interest in patients with the same or similar infections.

**11.4** Apart from differences among clinical specialists, there are likely to be differences between (i) the information and knowledge available to clinicians as a whole and (ii) the information and knowledge developed by scientists engaged in fundamental research, especially where there may be intellectual property rights to be protected. This chapter will leave the second topic for discussion in Chapter 29, *Discovery of HIV and Developments of Screening Tests*. Although scientific research overlapped in time with the events discussed in this chapter, and merged with them in 1984, progress in understanding of the aetiology of AIDS developed independently between the groups engaged in public debate and those pursuing confidential projects.

**11.5** These factors add further difficulty to what is inevitably a complex and difficult exercise: tracing changing theories of the cause of AIDS and assessing their relevance to scientific investigation and clinical practice.

**11.6** The controversies surrounding the possible cause of AIDS effectively ended by mid- to late 1984 with the confirmation that the lymphadenopathy-associated virus (LAV)/ human T-cell lymphotropic virus III (HTLV-III) was the pathogen responsible for transmitting infection. The developments in thinking up to that time are recounted at some length. Tragically, the majority of individuals infected with HIV – either those with bleeding disorders or following transfusion with infected blood – acquired the virus between early 1982 and mid-1984 when there was no settled understanding of the cause or causes of AIDS. There is natural, and wholly understandable, concern that in some way AIDS was ‘allowed’ to happen when it could, and should, have been controlled. If that concern is to be addressed, at the very least it is necessary to have information that is as reliable as possible about events as they unfolded.

### Early reports and first thoughts

**11.7** Early reports of the disease are discussed in the Preliminary Report and in Chapter 9, *Knowledge of the Geographical Spread and Prevalence of HIV 1*. The initial debate on AIDS, as published in 1981 and 1982, was heavily influenced by the fact that most of those reports dealt exclusively with homosexual men.<sup>3</sup> An association with some aspect of a homosexual lifestyle or disease acquired through sexual contact was promoted as a cause of the disease. Cytomegalovirus (CMV) infection, sometimes associated with cellular-immune dysfunction, was prevalent among male homosexuals and there was speculation at the end of 1981 that there was a causal link. Michael Gottlieb and colleagues reported that four young previously healthy homosexual men, whose clinical manifestations were similar to the group originally reported in June 1981,<sup>4</sup> all had CMV infection and this was suggested as a major factor in the pathogenesis (causation and development) of the immunocompromised state.<sup>5</sup> Other possibilities canvassed included abnormal responses

<sup>3</sup> Evatt ‘The tragic history of AIDS in the hemophilia population 1982–1984’, *Journal of Thrombosis and Haemostasis*, 2006; 4/11:2295–2301, (reprint) [PEN.016.1183] at 1185

<sup>4</sup> See Chapter 9, *Knowledge of the Geographical Spread and Prevalence of HIV/AIDS 1*, paragraph 9.18

<sup>5</sup> Gottlieb et al ‘Pneumocystis carinii pneumonia and mucosal candidiasis in previously healthy homosexual men’, *New England Journal of Medicine*, 1981; 1425–1431 [LIT.001.0779]

to Epstein Barr virus (EBV) or Hepatitis B virus.<sup>6</sup> It was thought that seminal fluid might be an important vehicle of CMV transmission. This suggested the possibility that common exposure predisposed male homosexuals to opportunistic infections.<sup>7</sup>

### *A genuinely new disease*

**11.8** AIDS seemed to be a genuinely new disease.<sup>8</sup> At the International Symposium on Infections in the Immunocompromised Host held in June 1982, a lecture on AIDS in homosexuals and drug addicts was 'the talk of the meeting'. Professor Hann said that after the lecture there was an atmosphere of extreme puzzlement. He explained:

[A]lthough we knew some viruses, like Epstein Barr virus, the glandular fever virus, other Herpes viruses like cytomegalovirus, could cause immune deficiencies, nothing remotely like this had ever happened before.

So we needed to prospectively study apparently normal gay people at that time, intravenous drug abusers et cetera, and see what it was that was making them immune deficient.<sup>9</sup>

**11.9** In relation to the cause of this syndrome, he said that the preferred belief among the experts present at the symposium was that it was most likely that a new viral agent or that several viruses might be involved.

**11.10** When the first cases were reported at the beginning of the 1980s, HTLV-III appeared to be a unique infection.<sup>10</sup> AIDS was considered to have no relevant history. It is now thought that HIV is a zoonosis – a pathogen transmitted from another species and in this case a descendant of a Simian Immunodeficiency Virus (SIV).<sup>11</sup> There are two types. HIV-1 is the more predominant, probably causing more than 98% of the human infections. It is believed that it was passed from chimpanzees to humans in West Africa in the early part of the twentieth century. HIV-2 has a different structure that is very closely related to a virus found in the sooty mangabey monkey species. Professor Andrew Lever, Professor of Infectious Diseases at Addenbrooke's Hospital, Cambridge, explained:

[T]he evidence is that HIV-2 crossed into humans from the sooty mangabey, whereas HIV-1 crossed into humans from the chimpanzee. Both of these, almost certainly – as I think it's well understood now – came into the human race, as far as we can tell, through the bush meat trade, where wild monkeys are caught and slaughtered and butchered and sold for food, and since both viruses are blood-borne and in fact in the monkey population they're transmitted predominantly by blood – by fighting, by biting and scratching – then it's relatively easy to think of how a virus may have been transmitted from fresh meat into someone who was handling that.<sup>12</sup>

<sup>6</sup> Professor Hann – Day 21, pages 43–44

<sup>7</sup> 'Pneumocystis pneumonia – Los Angeles', *MMWR* 5 June 1981; 30(21):1–3 [LIT.001.1026] at 1027

<sup>8</sup> Dr Winter – Day 15, page 111

<sup>9</sup> Day 21, pages 43–44

<sup>10</sup> Professor Lever's Report [PEN.015.0517] at 0518

<sup>11</sup> Zoonosis, or 'spillover', is relatively frequent, with up to 60% of known human diseases estimated to be zoonotic in origin. SARS (Severe Acute Respiratory Syndrome) is another, more recent example. 'Viral chatter' – tracing the emerging 'incursions' of zoonotic diseases – is an important part of virological research.

<sup>12</sup> Day 26, page 27

**11.11** Once passed to humans, SIV mutated to become HIV.<sup>13</sup> Over time, HIV spread from Africa to the West and, in particular, to the USA.<sup>14</sup>

**11.12** In the early 1980s, comment focused on the novelty of the emerging features of the disease, such as *Pneumocystis carinii* pneumonia (PCP) or Kaposi's sarcoma (KS), in apparently healthy homosexual males who had not previously had clinically apparent immunodeficiency. There was also speculation that homosexual men contracted the disease because their immune system was not working properly, having been compromised by so-called 'recreational' drugs taken for stimulation.

### **Risk factors**

**11.13** By mid-1982, the mix of homosexual and heterosexual patients, intravenous drug abusers and haemophilia patients suggested that risk factors might be different for different groups. At this stage, in the first half of 1982, a blood-borne virus, spread by sexual relations, had been postulated but there was great uncertainty.<sup>15</sup> Other mechanisms were suggested, especially in the case of haemophilia patients, and it has become clear with the passage of time that some haemophilia patients did indeed develop different immune disorders, not dissimilar to those associated with HIV but without a viral agent of transmission of infection and with apparently different outcomes.<sup>16</sup>

**11.14** Professor Lever said that information about infection in drug users was an additional piece of the jigsaw:

Until that time there were plausible arguments that what was being seen, which was effectively confined to the gay, homosexual population, might have had a number of causes and ... people initially started looking for things they could find, which was why cytomegalovirus and Hepatitis B came up, and the fact that these populations were almost uniformly positive for these viruses, whereas the general population has a much lower incidence overall, made them potential candidates. But there was also an uncovering of information about the gay lifestyle at the time, about sexual promiscuity and about drug abuse, which also distinguished that population to some extent, certainly in the level of it, from most other populations. So there was room for a lot of speculation as to what might be triggering the immunodeficiency.<sup>17</sup>

**11.15** It was speculated that abnormal exposure to pathogens in the rectum and in the gut associated with male homosexual practices was significant. However, intravenous drug users, as a population, did not characteristically indulge in homosexual practices: heterosexual transmission affected the range of speculation related to homosexual behaviour and pointed to something that was probably common to both types of sexual conduct. As put by Professor Lever, it would have been logical to be looking for the common element: what was going wrong with the patients' immune systems.<sup>18</sup>

<sup>13</sup> (1) Gao et al, 'Origin of HIV-1 in the chimpanzee *pan troglodytes troglodytes*' *Nature*, 1999; 397:436 [LIT.001.1178]; (2) Bailes et al, 'Hybrid origin of SIV in chimpanzees', *Science*, 2003; 300:1713 [LIT.001.1184]; and (3) Wolfe et al, 'Naturally acquired simian retrovirus infections in Central Africa hunters', *The Lancet*, 2004; 363:932 [LIT.001.1185].

<sup>14</sup> For a relatively recent (and technical) discussion of the spread of HIV/AIDS using sophisticated phylogenetic, molecular, historical and epidemiological techniques see Gilbert et al 'The emergence of HIV/AIDS in the Americas and beyond' *Proceedings of the National Academy of Sciences*, 2007; 104(47):18566–18570 [LIT.001.4483]

<sup>15</sup> For example in editorial comment in the *MMWR* of 16 July 1982 [LIT.001.0559]

<sup>16</sup> See the discussion of the 'antigen overload theory' later in this chapter.

<sup>17</sup> Day 26, pages 32–33

<sup>18</sup> Day 26, pages 36–37

**11.16** Other heterogeneous theories were discussed and were explored by different specialist groups. One, relating to retroviruses, was to become important but in retrospect it appears to be clear that there was as yet, in the first half of 1982, a lack of cross-fertilisation of ideas among those taking an interest in this new phenomenon.

## **A widening constituency and the infective agent theory**

### *A widening constituency*

**11.17** Reports of opportunistic infections among Haitian immigrants to the USA and additional cases of PCP in haemophilia patients in July 1982, and of intravenous drug abuse as a risk factor in September 1982, marked a further material change in context away from an exclusive focus on sexual behaviour.<sup>19</sup> The initial hypothesis linking the condition only to sexual behaviour could not be sustained: it was no longer possible to focus exclusively on such behaviour and theories related exclusively to homosexual conduct and lifestyle were largely discarded.

**11.18** Three US haemophilia patients who reported with opportunistic infections in July 1982 had all received frequent administration of Factor VIII concentrate.<sup>20</sup> No two had received concentrate from the same batches. PCP had not previously been reported among haemophilia patients who had no other underlying disease and who had not had therapy associated with immunosuppression.<sup>21</sup> Possible transmission of an agent through blood products was suggested.

### *Dr Bruce Evatt and the infective agent theory*

**11.19** The report of these cases reflected the findings and views of Dr Bruce Evatt of the US Centers for Disease Control (CDC). The CDC had a supervisory function relating to off-licence use of certain drugs. At the material time, pentamidine, an antibiotic with certain conventional applications, was used for the treatment off-licence of PCP. Controlled issue allowed the CDC to build up a national epidemiological map of putative diagnoses of the disease, hitherto extremely rare and, where it did occur, almost always confined to immunosuppressed patients such as those undergoing chemotherapy.<sup>22</sup> In early 1982, Dr Evatt had received a report of PCP in a haemophilia patient and similar reports relating to Haitian patients, although previously haemophilia had not been among the underlying disorders of patients for whom pentamidine had been requested for PCP.<sup>23</sup> His organisation began surveillance of requests for pentamidine for haemophilia patients who were contracting PCP and several applications were received in quick succession in June and July.<sup>24</sup> It was inferred within the CDC that a new form of immune suppression was occurring in the haemophilia community.<sup>25</sup> Dr Evatt was convinced that AIDS had reached haemophilia patients.<sup>26</sup> Dr Mark Winter, who became Consultant Haematologist at Kent and Canterbury Hospital in 1983, said that Dr Evatt was the doctor who identified the haemophilia patients in 1982 with what became known as AIDS.<sup>27</sup>

<sup>19</sup> See Chapter 9, *Knowledge of the Geographic Spread and Prevalence of HIV/AIDS 1*, paragraphs 9.20–9.22

<sup>20</sup> 'Epidemiologic Notes and Reports – Pneumocystis Carinii Pneumonia Among Person With Haemophilia A', *MMWR*, July 16 1982; 31:365–7 [LIT.001.0559] at 0560; Preliminary Report, para 8.12

<sup>21</sup> All three had died by December 1982.

<sup>22</sup> Dr McClelland – Day 21, pages 138–39

<sup>23</sup> 'Epidemiologic Notes and Reports – Pneumocystis Carinii Pneumonia Among Person With Haemophilia A', *MMWR*, July 16 1982; 31:365–7 [LIT.001.0559]

<sup>24</sup> Dr Winter – Day 16, page 23; Evatt 'The tragic history of AIDS in the hemophilia population 1982–1984', *Journal of Thrombosis and Haemostasis*, 2006; 4:2295–2301 (reprint), [PEN.016.1183] at 1185–6

<sup>25</sup> Dr McClelland – Day 21, pages 138–39

<sup>26</sup> Evatt, 'The tragic history of AIDS in the hemophilia population 1982–1984' *Journal of Thrombosis and Haemostasis*, 2006; 4:2295–2301 (reprint) [PEN.016.1183] at 1186

<sup>27</sup> Day 15, pages 112–113

**11.20** Dr Winter commented:

Prior to July 1982 the disorder was known as GRID, Gay Related Immuno-Deficiency, and it was these reports of July 1982 that really changed the favoured aetiological agent, obviously enough towards a virus. The fact that here were this small number of patients with a blood disorder, treated regularly with blood products, here were they with the same disorder, that made viral aetiology very much more likely than the previously favoured theories, and then obviously we only had to wait a few more months before there was much clearer evidence that it was likely to be a viral disorder even though the virus had not at that time been identified.<sup>28</sup>

**11.21** Not everyone was convinced and Dr Evatt's views were not generally accepted at the time. Opinion that the disease was likely to be due to a blood-borne transmissible agent hardened to some extent after July 1982 but unanimity was not achieved. There remained considerable divergence of views on the aetiology of the disease. Dr Evatt's views met with particular resistance among haemophilia clinicians.

**11.22** Specialists in infectious diseases also saw difficulties. Professor Lever told the Inquiry that, at that time, there were hints that this new illness might be an infection but that it did not have the usual characteristics of an infection. With chronic infections such as hepatitis, the immune system would be activated to try to clear the infection. One of the mysteries with AIDS was the apparent deterioration of the immune system: 'It was almost like a degenerative disease, things were failing, and there was no obvious evidence before testing came along that the body was doing anything about it.'<sup>29</sup>

**11.23** Professor Lever thought that individual physicians and the people at the CDC whose job it was to study the epidemiology would have been looking for a common element causing suppression of the immune system, taking into account the unusual infections and malignancies that were affecting different groups.<sup>30</sup>

**11.24** Epidemiological studies, begun shortly after the initial reports of the disease, confirmed that the constellation of symptoms seen in homosexual men was also seen in the additional groups found to be infected and in heterosexuals with multiple partners. The need for a more broadly-based hypothesis was reinforced by the report in December 1982 of four more cases of heterosexual haemophilia patients with opportunistic infections in the USA<sup>31</sup> and, in the same month, the report (by Dr Arthur Amman and others) of a possible transfusion-related case of AIDS in a 20-month-old child from San Francisco.<sup>32</sup> The child had been treated with an infusion of platelets from a donor who subsequently died of PCP. This case, and another of a child under 10 years of age, suggested that an association with sexual conduct was unlikely.

<sup>28</sup> Day 15, page 114. Similar views were later reported by Dr Margaret Ragni: 'AIDS and treatment of hemophilia patients', *Plasma Therapy and Transfusion Technology*, 1988; 9:173 [SGF.001.1314]

<sup>29</sup> Professor Lever – Day 26, page 35

<sup>30</sup> Day 26, pages 37–38

<sup>31</sup> 'CDC Update on acquired immune deficiency syndrome (AIDS) among patients with haemophilia A', *MMWR*, 1982; 31:644-652 [LIT.001.0576]

<sup>32</sup> 'CDC Possible transfusion-associated acquired immune deficiency syndrome [AIDS] – California', *MMWR*, 1982; 31:652–654 [SGH.008.5105] at 5108. Dr Amman and others reported the case in April 1983 in *The Lancet*: 'Possible Transmission by Means of Blood Products' [LIT.001.0405]



### *The 'San Francisco child' debate*

**11.25** There was, however, considerable divergence of opinion on the case of the infant from San Francisco. As noted in Chapter 9, *The Geographical Spread and Prevalence of HIV 1*, paragraph 9.32, the *Morbidity and Mortality Weekly Report (MMWR)* editorial of 10 December 1982 advised caution. Professor Christopher Ludlam, Director of the Edinburgh Haemophilia Centre during the reference period, commented that it was not a definite case of AIDS. He speculated that the child could have had a congenital immune deficiency, notwithstanding that there was an infected donor.<sup>33</sup> He agreed that it was a significant event, although not a 'clinching' one.<sup>34</sup> Professor Lever said that the case was 'compelling but not absolutely conclusive'. He also pointed out that the genetic background of the child was unknown, as was his particular susceptibility to illness which could have made him more prone to an infection. He thought that, taken with other knowledge at this time, it was 'more and more suggestive of an infectious agent and a transmission by blood products. But it doesn't close the door'.<sup>35</sup> Later, when discussing the differing hypotheses emerging around this time, Professor Lever returned to this case and commented that a very young child, months old, was not something to hang a whole case on because 'some two per cent of children are born with some oddity about them, some minor difference from the average'.<sup>36</sup>

**11.26** On the other hand, Dr Winter's view was that the report of infection in the San Francisco infant was a critical point in the developing history.<sup>37</sup> After that, it was no longer possible, in his view, to support the theory that the disease was related to the lifestyle of homosexuals rather than that it was caused by an infectious agent. He expressed his view strongly:

By December 1982 ... [a]ny clinician looking at this data would have to believe that AIDS was a transmissible disorder and that it could have been transmitted by blood and blood products. It was the only clinical interpretation of the data that was available.<sup>38</sup>

**11.27** On the evidence as a whole, however, Dr Winter was ahead of other opinion in arriving at this conclusion. It was inconsistent with Dr Peter Kernoff's reported views at the time and with the views of Professor Lever and Professor Ludlam, expressed in retrospect, among others. It is clear that a further major split in opinion was to develop, as Dr Winter indicated, but that was to come later.

### *Koch's postulates*

**11.28** At a workshop convened on 4 January 1983 in Atlanta there was a hostile reaction to Dr Evatt's argument.<sup>39</sup> As he reported it, there were calls to 'Show us the agent ... subject it to Koch's postulates'.<sup>40</sup> At the end of the workshop it was said that the biggest question of all remained what caused AIDS. In relation to the infective agent theory, Dr Louis Aledort, Director of the Haemophilia Center at New York and a respected US

<sup>33</sup> Day 18, page 117

<sup>34</sup> Day 18, page 117

<sup>35</sup> Day 26, page 50

<sup>36</sup> Day 26, page 101

<sup>37</sup> Day 16, page 7

<sup>38</sup> Day 16, page 8

<sup>39</sup> Research News: 'Health Officials Seek Ways to Halt AIDS' [LIT.001.1589]

<sup>40</sup> Evatt, 'The tragic history of AIDS in the hemophilia population 1982–1984' *Journal of Thrombosis and Haemostasis*, 2006; 4:2295–2301, (reprint) [PEN.016.1183] at 1188. For competing views, see Marx, 'Health Officials Seek Ways to Halt AIDS', *Research News*, 21 January 1983 [LIT.001.1589]

haematologist, was and remained for some time a prominent sceptic. He was one of a group of clinicians who found it particularly difficult to accept that blood products were transmitting an infectious agent.<sup>41</sup> Dr Aledort favoured the idea that haemophilia patients were exposed to a great number of foreign antigens in the course of treatment and experienced a high degree of antigenic stimulation that effectively wore out their immune systems: the 'antigen overload theory'.

**11.29** The resort to Koch's postulates by the CDC's opponents perhaps reflected the full extent of the divergence of opinion at the time. Robert Koch was a 19th-century German physician who set out criteria that he thought necessary to prove that an infectious agent (at the time typically bacteria) was the cause of a particular illness when transmitted from one person to another.<sup>42</sup> Professor Ludlam outlined the requirements:<sup>43</sup>

- The bacteria must be present in every case of the disease.
- The bacteria must be isolated from the host with the disease and grown in pure culture.
- The specific disease must be reproduced when a pure culture of the bacteria is inoculated into a healthy, susceptible host.
- The bacteria must be recoverable from the experimentally-infected host.

**11.30** If Koch's postulates were satisfied, that demonstrated to a satisfactory standard that a particular disease was caused by an infectious bacterial agent.<sup>44</sup> The postulates did not supply proof to the standard of a mathematical or scientific certainty, however, that the specific bacterial agent caused the specific disease. It remained a test of probability according to Dr Winter.<sup>45</sup> Consistent with Dr Winter's evidence, Professor Lever said that Koch's postulates were valuable as a guide but they were not the final definition of whether something was an infection. He also explained that the postulates were much more difficult to apply to viruses:

[B]ecause viruses only grow within living cells and if one doesn't have the appropriate cells in culture in which that virus can grow, or one cannot keep the appropriate cells alive, one cannot fulfil the second of Koch's original postulates.<sup>46</sup>

**11.31** In early 1983 the agent of transmission, HIV, had not been identified. It could not be known that, if there were an agent of transmission, it would necessarily share common characteristics with bacteria that would enable the postulates to be satisfied. Furthermore, AIDS was not a 'specific' disease. The disease manifestations of AIDS included PCP and KS but the full spectrum ranged from cases of proven cell-mediated immune deficiency without symptoms to non-specific symptoms associated with laboratory evidence of immune deficiency. The CDC definition for reporting purposes by this stage identified AIDS as a disease, at least moderately predictive of a defect in cell-mediated immunity, occurring in a person with no known cause for diminished resistance to that disease. Koch's postulates would have required adaptation for application to the identification of an infective agent for the transmission of AIDS.

<sup>41</sup> Professor Ludlam – Day 18, page 115

<sup>42</sup> Dr Winter – Day 16, page 5. (Koch is widely regarded as the founder of modern bacteriology and discovered the aetiological agents of anthrax, cholera and tuberculosis.)

<sup>43</sup> Day 19, pages 8–9

<sup>44</sup> Professor Lever – Day 26, pages 57–58

<sup>45</sup> Dr Winter – Day 16, page 6

<sup>46</sup> Day 26, page 55

**11.32** There are other reasons for concern that Koch's postulates may have been relied upon. Fully developed AIDS, as understood from the earliest stages of the epidemic, was associated with high mortality. Leaving aside the first two postulates, the infusion of blood from a known AIDS patient into a susceptible, healthy host – another human being – with an inherent risk of causing potentially fatal disease could not have been justified. By the time it was accepted that HIV was probably the agent of transmission, so that the first two postulates might have been tested, the risk of incurable and potentially fatal disease was so well established that it would have been unthinkable to expose a healthy, susceptible human host to infection to test the postulates.

**11.33** So far as the UK is concerned, Professor Ludlam stated that he had no recollection of Koch's postulates featuring in the discussion around this time (in 1983). He emphasised that in clinical medicine one worked the whole time with incomplete data and information, making assumptions that may not be backed up by scientific evidence.<sup>47</sup> In relation to the infant who had received a transfusion of platelets (reported in the *MMWR* of 10 December), Dr Winter thought that 'because you had ... three parts of the equation – the donor, the recipient and the blood transfusion – it could have been said to have fulfilled Koch's postulates.'<sup>48</sup> Professor Lever said that some clinicians took the approach that if most of the postulates were satisfied, it was more likely than not an infectious agent but that other clinicians did not agree with this approach.<sup>49</sup> Controversy reigned.

**11.34** By the end of 1982 and in to 1983 the aetiology of AIDS remained, technically, unknown so far as Koch's postulates were concerned: the full requirements of the postulates had not been fulfilled.<sup>50</sup> At the Atlanta conference the opponents of Dr Evatt's views regarded his evidence as anecdotal in the absence of proof to that standard. The CDC was dismayed by the outcome of the Atlanta conference.<sup>51</sup>

**11.35** Koch's postulates were an impossible test at the time. The demand for proof to that standard demonstrates the resistance among highly respected US clinicians to the infectious agent theory but leaves open the question whether that resistance was based on scientific grounds or reflected wider concerns about the implications for haemophilia therapy if the theory was given credibility.

### *Altered immunological states in haemophilia patients*

**11.36** On 29 January 1983, Dr Margaret Ragni and others reported altered immunological states in two multiply-transfused patients with severe haemophilia.<sup>52</sup> They commented:

The lymphadenopathy and immunological features in these two haemophiliacs bear a striking resemblance to the acquired immunodeficiency syndrome (AIDS) of homosexuals, intravenous drug abusers, and Haitian immigrants. These findings may represent a prodromal [early, often asymptomatic] phase or forme fruste [atypical manifestation] of AIDS. Transmission of an infectious agent in blood products seems likely.<sup>53</sup>

<sup>47</sup> Day 19, pages 11–12

<sup>48</sup> Day 16, page 6

<sup>49</sup> Day 26, pages 57–58

<sup>50</sup> Dr Winter – Day 16, pages 4–5.

<sup>51</sup> Evatt, The tragic history of AIDS in the hemophilia population 1982–1984, *Journal of Thrombosis and Haemostasis*, 2006; 4:2295–2301 (reprint) [PEN.016.1183] at 1188

<sup>52</sup> Ragni et al, 'Acquired immunodeficiency-like syndrome in two haemophiliacs', *The Lancet*, 29 January 1983, 213 [SNB.007.3455]. See also Dr Ragni's comments in 'AIDS and Treatment of Hemophilia Patients', *Plasma Therapy and Transfusion Technology*, 1988; 9:173 [LIT.001.0598]

<sup>53</sup> Ragni et al, 'Acquired immunodeficiency-like syndrome in two haemophiliacs', *The Lancet*, 29 January 1983, 213 [SNB.007.3455]

**11.37** Professor Ludlam commented that at this time it was unclear whether individuals with the features reported by Dr Ragni and her colleagues were likely to get AIDS but that the study provided further evidence for AIDS in haemophilia patients being caused by an agent transmissible in Factor VIII concentrate.<sup>54</sup>

**11.38** By the summer of 1983 there was continuing doubt in some segments of the haemophilia community, in the blood banking industry, and among physicians and the Food and Drug Administration (FDA) in the USA that AIDS was a blood-borne infection.<sup>55</sup> There was no consensus that the disease was transmitted by a virus and, until Robert Gallo's announcement in 1984, no generally accepted evidence of a candidate for transmission.<sup>56</sup>

**11.39** There were similarly differing views in the UK. Dr Winter was asked whether there was particular resistance to the transmissible agent theory, on the part of at least some haemophilia clinicians in the UK, because of the advantages of using concentrates. He said:

I think ... that was the case. The initial – if you like, the clinicians didn't want to believe any of this data, because we [had] just been through such a very major advancement in healthcare. So that would have been the mindset originally and then they are looking at this American data and the next thing is, okay, these patients – they are a very small number and there were no British ones and there were no German ones, so I'm just going to keep on looking at the situation, and now you have a situation, December 1982/January 1983, I can't ignore this any more. These patients must have a disorder that's caused by blood transfusion in the forms of the concentrates. So maybe in Britain things will be fine if we now just switch or do all we can to use British concentrate.

In America it was the same ... the clinicians didn't want to believe it, the commercial companies didn't want to believe it, the blood transfusion services didn't want to believe it because they were particularly sensitive about excluding certain risk groups as donors. There were lots of political issues around that. So none of the related agencies wanted to know this. That's why, if you like, I'm sure, this data took some time to really hit home.<sup>57</sup>

**11.40** He continued:

So deeply engrained in the psyche of haemophilia clinicians, as in the patients ... was the concept that British blood was likely to be much freer from viruses than American blood. So here we were in 1982, we already knew about hepatitis, we already knew about the increased risk from commercial donors. Here was now what looked like a transmissible disease that also appeared to be occurring in these same unsavoury American blood donors. This reaffirmed the view that these things weren't likely to happen in British blood donors.<sup>58</sup>

<sup>54</sup> Historical Summary of AIDS in Haemophilia 1981–1985 [PEN.015.0468] at 0468–9

<sup>55</sup> Evatt, 'The tragic history of AIDS in the hemophilia population 1982–1984', *Journal of Thrombosis and Haemostasis*, 2006; 4:2295–2301 (reprint) [PEN.016.1183] at 1189

<sup>56</sup> It is interesting to compare the development of thought in relation to hepatitis. See Chapter 15, *Knowledge of Viral Hepatitis 2, 1975 to 1985* paragraph 15.24. Alter et al applied the postulates, only to set them aside as research proceeded and the realities of the disease required a more flexible approach.

<sup>57</sup> Day 16, pages 28–29

<sup>58</sup> Day 16, pages 29–30

**11.41** On the evidence now available to the Inquiry there was, on one view, ample circumstantial evidence by early 1983 of an association between some blood products and transmission of infection. Infected patients had received large amounts of concentrate; none had prior opportunistic infections; their personal and environmental histories were different; and two were 10 years of age or less. It would have been open to infer that the whole group of infected patients would not fall within any of the other known at-risk categories of promiscuous homosexuals, heroin addicts and immigrants into the USA from Haiti. However, the proponents of the several theories were divided on a more basic level reflecting interests that were not wholly scientific in origin. The resistance of the haemophilia clinicians appears to have reflected their wish to continue to use factor concentrates of proven efficacy in treating their patients. The pharmaceutical industry had commercial interests to protect. Human nature rather than the strict application of scientific theory probably contributed to the persisting differences of opinion.

### Competing theories in 1983

**11.42** While a common cause was postulated in the haemophilia population and in homosexual and other groups by some commentators, there were unresolved issues. In particular, once it was established that AIDS was occurring in the haemophilia population as well as in other risk groups, there was an apparently inexplicable difference in the pattern of disease. The haemophilia patients did not develop KS, whereas this was common in homosexual AIDS patients. The difference in the pattern of disease presentation probably contributed to the belief that there were different aetiological agents behind the diseases in the two groups.<sup>59</sup>

**11.43** It is now reasonably clear that there are likely explanations for the difference. Professor Lever told the Inquiry that it is now thought there are two or three possible explanations for the absence of KS in haemophilia patients with HIV infection. One is that HHV8 (otherwise KSHV, the herpes virus responsible for KS) may be very poorly transmitted by blood-borne routes. Transmission does occur by these routes, but it is certainly less easily transmitted than HIV. The amount of HHV8 virus present in the blood may be far less than the many millions of copies of HIV that one finds. Second, it may be far more easily transmitted by the sexual route and that would also be plausible because other herpes viruses are transmitted by mucus membrane contact. Classically, herpes simplex type 1, which causes the cold sore, is transmitted mouth to mouth or by saliva. EBV, another herpes virus, causes glandular fever and is sometimes known as 'the kissing disease'. So it is quite likely that sexual transmission of HHV8 is far more efficient than any other route. The third possibility is that a preparation technique might have been effective to inactivate in blood products what is a large and also relatively fragile, complex virus. Or the explanation might be a combination of the above.<sup>60</sup> These possible explanations of the differences in disease profile were, however, quite unknown in the 1980s.

**11.44** There were other uncertainties at that time. Professor Lever told the Inquiry that there were many people who from the beginning thought there was an infectious cause and many who did not. He thought that the issue was that there was no physiological appearance of an infection. He continued:

<sup>59</sup> Professor Lever's Report [PEN.015.0517] at 0520. HHV8/KSHV, the cause of Kaposi's sarcoma, was finally identified in 1994.

<sup>60</sup> Professor Lever – Day 26, page 76

The fact that you get a rash with measles is probably only there to tell the rest of the population that you are infectious and should be kept away from. The fact that you get a very high fever in some diseases doesn't actually do you very much good but it tells other people that you are ill. That's how mothers know their babies are ill because they feel hot.<sup>61</sup>

**11.45** The geographical spread was also unusual, although not unprecedented. Professor Lever advised that some infections could spread very rapidly but in this case there was no continuity or explosion of a cluster in one particular area.<sup>62</sup> In the period 1982–83 these and other uncertainties led to a more broadly-based study by virologists of immune deficiencies in cases of AIDS infection.

### *Haemophilia research*

**11.46** The publication of cases of AIDS in haemophilia patients, first in June and then November 1982, had prompted several groups of researchers in the USA to carry out immune studies in groups of asymptomatic haemophilia patients. It was known that the absolute number of certain cells ('helper' cells known as  $T_4$  or CD4 cells) and the ratio of those cells to another group ('suppressor' cells known as  $T_8$  or CD8 cells) provided a measure of cell-mediated immunity, the effectiveness of the immune system. The researchers found widespread depression of  $T_4/T_8$  ratios in their subjects and also found that depressed  $T_4$  counts were very closely related to exposure to US commercial Factor VIII concentrates. The 'immune overload', or 'antigen overload', theory developed as an alternative to a transmissible agent theory as an explanation of these immune disorders: the fact that immune abnormalities occurred in asymptomatic haemophilia patients receiving single or multiple-donor products suggested that immunological defects might arise from blood product treatment alone.<sup>63</sup> It was also relevant to the view developed at the time that there was uncertainty about what did constitute AIDS.<sup>64</sup>

**11.47** The major pathological feature of AIDS was very profound immunosuppression, with characteristic suppression of  $T_4/T_8$  ratios and hyperglobulaemia (an excess of globulin in the blood). Researchers began to explore ideas based on the hypothesis that there was a relationship between these immune phenomena and the aetiology of AIDS. During 1982 and into 1983 immune studies of homosexual men with no symptoms of AIDS showed similar, if less marked, immune phenomena (notably suppressed  $T_4/T_8$  ratios) to those with overt diseases characteristic of AIDS.

**11.48** On 13 January 1983, the *New England Journal of Medicine (NEJM)* published an article by Michael Lederman and others entitled 'Impaired cell-mediated immunity in patients with classic hemophilia'.<sup>65</sup> They studied 19 patients and 19 controls and, within the haemophilia group, distinguished those who had received Factor VIII concentrates from those who had received only cryoprecipitate.<sup>66</sup> The  $T_4/T_8$  ratio results for the latter group did not differ from the controls. The results for the group who had received Factor

<sup>61</sup> Day 26, page 43

<sup>62</sup> Professor Lever – Day 26, page 43

<sup>63</sup> Ragni, 'AIDS and treatment of hemophilia patients', *Plasma therapy and transfusion technology*, 1988; 9:173 [SGF.001.1314] at 1317

<sup>64</sup> 'Update on Acquired Immune Deficiency Syndrome (AIDS) among Patients with Hemophilia A', *MMWR*, 10 December 1982 [SGH.008.5105] at 5108–10

<sup>65</sup> Lederman et al, 'Impaired cell-mediated immunity in patients with classic hemophilia', *New England Journal of Medicine*, 1983; 308/2:79–83 [PEN.012.0263]

<sup>66</sup> That is, in this case, 19 age-matched, apparently healthy people without haemophilia.

VIII concentrates were similar to those reported among populations of apparently healthy homosexual men. The authors thought that genetic haemophilia factors were unlikely to explain their findings. They stated:

A more likely possibility is that the immune dysfunction is acquired. Active infection with hepatitis B virus is probably not responsible, since none of the 11 patients in the group [treated with concentrates] had demonstrable hepatitis B surface antigenemia. The cause of the immuno-suppression in this population is not known ....<sup>67</sup>

**11.49** They commented that, among AIDS patients, epidemiological evidence would implicate a blood-borne pathogen as the cause of immunosuppression but offered no view as to whether this explained their findings.

**11.50** In the same issue of the *NEJM*, Jay Menitove and others also published immunology studies on apparently healthy haemophilia patients, differentiating those treated with cryoprecipitate obtained from volunteer blood donors and those treated with commercially prepared Factor VIII concentrates and further distinguishing groups according to dosage.<sup>68</sup> They set out to test the hypothesis that AIDS might be transmitted through Factor VIII infusion. They found that none of the cryoprecipitate users had abnormal  $T_4/T_8$  ratios while 57% of the users of commercial concentrates did have abnormal ratios. They noted that there had been speculation that AIDS might be transmitted to haemophilia patients through Factor VIII infusion. The article noted that the epidemiology of AIDS was suggestive of a blood-borne transmissible agent but it was not yet clear whether the abnormalities in cell-mediated immunity in patients with haemophilia and, in particular, in those who had also developed opportunistic infections were due to the putative blood-borne pathogen. The authors advised caution in the interpretation of the findings. They noted that the proposed explanations for AIDS included CMV infection, inhaled nitrates and exposure to foreign antigens, such as spermatozoa, and concluded:

Our data are consistent with the possibility that commercially prepared lyophilized factor VIII concentrates can induce an AIDS-like picture, but a large number of patients must be studied before a definite conclusion can be drawn. In addition, we cannot hypothesize about the emergence of this apparently new syndrome at this time. Whether the abnormalities found in our patients will evolve into clinical disorders remains to be determined, but we urge those involved in the care of patients who use factor VIII concentrate to follow them carefully for stigmata of AIDS and changes in immunologic status.<sup>69</sup>

**11.51** The opinions in these two articles in January 1983 were carefully qualified. Neither paper used the term 'immune overload' or any of the alternative expressions carrying the same meaning. However, to a greater or lesser extent each explored the underlying idea while not excluding a largely infective blood-borne cause of AIDS in haemophilia patients.

<sup>67</sup> Lederman et al, 'Impaired cell-mediated immunity in patients with classic hemophilia', *New England Journal of Medicine*, 1983; 308/2:79-83 [PEN.012.0263] at 0266

<sup>68</sup> Menitove et al, 'T-lymphocyte subpopulations in patients with classic haemophilia treated with cryoprecipitate and lyophilized concentrates' *New England Journal of Medicine*, 1983; 308:83-86 [LIT.001.0031]

<sup>69</sup> *Ibid* [LIT.001.0031] at 0033. They did not comment on the lack of fit between volunteer donors and commercial donor populations.

### *The 'immune overload' hypothesis*

**11.52** The hypothesis was that immune cellular dysfunction might be brought on by an 'overload' of normal immune responses, either by repeat introduction of foreign proteins contained in sperm or the repeated infusions of concentrates, or repeat infections with organisms such as CMV or EBV, leading to a state of immune suppression and presumably 'priming' the individual for an infection or other event leading to overt AIDS disease. Until early 1984, this theory gained support and, until the publication by Gallo of his identification of HTLV-III, was favoured by haemophilia specialists, some virologists and some immunologists.

**11.53** In an editorial in the same issue of the *NEJM*, Dr Jane Desforges commented that it was not yet known whether AIDS was secondary to multiple antigenic exposures, to a specific transmitted agent or to some other mechanism. The options were open.<sup>70</sup>

### *Antigen overload or a transmissible agent?*

**11.54** As indicated at paragraph 11.28 above, at the Atlanta meeting on 4 January 1983, Dr Evatt and his colleague, Dr James Curran, reported the findings and views of the CDC linking AIDS to a transmissible agent in blood products and noting that the risk for non-haemophiliacs was unknown but apparently small. The alternative theory was laid out. The hypothesis underlying Dr Aledort's theory was that prolonged exposure to foreign proteins had an impact on the immune system similar to that found in homosexual men and that AIDS was an end-stage development of these abnormalities.

**11.55** Both theories received media attention. There was comment on the issue in *The Observer* of 16 January 1983 in an article entitled 'Mystery Disease Threat'. The article commented on the infective agent theory. On the alternative point of view, the article quoted Dr Peter Kernoff from the Royal Free Hospital in London as saying:

"Assessing the risk is not a straightforward matter: we need much more hard evidence .... Factor VIII is a very valuable product and the advantages far outweigh the disadvantages."<sup>71</sup>

**11.56** Dr Winter thought that Dr Kernoff's comment reflected the position at the time:

He is a very respected figure looking at the data saying it is of concern, but we are talking about a product that has revolutionised the lives of patients and there is a major obvious benefit to this treatment. We will have to look at the risk that appears to be evolving. That was the situation of the day.<sup>72</sup>

**11.57** In the Department of Health and Social Security (DHSS), someone (name redacted) expressed the official view that:

[T]he value to severe haemophiliacs of clotting [Factors VIII and IX] far outweigh the possible and as yet unproven hazards of the transmission of acquired immune deficiency syndrome.<sup>73</sup>

<sup>70</sup> Desforges, 'Aids and Preventive Treatment in Haemophilia', *New England Journal of Medicine*, 1983; 308/2 [LIT.001.0040]

<sup>71</sup> 'Mystery Disease Threat', *The Observer*, 16.01.83 [DHF.001.7108]

<sup>72</sup> Day 16, pages 13–14

<sup>73</sup> Memo dated 18 January 1983: 'Factor 8 and the Observer Article' [DHF.001.7111]



**11.58** At the 19th Congress of the International Society of Haematology and 17th Congress of the International Society of Blood Transfusion in Budapest in August 1982, Dr Aledort discussed his experience with the cases of three haemophilia patients in the USA who had died from pulmonary infections characteristic of AIDS (as reported in the July *MMWR* – see paragraph 11.18 above). The theory was taken up by some haemophilia clinicians in the UK. On 15 January 1983, simultaneously with the two *NEJM* papers mentioned above, there was a report in *The Lancet* of altered immunology in English haemophilia patients.<sup>74</sup> The article, by Dr Peter Jones and others, Newcastle upon Tyne, noted that transfusion was immunosuppressive, in an as yet unidentified way, in renal transplantation and commented that an immunosuppressive syndrome associated with T-cell subset reversal had been noted in a small population of multiply-transfused, heterosexual haemophilia patients in New York. They commented on their own findings:

The alterations in T cell subsets in our survey may simply reflect temporary altered immune status in multitransfused individuals. But half our patients without T cell ratio reversal had been exposed to equally large quantities of blood. It could be that T cell ratio reversal is a normal defence mechanism to antigenic load, and that the patients without reversal show an abnormal lack of response.

None of our patients, who have all been exposed to commercial blood products of American origin, shows features of AIDS ....<sup>75</sup>

**11.59** The article by Dr Jones followed in date, but must have been submitted before, the workshop convened by the CDC in Atlanta on 4 January 1983.<sup>76</sup> At the date of its preparation, the antigen overload theory had a certain currency among other haemophilia clinicians in the UK. Professor Ludlam commented that this report of low  $T_4$  counts and  $T_4/T_8$  ratios suggested that the changes might be a response to antigenic load.<sup>77</sup> In his case, this initiated a research interest that came to have considerable importance for a time. Commenting later on a draft paper prepared for litigation in England and Wales 20 years ago,<sup>78</sup> he said:

[It was] possible that AIDS was arising in haemophiliacs because during the 1970s there was increasing use, massive increasing use of Factor VIII concentrates.

I mean, I calculated that at least using SNBTS concentrates, that in an average lifespan, you gave out a kilogramme of protein intravenously in an average severe haemophiliac. We are not designed to accept proteins in that magnitude intravenously. So one possibility was that actually – as we hinted earlier – maybe haemophilia as a whole was sliding into AIDS because of all the concentrate we were using. Quite separate from HIV or a putative virus.<sup>79</sup>

<sup>74</sup> Jones *et al.*, 'Altered immunology in haemophilia', *The Lancet*, 1983; 120 [DHF.001.7107]

<sup>75</sup> *Ibid.*, [DHF.001.7107]

<sup>76</sup> 'Health Officials Seek Ways to Halt AIDS', *Research News*, 21 January 1983 [LIT.001.1589]

<sup>77</sup> Historical Summary of AIDS in Haemophilia 1981–1985 [PEN.015.0468] at 0469

<sup>78</sup> Appendix 2 to Professor Ludlam's statement [PEN.015.0385] at 0400 onwards

<sup>79</sup> Professor Ludlam – Day 18, page 150

**11.60** In March 1983, Jonathan Goldsmith and others wrote an article published in *The Annals of Internal Medicine* in which they considered the similarities in T-helper/T-suppressor cell ratios in haemophilia patients and in homosexual men, Haitian refugees and narcotics addicts.<sup>80</sup> They noted that a characteristic feature of the altered cellular immune functions in homosexual men was reduced  $T_4/T_8$  ratios and that it had been suggested that these abnormalities were the result of continued exposure to sexually transmitted viral infections, particularly CMV infection. They studied 12 apparently healthy haemophilia patients to ascertain if they had similar abnormalities in their lymphocyte sub-populations. The similarities in biometric abnormalities were striking in 9 of the 12 patients studied. However, none of the haemophilia patients had been exposed to nitrates and all had stable antibody titres to CMV.

**11.61** The conclusion relating to the haemophilia patients was that:

The presence of an abnormal ratio of helper to suppressor T-cells in these patients is of uncertain significance, and this observation needs to be confirmed .... In addition, since the establishment of the ... Regional Haemophilia Centre ... in 1976, no cases of pneumonia or chronic infection have occurred in our patients .... Whether patients with these T-cell defects are at increased risk for development of malignancy has yet to be substantiated. Reports from the literature, however, suggest that patients with congenital bleeding disorders have a prevalence of malignant disease similar to the general population. At this time there is insufficient evidence to advocate a change in therapeutic practices in these patients. However, additional patients with hemophilia need to be evaluated to ascertain if the magnitude of exposure to clotting factor concentrates is associated with an increased incidence of malignancy or opportunistic infections.<sup>81</sup>

**11.62** In early 1983 the antigen overload theory was supported by haemophilia clinicians on both sides of the Atlantic. Professor Lever explained that it was a compelling theory at that stage.<sup>82</sup> He suggested that the theory had probably originated in New York amongst the physicians looking after patients with HIV and amongst the gay population in New York itself. He thought that 'a physician in New York' (a description that Dr Aledort would have fitted) had put the antigen overload theory forward as an alternative, less stigmatising theory. With the benefit of hindsight, it could be speculated that they felt that if it was perceived that there was an infectious cause the gay population might be more stigmatised for transmitting agents which caused disease. The stigma was very real. Professor Lever described the scenes that occurred during the first Canadian conference on AIDS held in Montreal in May 1985.<sup>83</sup> The stage was taken by different pressure groups protesting about what had been seen to be media perceptions or medical professional perceptions. The prostitute population complained that being referred to as 'vectors of disease' was very demeaning. In South Africa it was deemed to be politically better for there not to have been a virus originating in Africa which caused the infection. These reactions would have established themselves in the minds of people who had vested interests in there not being a virus.

<sup>80</sup> Goldsmith et al., 'T-lymphocyte subpopulation abnormalities in apparently healthy patients with hemophilia', *The Annals of Internal Medicine*, March 1983 [LIT.001.0055]

<sup>81</sup> Ibid [LIT.001.0055] at 0057

<sup>82</sup> Day 27, pages 29–30

<sup>83</sup> The Conference was held with a view to bringing together the ideas and proposals for strategy held by affected groups. It led to the formation of the Canadian AIDS Society in July 1986.

**11.63** Professor Lever was anxious, however, to put the issue in context. As already noted, he emphasised that the initial manifestations of HIV did not look like a normal infection. They looked like something that was leading to degeneration or deterioration in the immune system. There had not been another infection which clearly did that. That was why theories of protein overload and theories of abuse of specific drugs like amyl nitrate were brought up. The disease could have been a toxic effect in the immune system. All of the theories were as plausible as each other. None of them had a majority view at the very beginning. Professor Oliver James, Medical Assessor to the Inquiry, had a similar impression of the early development of these theories.<sup>84</sup>

**11.64** The antigen overload theory persisted in parallel with the transmissible agent theory and remained competitively tenable until the virus was isolated.<sup>85</sup> Various agents were considered as possible causes of the new disease.

### *Scottish research*

**11.65** In Scotland, interest in the topic developed in Edinburgh and in Glasgow. In the context of haemophilia therapy, Professor Ludlam began a series of tests, described by him as 'screening' tests, in about the beginning of 1983.<sup>86</sup> His studies started after the first three cases of AIDS in haemophilia patients had been reported in the USA in July 1982 and followed the course of research into clinical immune deficiencies in homosexual men with AIDS. As already noted, a characteristic feature of these immune deficiencies was a reduction in blood CD4 lymphocyte numbers and a decrease in CD4/CD8 ratios. Similar decreases in CD4 numbers and CD4/CD8 ratios were found in intravenous drug users. Professor Ludlam explained that it was uncertain whether these were due to viral infection, chronic antigen stimulation or another aetiological factor. This stimulated his research into the position in asymptomatic haemophilia patients.<sup>87</sup>

**11.66** Professor Ludlam studied a large number of patients and found a pattern of suppression that seemed to have at least some parallels with the New York studies. Professor Lever explained that in the absence of an illness that looked like conventional infection one would look around for competing theories.<sup>88</sup> To ensure control of the tests, Professor Ludlam had the forms for samples labelled 'AIDS study'.<sup>89</sup> This was later to give rise to suspicion on the part of some patients that he was carrying out experiments on his patients. In the view of this Inquiry that suspicion was without foundation. Professor Ludlam explained that by the spring of 1983, it was becoming clearer that strange things were happening to the immune systems of patients with haemophilia who were otherwise feeling well.<sup>90</sup> He explained what he was doing:

In 1982/83 in the absence of any patient with an AIDS-defining illness, the only way to potentially investigate individuals to assess their possible susceptibility to developing AIDS was to assess their immune function by laboratory testing. By 1983 it therefore seemed important, as it did to many other haemophilia physicians, to investigate the immune status of patients under my care....

<sup>84</sup> Day 27, pages 39–40

<sup>85</sup> Professor Lever – Day 27, page 30

<sup>86</sup> Professor Ludlam's Statement [PEN.015.0445] at 0448; Day 19, page 13

<sup>87</sup> 'Human Immunodeficiency Virus Infection in Haemophiliacs' [PEN.015.0385] at 0400–0401

<sup>88</sup> Day 27, page 40

<sup>89</sup> Day 35, page 19

<sup>90</sup> Ibid, page 21

I was surprised to observe that many patients had immune abnormalities very similar to those reported from homosexual men and haemophiliacs residing in North America.<sup>91</sup>

**11.67** He said in oral evidence:

It was – the interpretation that you could put upon those was puzzling us. I would say that similar abnormalities were shown in gay men who were otherwise feeling well. And the question is in fact: were all these patients or all these individuals in the United States actually already infected with a latent, if you like, AIDS virus?<sup>92</sup>

**11.68** While his patients had immune abnormalities similar to those reported in homosexual and other populations in the USA, it was inferred that they could not have been infected with an AIDS virus and that, at least in Edinburgh, patients' immune disturbances were due to a non-AIDS-causing agent.<sup>93</sup> This raised the possibility that haemophilia patients in the USA and elsewhere might not be infected with an AIDS virus.<sup>94</sup> In the event, his oral evidence was that there were three groups: those with abnormal immune systems who were subsequently shown to be infected with HIV; those with abnormal immune systems who were not infected with HIV; and those with normal immune systems who were infected but in whom changes in the immune system had not yet begun.<sup>95</sup>

**11.69** A letter to *The Lancet* of 30 April 1983 by Robert Gordon of the US National Institutes of Health (NIH) put the antigen overload theory in a way that provoked a response from Professor Ludlam. Having noted that observations of altered distribution of T-lymphocyte sub-populations in haemophilia patients with AIDS was consistent with the hypothesis that the disease was caused by a transmissible agent, presumably a virus, in blood products, Dr Gordon continued by saying that the observations were:

[A]lso compatible, however, with the possibility that repeated administration of factor VIII concentrate from many varied donors induces a mild disorder of immune regulation by purely immunochemical means, without the intervention of an infection.<sup>96</sup>

**11.70** A response from Professor Ludlam and others appeared in *The Lancet* of 28 May 1983. It referred to Dr Gordon's letter and to the ongoing study of haemophilia patients in south east Scotland. By this stage in Dr Ludlam's continuing research programme, 23 patients who had received exclusively SNBTS Factor VIII in the past five years, most of whom had never received commercial concentrate, had been studied. In the majority of these patients, the  $T_4/T_8$  ratios were reduced. The letter stated:

Since there are no known cases of AIDS in our blood donor population it seems likely that the immunosuppression observed in haemophiliacs, as reflected by reduced T lymphocyte helper/suppressor ratios, results from infusion of foreign

<sup>91</sup> Professor Ludlam's Statement [PEN.015.0445] at 0448

<sup>92</sup> Day 35, page 21

<sup>93</sup> Day 19, pages 18 and 21

<sup>94</sup> Day 19, pages 16–18

<sup>95</sup> Day 19, pages 18–20. It was later found, in 1985, that those who were infected with HIV had the same abnormal T lymphocyte subsets after as they had had before transfusion of material infected with the virus, confirming to the satisfaction of Professor Ludlam and his colleagues that the abnormal T lymphocyte subsets were a result of the intravenous infusion of Factor VIII concentrates per se and not HIV infection: Ludlam et al, 'human T-lymphotropic virus type III (HTLV-III) infection in seronegative haemophiliacs after transfusion of Factor VIII', *The Lancet*, 3 August 1985 [SNB.008.3434] at 3436

<sup>96</sup> Gordon, 'Factor VIII products and disordered immune regulation' *The Lancet*, April 30 [LIT.001.0911]

protein or a ubiquitous virus rather than a specific AIDS virus in factor VIII concentrates.<sup>97</sup>

**11.71** Professor Ludlam's letter to *The Lancet* was published at or about the time that the results of Montagnier's work were coming into circulation.

**11.72** The course of study of immune abnormalities amongst haemophilia patients involved a number of projects and teams and continued into 1984 with many published papers, including Professor Ludlam's own work. The work demonstrated a range of immune disturbances similar to those observed in other risk groups: a reduction in CD4 counts, disturbed CD4/CD8 ratios and other immune abnormalities. In a summary of the position as he saw it at about this time, Professor Ludlam observed that there were several candidate viruses in the field, some known and some unknown or mutations of known viruses. In the case of homosexual men, 'antigen overload' from semen in the rectum and 'recreational drugs', such as amyl nitrate and isobutyl nitrate, were candidates. Proteins other than Factor VIII/IX in clotting factor concentrates used to treat haemophilia were another.<sup>98</sup> On his approach, it was inappropriate in mid to late 1983 to make an assumption that the AIDS in people with haemophilia was of similar aetiology to the AIDS in the other groups. It was known that, clinically, the spectrum of AIDS-related conditions differed to some extent as between the groups and so clinicians considered the possibility that they had arisen simultaneously, or nearly simultaneously, but were of different aetiologies.<sup>99</sup>

**11.73** At the Glasgow Royal Infirmary (GRI), Professor Charles Forbes was interested in the same phenomenon. His group's research on immune disorders was published in October 1983.<sup>100</sup> He said:

It was quite apparent that there was an association between the administration of large amounts of Factor VIII concentrate and the immune process, which was suppressed in many patients. A variety of other investigators were finding the same kind of abnormalities using a range of biochemical tests and the real question was what did this mean? Was there something in the Factor VIII or IX concentrates that did suppress these tests of immunity?<sup>101</sup>

**11.74** He explained:

We became interested because of the ability to measure so many of the factors in blood. And we were kind of thrown off the scent at this time by finding that a lot of our patients who had been highly treated, a lot of protein given to them, had abnormalities of various kind[s], not all the same kind, and we thought that it must be that their immune system was being suppressed by something in the plasma that they were given, and that was a view we took and explored for several years. And I think it was probably accurate to say that there were abnormalities but what they meant, we didn't know, and of course, some of it probably was that they were infected with the unknown virus, HIV. So we were looking for something but we didn't know what we were looking for at the time.<sup>102</sup>

<sup>97</sup> Ludlam et al, 'Disordered immune regulation in haemophiliacs not exposed to commercial Factor VIII' *The Lancet*, 28 May 1983 [LIT.001.0416]

<sup>98</sup> Professor Ludlam – Day 18, page 105

<sup>99</sup> Professor Ludlam – Day 18, page 109

<sup>100</sup> Froebel et al, 'Immunological abnormalities in haemophilia: are they caused by American Factor VIII concentrate?', *British Medical Journal*, 1983; 287:1091–1093 [LIT.001.0215].

<sup>101</sup> Amended Witness Statement of Professor Charles Forbes [PEN.015.0254] at 0256–7, para 9

<sup>102</sup> Day 17, pages 89–90

**11.75** So far as he was concerned, the mystery has not been resolved even now.<sup>103</sup> His evidence about the state of knowledge in the early 1980s was not clear.<sup>104</sup> He thought, however, that there was a lot of doubt and argument at the time: knowledge was not hard and fast.<sup>105</sup>

***The infective agent theory***

**11.76** As noted in paragraph 11.55, an article was published in *The Observer* in January 1983 commenting on the competing theories. In relation to the infective agent theory, it stated:

A commercial blood product imported into Britain from the United States, may pose a grave threat to the health of haemophiliacs who inject it to encourage clotting ....

[I]t is being linked in America with a devastating and mystifying disease previously associated with homosexuals, which causes a serious breakdown in the body's immunity system.

Officials at the Government's Center for Disease control ... have described the spread of the disease as 'an impending epidemic' among haemophiliacs ....

In the past 10 months the disease has spread from the homosexual community to include haemophiliacs, Haitian immigrants, drug abusers, a handful of heterosexuals and some children. The cause remains baffling. One theory is that an infection agent is transmitted directly, either sexually or through contaminated blood products, in a similar manner to hepatitis B ....

Although no cases of AIDS have been reported from British haemophiliacs, the deaths of at least 10 American haemophiliacs, are now known to be caused by the disease following a survey of nearly 6000 haemophiliacs.<sup>106</sup>

**11.77** An article in the *New Scientist* of 3 February 1983 commented that there was a risk that AIDS was transmitted by blood products. It stated that the hunt for the cause of the disease:

[H]as now labelled as a prime suspect some unknown blood-borne virus.

....

In the last year, a task force under Dr Harold Jaffe at the Center for Disease Control in Atlanta, Georgia, has found seven cases of AIDS among haemophiliacs .... Jaffe believes that the spread of the disease may be connected with new preparations of factor VIII concentrate – the blood-clotting agent given to haemophiliacs – which are made up from blood from large numbers of donors, rather than one individual.

If this is correct, any patient in hospital who is given a blood transfusion could be at risk if one of the donors of the blood carries the virus.

No cases of AIDS among British haemophiliacs have been reported so far – even though 50 per cent of the factor VIII used in Britain comes from the US.<sup>107</sup>

---

<sup>103</sup> Day 17, pages 90–91

<sup>104</sup> Amended Witness Statement of Professor Charles Forbes [PEN.015.0254] at 0257

<sup>105</sup> Day 17, pages 96–97

<sup>106</sup> 'Mystery Disease Threat', *Observer*, 16.01.83 [DHF.001.7108]

<sup>107</sup> 'AIDS – transfusion patients may be at risk', *New Scientist*. 03 February 1983 [DHF.001.7119]

**11.78** On 1 March 1983, a paper on AIDS was produced by the UK Haemophilia Centre Directors' Hepatitis Working Party.<sup>108</sup> It was sent to the DHSS on 11 April 1983. This paper summarised the position to that date, based on information from the CDC at Atlanta. Aetiology was explored, with the infectious agent theory being favoured as the most likely cause. The concluding paragraph stated that it was likely that batches of Factor VIII concentrate which might contain the AIDS agent had been in use since the beginning of 1980. The CDC had therefore requested the UK Haemophilia Centre Directors to report cases of AIDS which might be related to transfusion of US concentrate. A detailed list of possible symptoms, diseases and signs associated with AIDS formed part of the survey sent to all centre directors.<sup>109</sup>

**11.79** Dr Winter told the Inquiry:

I think by that stage all haemophilia clinicians were signed up to the infectious theory because of the evidence of the San Francisco child. There was no other construction you could put on that evidence. So I think these minutes are just reflecting – they are setting out the other theories and discounting them because of the new haemophilia data.<sup>110</sup>

**11.80** Despite Dr Winter's view, it is clear that in fact there was not unanimity by this stage. However, the view of the UK Haemophilia Centre Directors' Hepatitis Working Party can be taken to be broadly representative of opinion in the profession.

**11.81** In *The Annals of Internal Medicine* of March 1983, an editorial and a series of articles discussed the evidence available up to that time and lent further support to the transmissible agent hypothesis.<sup>111</sup> Dr Evatt and Dr Curran were two of the three authors of the editorial. It gave further information about the preparation of concentrates. In the US, plasma pools contained up to 22,500 individual donations and approximately 500,000 international units of anti-haemophilic factor. The average patient with severe haemophilia received 30,000 to 50,000 units per annum from 5 to 10 separate lots and was thereby exposed to tens of thousands of donors each year. Haemophilia patients receiving blood products were said to be at the highest risk of contracting AIDS. Substantially the same material was contained in the UK Haemophilia Centre Directors' Hepatitis Working Party report referred to in paragraph 11.78, above.

**11.82** In March 1983, Dr Peter Foster of the PFC (the Protein Fractionation Centre, the manufacturer of NHS blood products in Scotland) gave a series of presentations to haemophilia clinicians and haematologists in Edinburgh and Dundee.<sup>112</sup> He was somewhat guarded in expressing his opinion. He mentioned that AIDS might be caused by transmission of an infectious agent. In evidence, he said that at that time his perception of the risk had been somewhere between a possibility and a probability. He was not definitive, but thought that the risk should be taken into account by the PFC.<sup>113</sup> As an SNBTS scientist, that was a reasonable position to adopt at the time. An infectious aetiology was still

<sup>108</sup> 'The Acquired Immune Deficiency Syndrome (AIDS)' [DHF.001.7178]

<sup>109</sup> UK Haemophilia Centre Directors' Hepatitis Working Party – Acquired Immune Deficiency Syndrome Survey [DHF.001.7183]

<sup>110</sup> Day 16, page 34

<sup>111</sup> Curran, Evatt and Lawrence, 'Acquired Immunodeficiency Syndrome – The Past as Prologue', *Annals of Internal Medicine*, 98/3, March 1983 [LIT.001.0047]

<sup>112</sup> Preliminary Report, para 11.113

<sup>113</sup> Dr Foster – Day 23, pages 10–11

not settled. The editorial in *The Lancet* of 2 April 1983, 'Acquired Immunodeficiency in Haemophilia', commented that the links with blood or blood products must be regarded as not proven.<sup>114</sup>

**11.83** The UK public health view as reflected by Dr Spence Galbraith, Director of the Communicable Disease Surveillance Centre (CDSC) in England and Wales, was set out in a letter to the DHSS in May 1983. He enclosed a paper setting out his views in support of the transmissible agent theory.<sup>115</sup> His view, which he supported by detailed discussion, was that the AIDS epidemic in the USA was probably due to a transmissible agent and that the agent was probably transmitted by blood and blood products.

### The comparative position in mid-1983

**11.84** Professor Lever commented on the competing theories at this time:

There were competing hypotheses as to what was causing the immunodeficiency, some of which had quite powerful advocates. I think ... the balance of opinion or the balance of evidence was in favour of an infectious agent at that stage. However, as one knows, the amount of distress and concern and worry, sometimes unnecessarily, that you can induce in people by raising the fear of an infectious agent in something like a blood product would be undesirable unless it was absolutely certainly the case, or as near certain as you could be that that was the case.

I think people would not necessarily have been very understanding had this turned out to be a false alarm and individuals had either bled or died by withdrawal of the clotting factors and then it having been found that there was not the threat which had been assumed.<sup>116</sup>

**11.85** Professor Ludlam said that the inferences in his studies in 1983 were confirmed when anti-HTLV-III (HIV) testing became available in late 1984 and all but two of the patients in the 1983 study were found to have been negative for HIV in 1982 and in 1983.<sup>117</sup>

**11.86** Professor Ludlam's work was to receive attention in June 1983. When Dr Foster reported on the World Federation of Haemophilia (WFH) and International Society on Thrombosis and Haemostasis (ISTH) meeting in June 1983, he recorded that some participants had attempted to make a number of points regarding features of haemophilia patients with T-cell abnormalities: in essence, North American studies correlated lowered helper-suppressor ratios with lifetime exposure to Factor VIII or with age, whereas European studies correlated the lowered ratios with use of imported concentrates and not with local concentrates. Many European participants were implying that USA products were 'bad news'. The North American response had been 'to cite Ludlam *et al*' and then to attack the validity of the data. The general feeling appeared to be that a low CD4/CD8 ratio in haemophilia patients would not necessarily indicate a pre-AIDS condition. Dr Foster's own

<sup>114</sup> 'Acquired Immunodeficiency in Haemophilia', *The Lancet*, 2 April 1983 [LIT.001.0408]

<sup>115</sup> Letter [MIS.001.0001]. Re-typed letter [MIS0010005]. See also Chapter 9, *Knowledge of the Geographic Spread and Prevalence of HIV/AIDS 1*, for further discussion of this letter.

<sup>116</sup> Day 26, page 92

<sup>117</sup> Day 19, page 40 (Of the two patients positive for HIV at that time, one died of AIDS, the other from bleeding.)



feeling had been of an attempt to suppress AIDS 'hysteria', although some of the more scientific criticism of the T-cell situation did appear to him to make some sense. He was at a disadvantage, as were others, in one respect: Dr Evatt had not submitted an abstract and delegates were left to make their own notes of his address.<sup>118</sup> He noted that Dr Evatt had explained that none of the known haemophilia cases had any other risk factor.

**11.87** There was a clash between Dr Evatt and Dr Aledort that reflected the depth of feeling at the time. Douglas Starr, in *Blood: An Epic History of Medicine and Commerce*, commented:

Bruce Evatt had been invited to speak, but he felt himself set up in a way. Though Aledort was supposed to give a brief introduction, instead he swung into a lengthy discourse on how little scientists knew about the disease. Evatt, when his turn came, felt he had to defend how much they *did* know.<sup>119</sup>

**11.88** The WFH was an influential body, comprising scientists, doctors, nurses and patients.<sup>120</sup> It concluded that there was insufficient evidence to cause changes in the treatment of haemophilia. Once more, however, the question appears to have turned on whether there was transmission by an infective agent to the exclusion of the risks inherent in the antigen overload theory.

**11.89** Professor Lever was asked when the early theories began to be disregarded. He responded that until the infectious agent had been found, theories like that would always have some degree of credibility. Once Montagnier and Barré-Sinoussi had identified something and 'certainly by the time Gallo had published', there was only a small fraction of individuals who still clung on to a theory of anything other than infection. He continued:

Up until that time I think it's a gradation. There was a gradual acceptance that it couldn't just be put down to immunological-based theories and that the epidemiology looked more and more like an infectious agent.<sup>121</sup>

### **May 1983: Identification of LAV**

**11.90** The continuing controversy in early summer 1983 initially paid little regard to the work of Montagnier and Barré-Sinoussi in France that was to become of real importance as the middle years of the decade passed. On 20 May 1983, an article appeared in *Science* reporting that the team of scientists at the Institut Pasteur in Paris had isolated a retrovirus, which they named lymphadenopathy-associated virus (LAV), from cultures of T-lymphocytes derived from the lymph nodes of a patient with signs and symptoms thought to precede AIDS.<sup>122</sup> There is more detailed discussion of this development in Chapter 29 *The Discovery of HIV and Development of Screening Tests*.

**11.91** The full significance of the French discovery was not widely understood in 1983 and later Montagnier was to recognise that the results remained controversial until Gallo

<sup>118</sup> Dr Foster's Witness Statement [PEN.015.0101] at 0109

<sup>119</sup> Starr D, *Blood: An Epic History of Medicine and Commerce*, 1998, Harper, London, pages 281–282 [LIT.001.2936] at 2951 (emphasis in original)

<sup>120</sup> Dr Winter – Day 16, page 61

<sup>121</sup> Day 26, page 41

<sup>122</sup> Barré-Sinoussi et al, 'Isolation of a T-lymphotropic retrovirus from a patient at risk for acquired immune deficiency syndrome (AIDS)', *Science*, 1983; 220: 868–871 [LIT.001.0058]

and his group announced their discovery of HTLV-III in the spring of 1984.<sup>123</sup> Nevertheless, it seems likely that the article was known to Scottish scientists by 15 June 1983 and hardened opinion in favour of an infective agent, at least as a working hypothesis.<sup>124</sup>

**11.92** Reports of cases led to the identification of products possibly associated with transmission. Dr Foster's report from the WFH and ISTH meetings stated that of the 16 US cases one was a mildly affected Haemophilia B patient who also received two units of New York blood.<sup>125</sup> Of the 14 cases of AIDS reported to the UK CDSC by 31 July 1983, one was a haemophilia patient and it was noted that he had received Factor VIII imported from the USA.<sup>126</sup> There was growing apprehension that the disease was associated with commercial blood products from the USA. Dr Foster's report of the contribution of Dr Evatt included comments relevant to the present chapter. In summary, Dr Foster noted:

- The June 1983 figures at CDC showed that the total number of USA confirmed cases was marginally higher than would be predicted from an exponential growth, consistent with the view that AIDS is caused by a transmissible agent.
- Epidemiology strongly suggested a transmissible agent (AIDS had been found in spouses, male and female, siblings etc.)
- AIDS fell into two categories: those who developed KS and those who developed opportunistic infections.
- Haemophilia patients were in the group which developed opportunistic infections.
- AIDS was still located mainly in key urban areas in the USA (New York, San Francisco, Los Angeles) but the haemophilia cases were generally located in non-AIDS areas. This was strong evidence for transmission by Factor VIII.
- Common lots of Factor VIII concentrate seemed to be 'rare or non-existent'. Haemophilia patients who received material from two known Factor VIII lots prepared from plasma containing two AIDS donations had been followed for two years with no signs of AIDS at that stage.
- The haemophilia patient with AIDS in Cardiff received products from Armour and Immuno as well as NHS concentrates. Other suspected cases had received products from Hyland (reported from Israel) and Hyland and Immuno (reported from Sweden).<sup>127</sup>

**11.93** On 23 June, the recital of a Council of Europe resolution noted that AIDS 'may be caused by an infectious agent transmissible by blood and blood products'.<sup>128</sup>

<sup>123</sup> 'A History of HIV Discovery', *Science*, 2002; 298:1727 [LIT.001.3767] at 3768; Preliminary Report, para 8.83

<sup>124</sup> The Barré-Sinoussi article may have been the 'recent work' showing an association between AIDS and a human t-cell leukaemia virus referred to at a meeting on 15 June 1983 of the Factor VIII safety sub-committee: Minutes of FVIII Safety Sub-Committee Meeting held on 15th June 1983 [SNF.001.3730]. An alternative possibility is a different article in the same issue of *Science*: Gallo et al, 'Isolation of human T-cell leukemia virus in [AIDS]', *Science*, 1983; 220: 865–867

<sup>125</sup> Dr Foster appears to have prepared two reports: [SNF.001.3714] and [SNF.001.3712]; the one referred to is the latter of these.

<sup>126</sup> Haemophilia Centre Directors AIDS Investigation – Surveillance of AIDS Cases in Patients With Blood Coagulation Disorders [SNB.001.7556]. See reference to this case in Dr Craske's update in September 1983. The case was also highlighted in a letter to *The Lancet* of 19 November, 1983 [LIT.001.0413]

<sup>127</sup> Dr Foster's Memo [SNF.001.3712]

<sup>128</sup> Recommendation No R(83)–B of the Committee of Ministers to Member States on Preventing the Possible Transmission of Acquired Immune Deficiency Syndrome (AIDS) from Affected Blood Donors to Patients Receiving Blood or Blood Products [DHF.002.2149]

**11.94** On 13 July 1983, Dr Galbraith's paper of May<sup>129</sup> was discussed at a meeting of the Biological Products Sub-Committee of the Committee on Safety of Medicines.<sup>130</sup> It was minuted that the cause of AIDS was unknown but that an infectious aetiology seemed likely. The minute proceeded:

A previously unrecognised or new agent may be responsible, but repeated exposure to, or reactivation of, known agents, (eg CMV, EBV) may be involved. Heightened susceptibility may be an important factor, e.g. immunological deficiencies induced by unusual sexual practices or exposure to blood products. Based on the clinical evidence, transmissibility of the supposed agent(s) appears to be low, requiring intimate contact or introduction into the tissues.

Patients who repeatedly receive blood clotting-factor concentrates appear to be at risk, but the evidence so far available suggests that this risk is small. The risk appears to be greatest in the case of products derived from the blood of homosexuals and IV drug abusers resident in areas of high incidence (eg New York and California), and in those who repeatedly receive concentrates in high dosage.<sup>131</sup>

### Developments during the remainder of 1983

**11.95** Over the remainder of 1983, there were reports of increasing numbers of infections.<sup>132</sup> On 28 September, there was a meeting of the Central Blood Laboratories Authority.<sup>133</sup> It was noted that the Medical Research Council (MRC) had set up a working group on AIDS. The working group first met on 10 October 1983.<sup>134</sup> In their discussion of aetiology, there was a 'passing allusion' to the antigen overload hypothesis. The 'more widely held view' noted was that AIDS was due to a novel 'AIDS agent'. Retroviruses were considered and it was noted that HTLV was a possible candidate on the basis of its known tropism for T-helper cells.<sup>135</sup> The comment proceeded:

However a critical evaluation of the data led to the view that it was more probably an opportunist was unlikely [*sic* – likely]<sup>136</sup> to be the aetiological agent. The assumption that the agent was necessarily a virus was challenged and the need to keep an open mind on organisms such as protozoa was stressed.<sup>137</sup>

**11.96** The group was careful to reserve its opinions. It was said that the 'best and brightest' in the UK (at the MRC) were still very confused as to the causal agent. It was suggested that systematic antimicrobial therapy might provide leads on such agents. It was noted that blood product associated cases could enable some of these alternative hypotheses to be tested. Specifically in relation to epidemiology, but probably more generally, there was a lack of confidence in US studies which were thought to be insubstantial and not of the highest quality.

<sup>129</sup> Action on AIDS [MIS.001.0001]; Re-typed letter and paper [MIS.001.0005]

<sup>130</sup> Committee on Safety of Medicines – Sub-Committee on Biological Products, Minutes of the Meeting held on 13 July 1983 [MIS.001.0291]

<sup>131</sup> Ibid [MIS.001.0291] at 0292

<sup>132</sup> Dr Craske's report of 10 September 1983 [SNB.001.7556]; his report to the UK Working Party on Transfusion Associated Hepatitis on 27 September [SNF.001.1039], as noted by Dr McClelland and by Dr. Mitchell [SNB.001.3443]; and Dr Craske's report to the UKHCDO Hepatitis Working Party for 1982–83 [SNF.001.0948]

<sup>133</sup> Minutes of the Eighth Meeting of the Central Blood Laboratories Authority held on 28 September 1983 [DHF.001.4807]

<sup>134</sup> Minutes [SNF.001.3759]; Preliminary Report, para 8.54

<sup>135</sup> Tropism is the response of an organism to an external stimulus by growth in a direction determined by the stimulus. At this stage HTLV-III had not been discovered, but HTLV-I had been and was the subject of study.

<sup>136</sup> Notwithstanding the approval of the Minutes at the next meeting the Inquiry considers that the word 'unlikely' should read 'likely'

<sup>137</sup> Minutes [SNF.001.3759] at 3761

**11.97** Meantime, as events were to prove, UK patients were being infected with HIV. It is of interest to note the reasons for casting doubt on US epidemiological research:

The erasure of patients' names from the records held at the Centres for Disease Control in Atlanta as a result of political pressure would limit the ability of CDC to conduct proper epidemiological studies. The organisation of epidemiology in the United Kingdom was well suited to studying this problem. The importance of establishing such studies early in the emergence of disease was again stressed. Further emphasis was given to the concept of identifying early phases of the disease for testing aetiological hypotheses. It was emphasised that at this stage national collaboration was possible and indeed essential on items such as an AIDS case-control study and active surveillance ... The close liaison between clinical and laboratory medicine in the UK was again stressed as an important background for such work. Blood transfusion policy was discussed in relation to the possibility of using 'clean' donor panels for blood products.<sup>138</sup>

**11.98** This rather optimistic view of the situation in the UK is challenged by the difficulties in obtaining comprehensive data, not least caused by the insistence of haemophilia directors on the confidentiality of patient details (discussed in Chapter 10, *Knowledge of the Geographical Spread and Prevalence of HIV/AIDS 2*, paragraph 10.101). This Inquiry has found no objective support for the MRC's relative lack of confidence in the CDC's epidemiological research.

**11.99** On 14 October 1983 the UK Central Blood Laboratory Authority's central committee for research and development in blood transfusion Working Group on AIDS in Relation to Blood Transfusion first met. The record of the meeting noted:

Epidemiological Features of HTLV infection

The epidemiological features of AIDS suggest that an infectious agent is responsible for the condition but as yet no aetiological factor has been unequivocally associated with the disease.<sup>139</sup>

**11.100** The paper proceeded to comment on evidence of HTLV infection in homosexuals and in AIDS patients, among other topics, and continued:

Recently two variant viruses have been found in association with a few AIDS patients. Cherman et al have described a retrovirus isolated from a French homosexual .... Recent evidence suggests that this virus is distinct from HTLV ... (Montagnier.Pers.Comm). A virus related to HTLV but distinct from HTLVI and HTLVII has recently been demonstrated in proviral form in a few AIDS patients.

The inherent difficulty in interpreting the significance of HTLV infection in AIDS patients is that these individuals are highly susceptible to a wide range of opportunistic infections, a category into which HTLV might fall. Furthermore the establishment of infections requiring intimate contact is likely to be favoured in populations with a high degree of sexual promiscuity, a social feature which appears to be common in AIDS victims.<sup>140</sup>

<sup>138</sup> Ibid [SNF.001.3759] at 3762–3763

<sup>139</sup> Minutes [DHF.002.4834] at 4838

<sup>140</sup> Ibid [DHF.002.4834] at 4839

**11.101** In the *British Medical Journal* of 15 October 1983, Karin Froebel and others (Professor Forbes' Glasgow group) reported on a study of changes in T-cell ratios in Scottish haemophilia patients exposed to Scottish and US Factor VIII concentrates.<sup>141</sup> They carried out a 'controlled' experiment to compare the cellular immunity of patients who had received solely Scottish product and a comparator group who were administered Profilate (Alpha) Factor VIII. Their conclusion was that:

Our results ... argue against a disease vector that is specific to American blood products. In terms of lymphocyte abnormalities, Scottish patients with haemophilia yield results that are consistent with those seen in the acquired immune deficiency syndrome and in acute viral infection. Whether these abnormalities in the T cell ratios ... are sufficient to render the patients immunodeficient and therefore, possibly, in a prodromal stage of the acquired immune deficiency syndrome, will become apparent as the patients are followed up clinically.<sup>142</sup>

**11.102** The paper was mentioned in *The Guardian* of 14 October 1983 in an article by Andrew Veitch, medical correspondent. He noted the findings and commented that, on the basis of the research, US Factor VIII appeared to be no more dangerous than the Scottish version. The headline and opening comments were:

Aids 'not imported in blood'

Fears that more haemophiliacs may contract Aids from contaminated US supplies of the blood clotting factor VIII will be calmed, at least temporarily, today.<sup>143</sup>

**11.103** The tone of the article was somewhat sceptical. Mr Veitch noted, without comment, emerging evidence in England that implicated US Factor VIII in the infection of haemophilia patients.

**11.104** The Glasgow paper appeared to accept the hypothesis that immunodeficiency might be diagnostic, in itself, of a prodromal state of AIDS. In that sense it was less cautious than Professor Ludlam's published views at this stage.

**11.105** The first World Health Organization (WHO) European conference on AIDS, entitled 'AIDS in Europe, Status Quo 1983', was held in Aarhus, Denmark between 19 and 21 October 1983.<sup>144</sup> The press release for the conference, dated 30 September 1983, noted that the AIDS epidemic continued to 'baffle' scientists.<sup>145</sup> It stated that the epidemiological evidence showed clearly that AIDS was contagious and that it was probably transmitted by blood contact. No infectious agent had so far been identified but a strong candidate was a C-type retrovirus.<sup>146</sup> Latency periods were thought to range from a few up to 18 months. It was still not clear what symptoms preceded fully-developed AIDS. Neither was there precise information about the number of AIDS victims who harboured the

<sup>141</sup> Froebel et al, 'Immunological abnormalities in haemophilia: are they caused by American factor VIII concentrate?', *British Medical Journal*, 1983; 287:1091 [LIT.001.0215]

<sup>142</sup> Ibid [LIT.001.0215] at 0216

<sup>143</sup> *The Guardian*, 14.10.83 [SGF.001.0948]

<sup>144</sup> 'International Notes Acquired Immunodeficiency Syndrome (AIDS) – Europe', *MMWR*, 1983; 32(46):610–611 [LIT.001.0555]. See also cutting from *Daily Telegraph*, 20 October 1983 [DHF.001.4959]

<sup>145</sup> Press Release [SGF.001.0949]

<sup>146</sup> The class of 'C-type retroviruses' include avian leukosis virus and salmon lymphoma virus. It was later thought that HIV belonged to a different class of retroviruses, 'lentiviruses'. See Chapter 29 *The Discovery of HIV and Development of Screening Tests* at paragraph 29.4, footnote 6, for Professor Lever's view that more recent research suggests that, while certainly a retrovirus, HIV may not properly belong to the lentivirus genus, either.

putative infectious agent. In any case the very poor prognosis for AIDS victims made it essential to gather as much information as possible in a co-ordinated way, in order to help contain the disease through preventative measures and to set up international research projects.

**11.106** The fact that the meeting aimed to summarise the available information about the nature of prodromal (early) symptoms of AIDS and the effectiveness of the different therapeutic strategies reflected a low level of accepted knowledge of the fundamentals of the epidemic and the aetiology of the disease.

### End of 1983

**11.107** Dr Brian McClelland and Mr John Watt represented the SNBTS at a WHO Conference in Geneva between 22 and 25 November 1983.<sup>147</sup> Others attending included representatives from the CDC and Professors Montagnier, Leikola and Zuckerman. The draft report of the meeting was distributed on 14 December with a request for comments by 6 January 1984.<sup>148</sup> The aetiology of the disease was said to be unknown but the epidemiological pattern was said to be most consistent with a transmissible agent. Transmission appeared to occur by blood sharing; the most likely cause was a virus. Coagulation factor concentrates had been implicated and methods of inactivation were being developed but these could not be evaluated until the causative agent was discovered.

**11.108** The only new observation recorded was that an aetiological role for retroviruses had been considered because they were known to be capable of causing immunosuppression and neoplastic diseases (such as tumours) in animals after long latency periods. HTLV was suggested as a possibility.<sup>149</sup>

**11.109** There appear to have been two clear schools of thought at the end of 1983. There was no settled consensus as to the cause of AIDS or the diagnostic significance of the cellular abnormalities identified in laboratory tests. For many, the almost simultaneous appearance of acquired immune deficiencies in homosexuals, IV drug abusers and haemophilia patients pointed to a single transmissible agent. For others, there were cohort differences that distinguished the patient groups and suggested that different pathologies might be involved.

**11.110** The factors that were adduced in support of the antigen overload theory at this stage were:

- The low absolute and relative numbers of haemophilia patients with signs and symptoms of overt disease.
- The apparent absence of recorded disease in populations with a high exposure to imported commercial Factor VIII (notably in Germany).<sup>150</sup>
- Uncertainty whether there was one single cause of AIDS.
- The clinical differences between haemophilia patients and others with severe immune abnormalities.

<sup>147</sup> Dr McClelland was Director of the Edinburgh and East of Scotland Blood Transfusion Service. Mr Watt was Director of the PFC. See Preliminary Report, para 8.65 for a more extensive summary of the meeting.

<sup>148</sup> Draft Report [SNF.001.2575]; Covering Letter [SNF.001.2574]

<sup>149</sup> Dr McClelland's initial report for the Scottish Regional Transfusion Directors' meeting on 8 December 1983 [SNF.001.0552] contained no new data on transmission.

<sup>150</sup> Draft Report [SNF.001.2575] at 2609. It appears frequently to have been overlooked that Germany had reported a few cases of AIDS in haemophilia patients to the WHO by this time.

**11.111** There are several problems with this position. By no means all homosexual men contracting AIDS had KS and some developed PCP. Lack of evidence of KS in haemophilia patients did not distinguish them from the group of infected homosexuals as a whole. Further, to exclude KS from the constellation of conditions to which haemophilia patients might be exposed at this stage would have been speculative. The most that one could have said was that no cases had been diagnosed. Many individuals in both groups had PCP.

**11.112** The epidemiological evidence inevitably depended on the reliability of reports. But whereas by January 1983 there had been only eight cases out of a total haemophilia population in the USA of about 20,000, the total number increased during the year to 21.<sup>151</sup> The rate was increasing as it had in the case of homosexual men.

**11.113** Professor Ludlam thought that the antigen overload theory was still on the table but, increasingly, that appears to have depended on finding alternative explanations for emerging evidence favouring the transmissible agent theory.<sup>152</sup>

#### January to mid-May 1984

**11.114** It appears that the picture became clearer still in early 1984. There was a report in *The Annals of Internal Medicine* for January 1984 of AIDS in the elderly wife of a haemophilia patient.<sup>153</sup> Her husband had received Factor VIII concentrate and subsequently died from PCP and probable AIDS.

**11.115** The same issue of *The Annals of Internal Medicine* noted the case of the San Francisco child in a report of an NIH conference entitled 'Acquired Immunodeficiency Syndrome: Epidemiologic, Clinical, Immunologic, and Therapeutic Considerations'.<sup>154</sup> One of the contributors, Dr Edward Gelmann, commented on the arguments for and against the hypothesis suggesting that a retrovirus might be involved in the aetiology of AIDS. His conclusion was that:

The significance of the association between human T-leukemia virus and the acquired immunodeficiency syndrome is not known. There are no data to disprove that there may be an etiologic role for this virus in the syndrome. The elucidation of this role is hindered by the low levels and transient nature of the virus expression. Molecular analysis of the cloned viral genome from one of the patients described may shed further light on the significance and pathogenic potential of this isolate. On the other hand, human T-leukemia virus may represent another new or reactivated opportunistic infection in persons predisposed by the underlying immunodeficiency.<sup>155</sup>

**11.116** The evidence of T-leukemia virus infection in AIDS cases had come in particular from Dr Gallo's laboratory. So far as published, it was clearly not considered to be conclusive at this stage. However, by this time at least 11 possible cases of transfusion-associated AIDS, together with cases of sexual partners of risk group members and certain infants connected with risk group members, had been identified in addition to the groups

<sup>151</sup> Professor Ludlam's Statement [PEN.015.0385] at 0398–0399

<sup>152</sup> Day 18, page 119

<sup>153</sup> Pitchenik et al, 'The Acquired Immunodeficiency Syndrome in the Wife of a Hemophiliac', *Annals of Internal Medicine*, 1984; 100:62–65 [LIT.001.0681]

<sup>154</sup> Fauci et al, 'Acquired Immunodeficiency Syndrome: Epidemiologic, Clinical, Immunologic, and Therapeutic Considerations', *Annals of Internal Medicine*, 1984; 100:92–106 [LIT.001.1573]

<sup>155</sup> Ibid [LIT.001.1573] at 1585

previously described. The previous, erroneous assumption that there was something intrinsic to homosexuality itself or other forms of sexual behaviour that was causally related to the syndrome had effectively been dismissed but this had not resolved the issue of aetiology.

**11.117** On 9 January 1984, the Blood Products Sub-Committee of the Haemophilia Society produced a paper reviewing blood products supply and related issues in the UK. On the topic of AIDS, the paper stated:

No discussion of blood products can be complete at present without referring to AIDS. Unfortunately facts are in very short supply. No infective agent has been identified for AIDS, and there is no reliable evidence that the disease is transmitted through blood products (although this still seems the most popular theory) ....

Certainly the immunological abnormalities which may be associated with AIDS are observable in haemophiliacs not exposed to commercial concentrates (e.g. in Scotland and Australia) ....

There is also a theory that the AIDS agent is closely associated with Hepatitis, the AIDS agent being in some way harboured by the hepatitis virus.<sup>156</sup>

**11.118** The letter to *The Lancet* by Professor Ludlam and others already referred to in paragraph 11.70 was cited in support of the reference to Scotland. The letter had noted that it seemed likely that immunosuppression observed in haemophilia patients resulted from infusion of foreign protein or a ubiquitous virus rather than a specific AIDS virus in Factor VIII concentrates. It did not say expressly that the abnormalities were those which might be associated with AIDS and Professor Ludlam was characteristically cautious in expressing his views. However, in general the paper reflected the continuing uncertainty about the aetiology of AIDS that was prevalent at the time among haemophilia doctors.

### *The balance of opinion*

**11.119** The approach adopted in the opinions of leading public health and transfusion doctors and blood product scientists was different. There were protagonists for and against an infective agent aetiology but the balance of opinion was, in general, in favour of an infective agent.

**11.120** On 12 January 1984, the *NEJM* published the results of a study by Curran and others of patients in the USA with AIDS and no recognised risk factors.<sup>157</sup> Patients who appeared to have been infected by blood transfusion were identified. At least one high-risk donor was identified for each of the seven cases in which investigation of the donors was complete. The authors concluded that their findings strengthened the evidence that AIDS might be transmitted in blood.

**11.121** An editorial in the same issue, by Joseph Bove, Yale University School of Medicine, advised caution in assessing the conclusions in the Curran paper. Having recited the data, he stated:

<sup>156</sup> Blood products Sub-Committee Paper [DHF.001.5151] at 5154

<sup>157</sup> Curran et al, 'Acquired Immunodeficiency Syndrome (Aids) Associated with Transfusions', *New England Journal of Medicine*, 1984; 310(2):69-75 [LIT.001.0695]



The apparent conclusion, and the one favoured by Curran et al., is that some cases of AIDS are caused by a blood-borne agent that is transmitted by transfusion. This conclusion also requires that there is a carrier state during which a person with infectious disease is healthy enough to be accepted as a blood donor. Although other epidemiological studies have also suggested such a carrier state, these transfusion-associated cases provide an opportunity to evaluate it more carefully and to study the critical aspect of recipient susceptibility.<sup>158</sup>

**11.122** The comment noted that the paper did not provide information about what happened to the recipients of other blood components from the suspect donors, whose donation would normally be channelled into component production. It proceeded:

If recipients of other components from the suspected donation remain healthy, one must either postulate an agent of low infectivity and assign major importance to host factors or question the basic assumption of blood-borne spread.<sup>159</sup>

**11.123** In the UK, a meeting was arranged by the National Institute for Biological Standards and Control (NIBSC), scheduled for 9 February 1984, to examine the infectious hazards of blood and blood products, with particular reference to hepatitis and AIDS.<sup>160</sup> The outcome of the discussion can only be regarded as inconclusive. Professor Tedder of the Middlesex Hospital Medical School posed the question whether AIDS could be caused by transmission of an infectious agent in blood and blood products. He commented that one possible explanation for the occurrence of AIDS in recipients of blood and blood products was due to a filterable agent, 'presumably a virus', but he noted that another possible explanation was 'an overwhelming of the immune system by repeated infusion of foreign (and possibly altered) proteins', concluding that 'the true explanation may lie between the two extremes'.<sup>161</sup> Dr Geoffrey Schild (NIBSC) suggested the possible importance of genetic susceptibility.<sup>162</sup> While some of the contributions appear to have proceeded on the hypothesis that AIDS could be transmitted by blood products, the record does not disclose an agreed answer to Professor Tedder's question.

### *Growing concern*

**11.124** There was growing concern in Scotland. By letter dated 15 February 1984 Professor John Cash, Medical Director of the SNBTS, wrote to Dr Albert Bell at the Scottish Home and Health Department (SHHD). He suggested that a UK group should be formed for coordinating research into blood transfusion and AIDS. He said:

[T]here should be formed a single UK group responsible to the Departments of Health for co-ordinating research in the area covering the interface between blood transfusion and AIDS. This group should have representatives of existing smaller groups already in existence – haematologists and haemophilia centre directors and of the SNBTS Directors.<sup>163</sup>

<sup>158</sup> Bove, 'Transfusion Associated Aids – A Cause for Concern', *New England Journal of Medicine*, 12 January 1984 [LIT.001.0702]

<sup>159</sup> Ibid [LIT.001.0702]

<sup>160</sup> Draft Minutes [SNB.004.8628]; Preliminary Report, para 8.75

<sup>161</sup> Ibid [SNB.004.8628] at 8630

<sup>162</sup> Ibid [SNB.004.8628] at 8635

<sup>163</sup> Letter [SNB.004.8639]; Preliminary Report, para 8.77

**11.125** The major areas of research proposed were listed and Professor Cash asked Dr Bell to bring those matters to the attention of the appropriate authorities.

**11.126** Meanwhile events were proceeding apace. Dr Evatt and others (including Dr Curran) returned to the subject in *The Annals of Internal Medicine* in April 1984.<sup>164</sup> In all but two of the 22 haemophilia cases examined by this time the standard risk factors had been excluded. The common factor was exposure to Factor VIII or Factor IX concentrates and all but one had also received other blood components. The discussion commented that the hypothesis that AIDS developed in the patients as a result of an infectious agent transmitted by blood products seemed logical. That had been Dr Evatt's view from early 1982. It seems unlikely that it would have been sufficient of itself to overcome the reservations of others. At this point, before publication of Gallo's work, the issue was clearly unresolved to general expert acceptance, at least in the haemophilia community.<sup>165</sup>

**11.127** The views of adherents of the 'antigen overload' theory among haemophilia clinicians at this time were reflected in a paper prepared by Professor Ludlam in 1990.<sup>166</sup> It contained a comprehensive analysis of the competing theories, and served to underline the state of uncertainty among haemophilia clinicians, as seen by Professor Ludlam, about the aetiology of AIDS until Gallo's publication. The paper was prepared for pending litigation in England and Wales.<sup>167</sup> However, it reflected Professor Ludlam's published research and he confirmed that it reflected the way of thinking at the time. In summary, as an alternative to a viral aetiology, immune abnormalities observed in asymptomatic haemophilia patients might be due to the following:<sup>168</sup>

- A previously undescribed feature of haemophilia.
- Chronic liver disease.
- Large amounts of foreign proteins in plasma preparations.

**11.128** Professor Ludlam summarised the evidence for the immune abnormality being due to blood products and not a virus and the contrary proposition that the immune changes could have been due to a putative AIDS virus, repeating the discussion already dealt with that had evolved over time, particularly as reflected in his own research. He said:

I think one of the things that we were just wondering ... was that maybe the AIDS in people with haemophilia was actually of a different aetiology from that in gay men ....

....

[M]aybe haemophilia as a whole was sliding into AIDS because of all the concentrate we were using. Quite separate from HIV or a putative virus.

Q: Just looking on AIDS almost as an end stage, as it were, in the progressive demolition of the immune system?

A. From Factor VIII concentrate per se or the proteins, the contaminant.<sup>169</sup>

<sup>164</sup> Evatt et al, 'The Acquired Immunodeficiency Syndrome in Patients with Hemophilia', *Annals of Internal Medicine*, 1984; 100:499-504 [LIT.001.0689]

<sup>165</sup> Dr McClelland's Witness Statement [PEN.015.0307] at 0324

<sup>166</sup> Professor Ludlam – Human Immunodeficiency Virus Infection in Haemophiliacs [PEN.015.0385] 30 October 1990

<sup>167</sup> Day 18, page 20

<sup>168</sup> Day 18, page 143, Professor Ludlam – Human Immunodeficiency Virus Infection in Haemophiliacs [PEN.015.0385] at 0401–0402

<sup>169</sup> Day 18, pages 149–150

**11.129** This answer is revealing. It suggests that, as an adherent of the antigen overload theory, Professor Ludlam had in mind that there was no significant clinical difference between the acquired immune deficiency syndromes in haemophilia patients and other groups and that each might be a progressive and potentially fatal complication in haemophilia. Fundamental to the theory was the hypothesis that factor concentrates by themselves were contributing to the development of serious acquired immune deficiency.

**11.130** Professor Ludlam was pressed on the question whether physicians examining the problem could have thought that antigen overload was the whole explanation of immune abnormalities in haemophilia patients. He said:

I think that became increasingly less tenable with the unfortunate case reports of a spouse and a child of a haemophiliac developing AIDS ... Because that was evidence of a presumed sexually transmissible agent, furthermore, sadly being passed to the child.<sup>170</sup>

**11.131** Professor Ludlam was referred to an article by Drs Barbara and Tedder published in October 1984.<sup>171</sup> The article suggested that 'little significance should be attached to reports of abnormal lymphocyte profiles in haemophiliacs'. He ultimately accepted that 'by October 1984, there was little doubt that HTLV-III was the cause of AIDS', including in people with haemophilia.<sup>172</sup>

### *The 'antigen overload' theory in retrospect*

**11.132** In retrospect it appears that the antigen overload theory was not a satisfactory answer to the question whether there was AIDS associated with haemophilia. On the face of it, Dr Aledort's view, and the development of the antigen overload theory generally, led to the conclusion that heavy and prolonged use of factor concentrates, and in particular Factor VIII, could be expected, in some cases, to damage the blood disorder patient's immune system in a way similar to the damage found in homosexual men who were exposed to the risk of progression to AIDS. That had to include the possibility of a fatal prognosis in some cases at least. It provided an explanation for the development of immune abnormalities in some patients, due solely to the administration of factor concentrates, but implicit in it was a risk of progressive damage. That process might result in an immune deficiency state indistinguishable from that in asymptomatic homosexual patients who were at risk of AIDS. Without evidence of relative rates of progression, the outcome for the patient might be the same whatever the aetiology of the cellular immune deficiency.

**11.133** Further, the possibility of antigen overload as a causative factor could not exclude the concurrent possibility of infection transmitted in blood and blood products, with a fatal prognosis in some cases. The two aetiologies postulated were not mutually exclusive. The positive risk could not exclude the increasing probability that haemophilia patients might also develop AIDS due to viral transmission. At best it was an additive risk. At worst it was an aggravating feature that could increase the threat to the patient exposed to an infective agent.

<sup>170</sup> Day 18, page 155. Ragni et al, 'Acquired immunodeficiency syndrome in the child of a haemophiliac', *The Lancet*, 19 January 1985 [LIT.001.5042]

<sup>171</sup> Day 19, page 1. Barbara and Tedder, 'Viral Infections Transmitted by Blood and Its Products', *Clinics in Haematology* [LIT.001.3739]

<sup>172</sup> Day 19, pages 5 and 7

**11.134** Less than three years had passed from publication of the first cases of AIDS, however. Despite intensive research and debate, there was no consensus as to the cause of the immune abnormalities observed in the haemophilia community, where they affected patients with severe Haemophilia A in particular. There was ample scope for continuing research and debate. How that might have developed would be a matter of pure speculation, however, as there was about to be a major change in direction.

### **May to October 1984: identification of HTLV-III**

**11.135** Dr Gallo and his group announced the discovery of HTLV-III on 23 April 1984 at a press conference in Washington.<sup>173</sup> As described in Chapter 29, *The Discovery of HIV and the Development of Screening Tests*, they concluded that HTLV-III might be the primary cause of AIDS and found antibodies to HTLV-III in a majority of patients with AIDS, thus opening the way to future testing of those infected by the virus.

**11.136** With the development of HTLV-III testing, following US research based on Dr Gallo's work, further cases of infection emerged and the discovery laid the basis for the general consensus that has prevailed ever since.

**11.137** Gallo's finding that HTLV-III caused AIDS is discussed in more detail in Chapter 29, *The Discovery of HIV and the Development of Screening Tests*. Confirmation of his findings was provided by Jay Levy and others, writing on the recovery of retroviruses from Factor VIII concentrates and processes to inactivate them.<sup>174</sup> Levy's findings on virus inactivation were, in turn, referred to in the US CDC update on AIDS in persons with haemophilia published in the *MMWR* of 26 October 1984.<sup>175</sup> For present purposes, the ability to infect Factor VIII concentrate with the AIDS virus, freeze dry it and thereafter heat it to reduce residual virus titre to an undetectable level were important stages in proof of a viral aetiology for AIDS. Nine patients were discussed. They had no risk factors for AIDS other than haemophilia therapy. The Editorial Note in the *MMWR* stated:

[T]he occurrence of nine cases with no known risk factor or exposure other than the use of factor VIII preparations implicates these products as potential vehicles of AIDS transmission.<sup>176</sup>

**11.138** These were significant findings. As a practical matter, after Gallo, work in the USA turned towards identification of infection in individuals and virus inactivation in manufacture.

### **The view in the UK in 1984**

**11.139** Even after the reports from Montagnier and Gallo, there continued to be comments published in the UK suggesting that immunological compromise in patients with haemophilia might be due to the repeated challenge of the immune system inherent in administration of Factor VIII concentrates manufactured from large pools. On 30 June 1984 *The Lancet* published an article by Dr Robert Carr and others (Professor Ludlam's Edinburgh group), related to a study of 47 patients with haemophilia who had been

<sup>173</sup> Preliminary Report, para 8.84

<sup>174</sup> Levy et al, 'Recovery and inactivation of infectious retroviruses added to factor VIII concentrates', *The Lancet*, 1984; II:722-23 [LIT.001.0434]

<sup>175</sup> 'Update: Acquired Immunodeficiency Syndrome (AIDS) in Persons with Hemophilia' *MMWR*, 1984; 33(42):589-591 [PEN.013.0186]

<sup>176</sup> 'Update: Acquired Immunodeficiency Syndrome (AIDS) in Persons with Hemophilia' *MMWR*, 1984; 33(42):589-591 [PEN.013.0186] at 0187

treated exclusively with SNBTS Factor VIII and Factor IX concentrates.<sup>177</sup> In Haemophilia A patients, the number of T-cells was depressed, resulting in a reduction of the helper/suppressor ratio in about half the patients. In Haemophilia B, the helper/suppressor ratio was also depressed, attributable to a slight increase in the suppressor number and a slight decrease in the helper number. It was suggested that these immunological abnormalities resulted from transfusion of foreign proteins in blood products rather than from an infective agent in the blood products giving rise to AIDS. It was also commented that at least a year had passed since the most recent batch of plasma used to prepare these concentrates had been collected.

**11.140** The final comment in the article was:

Furthermore, the relation between the lymphocyte subset abnormalities in symptomless haemophiliacs and the likelihood of eventual frank AIDS remains unclear although it may be connected with HLA status.<sup>178</sup>

**11.141** The article must have been written and presented for publication some months earlier than its date (30 June) and Gallo's discovery would not have been known to the authors. It forms an important bridge between Professor Ludlam's earlier 1983 letter and the discovery in late 1984 of the infection of the Edinburgh Cohort (a group of Edinburgh haemophilia patients infected by NHS products, discussed in Chapter 10, *Knowledge of the Geographical Spread and Prevalence of HIV/AIDS 2*). Briefly, at this date it remained an acceptable view among certain experts in the UK that full-blown AIDS in haemophilia patients might be the end-stage of progressive immune compromise caused by something other than a specific AIDS infective agent, an unidentified component of concentrates or a non-specific effect of foreign proteins.

**11.142** Therefore, at least until June 1984 some haemophilia clinicians clearly remained sceptical of the claims that AIDS was caused by a transmissible virus. Some in the scientific community took a different approach and researched the development of a laboratory test, as had happened in the USA.

**11.143** On 7 July 1984 *The Lancet* published a letter by Mads Melbye and others.<sup>179</sup> A study of 22 haemophilia patients from Denmark who had been treated with Factor VIII concentrate purchased from US and European commercial sources demonstrated a high prevalence of antibodies to LAV: 14 of the 22 were positive.<sup>180</sup> Clinicians caring for haemophilia patients were advised to consider alternative forms of therapy for new patients not yet exposed to 'Cryoprecipitate concentrate', factor concentrate in UK nomenclature. The authors stated that, until screening tests or inactivation techniques were in widespread use, commercially available cryoprecipitate products should be considered as 'probably contaminated'.

**11.144** This was followed by a letter in *The Lancet* dated 18 August 1984 by Rosemary Ramsay and others (including Dr Evatt) of the CDC giving additional information about a number of US cases. They argued that the serological data described, indicating a high risk

<sup>177</sup> Carr et al, 'Abnormalities of circulating lymphocyte subsets in haemophiliacs in an AIDS-free population', *The Lancet*, 1984; 1431-1434 [LIT.001.0425]; Preliminary Report, para 8.86

<sup>178</sup> Carr et al, 'Abnormalities of circulating lymphocyte subsets in haemophiliacs in an AIDS-free population', *The Lancet*, 1984; 1431-1434 [LIT.001.0425] at 0428. HLA, human leukocyte antigen, is the immune system's recognition protein. It is discussed in more detail, in the context of HCV, in Chapter 13, *Knowledge of Viral Hepatitis Now*.

<sup>179</sup> Melbye et al, 'High prevalence of lymphadenopathy virus (LAV) in European haemophiliacs', *The Lancet*, 1984; 40-41 [LIT.001.0423]

<sup>180</sup> Interestingly, when the research was published in December, it was said that 59% of the Danish patients were infected. 59% of 22 would be 13, not 14.

of exposure to LAV for heavy users of Factor VIII concentrate, supported the contention that LAV was transmitted by some blood products. They studied 25 Haemophilia A patients and four with Haemophilia B, none of whom had symptoms associated with AIDS:

Haemophilia A patients who were seropositive for LAV had used significantly more factor VIII concentrate than had patients sero-negative for LAV. This association would be expected if factor VIII concentrates contain LAV or its proteins. In contrast, the haemophilia patients with AIDS had a significantly lower antibody prevalence, perhaps because patients with AIDS have a declining antibody response to antigen despite paradoxically higher levels of circulating immunoglobulins. 4 patients with haemophilia B were negative for LAV antibody and had normal cellular immunity. Patients with haemophilia B, in general, have not been found to have the degree of immune abnormalities seen in haemophilia A.

These serological data, indicating a high risk of exposure to LAV for heavy users of factor VIII concentrate, support the contention that LAV may be transmitted by some blood products.<sup>181</sup>

**11.145** Although not published until October 1984 in *Clinics in Haematology*, the transfusionist John Barbara and virologist Richard Tedder had written in about May or June that:

The characteristics of agents lending themselves to transmission by blood or blood products centre around their presence in blood, or its components, which has been taken from *apparently healthy donors*. Thus these agents often will have a combination of a long incubation period with a prolonged and high-level viraemia.<sup>182</sup>

**11.146** It was inferred that agents transmitted by blood and blood products must have a 'silent period' because the donor appeared healthy when blood was given. In relation to HTLV-III, the paper noted the cases of possible transmission of AIDS by transfusion and continued:

The transmission of AIDS by pooled clotting factor concentrates is less controversial. Since, as a group, haemophiliacs are well studied, it is unlikely that there should have been an illness like AIDS unrecognized before 1980. Little significance should be attached to reports of abnormal lymphocyte profiles in haemophiliacs; nevertheless there is no doubt that there have been deaths of haemophiliacs due to AIDS in the absence of other established risk factors and that, unlike those associated with transfusion, these cases were scattered throughout the USA. In addition there is a report which seems to have identified the transmission of AIDS from a haemophiliac (asymptomatic at that time) to his wife.<sup>183</sup>

**11.147** The paper went on to note the isolation and characterisation of LAV/HTLV-III and the likely aetiological link to AIDS.

<sup>181</sup> Ramsey et al, 'Antibody to Lymphadenopathy-Associated Virus in Haemophiliacs With and Without AIDS', *The Lancet*, 1984 [LIT.001.0421] at 0422

<sup>182</sup> Barbara and Tedder, 'Viral Infections Transmitted by Blood and its Products', *Clinics in Haematology*, October 1984; 13/3 [LIT.001.3739] (emphasis in original)

<sup>183</sup> Ibid [LIT.001.3739] at 3749

**11.148** Professor Ludlam was asked to comment on the statement that little significance should be attached to reports of abnormal lymphocyte profiles in haemophilia patients. He said:

They are virologists and until the virus was identified and the antibody test developed, there was no other way of studying this condition other than by immune tests. These were patients who presented, when they developed AIDS, with profound immune deficiency and they were therefore investigated for immune deficiency with laboratory investigations.

....

Q. Yes, but I suppose the point they seemed to me to be making was that, firstly, this is plainly being written after the work by Gallo in the earlier part of 1984, which had linked AIDS and HTLV-III, and they seem to be saying, firstly, that, as far as they are concerned, the hunt is over, and the agent which is causing AIDS in people of homosexual orientation and also people with haemophilia, the hunt is over. Is that what they are saying?

A. I think by October 1984 there was little doubt that HTLV-III was the cause of AIDS ... I'm very happy to accept that. However, we don't know or we didn't know until the antibody test was produced, just how many people might have been infected. We don't know whether everyone was equally susceptible. It may be those who had abnormal immune tests were more susceptible to the virus when exposed to it. So I'm happy – very happy to agree.

....

Q. I can certainly understand, professor, the point you make, that there were many unanswered questions, and indeed even today there seem still to be unanswered questions, but your acceptance that you indicated a moment ago that by the autumn of 1984 that this virus, HTLV-III, was the cause of AIDS, including in people with haemophilia; does your acceptance extend to that?

A. Yes.

Q. Right. The point that Drs Tedder and Barbara make in this paragraph however, about it being unlikely that there should have been an illness like AIDS in people with haemophilia caused by some other phenomena, that was a valid point even in 1983, was it not?

A. Yes.<sup>184</sup>

### *Autumn 1984: a viral aetiology*

**11.149** Given Professor Ludlam's prominence in the development of alternative theories, the autumn of 1984 can be seen as the point at which a viral aetiology for AIDS was established, notwithstanding that there remained unanswered questions. It followed that some patients receiving factor concentrate therapy for haemophilia and other coagulation deficiencies were known at that stage to have been exposed to the risk of transmission of HTLV-III/HIV. Attention began to focus on the progression of disease from infection.

---

<sup>184</sup> Day 19, pages 4–7

**11.150** On 1 September 1984, *The Lancet* published the article by Dr Rachanee Cheingsong-Popov and others (including Professor Tedder). HTLV-III and LAV-1 were indistinguishable. The high incidence of HTLV-III antibodies in haemophilia patients found in this and other studies had to be set against the relatively low incidence of overt AIDS in this risk group so far – roughly one per thousand haemophilia patients in the UK.

**11.151** The article defined the hypothesis for the cause of AIDS in these terms:

Recent evidence has strongly implicated newly identified retroviruses as the cause of AIDS and PGL.<sup>185</sup> These viruses have been termed lymphadenopathy-associated or immunodeficiency-associated virus (LAV/IDAV) and human T-lymphotropic virus type III (HTLV-III), and they seem to have more similarities than differences. To date the evidence implicating them aetiologically comprises a high frequency of virus isolation from AIDS and PGL patients and high prevalence of specific antibody in these subjects. A notable feature of these retroviruses is their tropism for the T “helper” (T4<sup>+</sup>) lymphocytes, which typically are depleted in AIDS patients.<sup>186</sup>

**11.152** The detection of HTLV-III antibodies in all but one of the AIDS patients studied was said to strengthen the evidence for an aetiological relationship to AIDS. The prevalence of HTLV-III seropositivity in PGL patients was said to confirm the notion that HTLV-III was not the cause only of AIDS but was also the cause of PGL in epidemiologically related risk groups.

**11.153** The authors commented that even if the causal relationship with AIDS and PGL was established, as the evidence strongly suggested:

[W]e should not assume that these disorders will develop in all patients infected with this retrovirus .... Although it is too early to draw firm conclusions, it seems possible that overt disease will not develop in at least some, and perhaps the majority of seropositive subjects.<sup>187</sup>

**11.154** An apparent carrier state was also described.

**11.155** The article made reference to an accompanying paper by Professor Brian Gazzard and others. That paper referred to earlier US research relating to sexual contacts of AIDS patients, the recent discovery of LAV/HTLV-III and the accompanying paper supporting the aetiological association with AIDS/PGL. The main object of the study was explained as being:

[T]o observe the clinical spectrum of disease in men who had had sexual contact with AIDS or PGL patients, and to correlate development of symptoms with HTLV-III positivity.<sup>188</sup>

<sup>185</sup> Persistent generalised lymphadenopathy: enlarged lymph nodes, a condition that occurs frequently in the latent period of HIV infection.

<sup>186</sup> Cheingsong-Popov et al, 'Prevalence of antibody to human T-lymphotropic virus type III in AIDS and AIDS-risk patients in Britain', *The Lancet*, 1984; 477–480 [LIT.001.0417]; Preliminary Report, para 8.92

<sup>187</sup> Cheingsong-Popov et al, 'Prevalence of antibody to human T-lymphotropic virus type III in AIDS and AIDS-risk patients in Britain', *The Lancet*, 1984; 477–480 [LIT.001.0417] at 0419

<sup>188</sup> Gazzard et al, 'Clinical Findings and Serological Evidence of HTLV-III Infection in Homosexual Contacts of Patients with AIDS and Persistent Lymphadenopathy in London', *The Lancet*, 1984; 480–483 [DHF.002.5914]



**11.156** They reported that several of the group's findings were consistent with the hypothesis that HTLV-III was the sexually transmitted agent responsible for both AIDS and PGL and that it might be associated in certain cases without symptoms. It was a very early description of the natural history of the disease.

**11.157** On 11 September 1984, the SNBTS Directors met.<sup>189</sup> Dr McClelland reported that Professor Tedder had acquired a significant quantity of reagents from the USA and was establishing anti-HTLV-III assays.<sup>190</sup> The work of the English scientists was intimated to all of the Directors in Scotland at this stage.

**11.158** Within Scotland, there was active exchange of data and other information between the SNBTS in Edinburgh and scientists in Glasgow following a letter from Dr Perry to Dr Froebel at the GRI on 15 October 1984 in which Dr Perry asked for information about Glasgow data on HTLV-III and offered samples of Factor VIII for screening purposes.<sup>191</sup> Scottish scientists were also collaborating actively with colleagues abroad in developing knowledge of the disease and its prevalence.

### October to December 1984: growing awareness

**11.159** Knowledge of AIDS among haemophilia patients, of its prevalence and aetiology, continued to accumulate in this period, in the USA and in the UK. Evidence of transmission became more clearly focused in the UK on 23 October 1984. Dr Craske of the Public Health Laboratory Service (PHLS), Withington Hospital, Manchester, circulated a letter advising that a batch of Factor VIII concentrate produced by the Blood Products Laboratory (BPL, the English manufacturer of NHS blood products) had been found to be infected with HTLV-III. He warned of the possible risk of infection with HTLV-III and subsequent development of AIDS.<sup>192</sup> Professor Cash, Professor Ludlam and Dr Perry, amongst others, received copies of the letter.<sup>193</sup>

**11.160** Dr Craske's letter of 23 October 1984 provided a direct sequential link between infection in donated blood included in a plasma pool and transmission of AIDS to haemophilia patients and was, at least, highly persuasive evidence of a causal relationship. He stated:

You will have already heard that one of the donors who contributed to the plasma pool used in the manufacture of the batch of factor VIII ... was recently admitted to hospital with clinical features consistent with the diagnosis of AIDS. I am afraid that this has now been confirmed. The patient has developed Pneumocytosis carinii pneumonia and two specimens of serum collected in September and October 1984 have been found to be positive for antibody to HTLV-3 by competitive radioimmunoassay (RIA).

....

From studies already underway on recipients of batches of factor VIII transfused to the two haemophilia A patients who contracted AIDS in 1983, we have already provisionally identified one batch of factor VIII which was transfused to one of the AIDS patients and was associated with seroconversion to HTLV-3

<sup>189</sup> Minutes [SGH.001.0445]

<sup>190</sup> Ibid [SGH.001.0445] at 0446

<sup>191</sup> Letter [SNB.004.8715]

<sup>192</sup> Letter [SNF.001.4020] See also Chapter 10 *Knowledge of the Geographic Spread and Prevalence of HIV/AIDS 2*, paragraph 10.13 for discussion on Dr Craske's discovery of HTLV-III infected concentrate.

<sup>193</sup> Circulation stamp dated 13 November [SNF.001.4020]

antibody positive in seven out of thirteen recipients. One of the patients who acquired HTLV-3 infection subsequently developed AIDS, a second developed thrombocytopenia, and the other five have remained symptomless.<sup>194</sup>

**11.161** Dr Craske commented that further research was required to confirm the association of HTLV-III infection and transfusion. However, against the background of earlier published work, this letter was significant in giving wide publicity within the medical and scientific community in the UK to the risk of transfusion-transmitted HTLV-III in haemophilia patients. It helps to identify a time from which there was, or should have been, general acceptance of risk associated with factor concentrates. There were, in addition, other contemporaneous sources of information pointing in the same direction and medical practitioners began to consult scientists to investigate the incidence of infection in their own patients (see Chapter 10, *Knowledge of the Geographical Spread and Prevalence of HIV/AIDS 2*, paragraphs 10.3–10.5). The results of testing by Professor Tedder and his colleagues of samples submitted by clinicians demonstrated the association of HTLV-III infection with the transfusion of factor concentrates.

### Developments in 1985

**11.162** In January 1985, '[AIDS] – an overview' by James Gracie and others was published in the *Scottish Medical Journal*.<sup>195</sup> The authors, Dr Gracie, Dr Froebel, Dr Madhok, Professor Lowe and Professor Forbes, practised at the Regional Haemophilia Centre, GRI. The article presents a picture of the generally held views at that Centre at the time of its preparation (December 1984). Overall, the authors stated that it seemed certain that a specific transmissible agent was responsible for AIDS. Other theories were dismissed.

**11.163** Emerging data on AIDS in patients who did not belong to any at-risk group but who had received blood transfusions were commented on as having serious implications. It had become necessary to look at the safety procedures used in obtaining blood and blood products.<sup>196</sup> The article made no mention of the Edinburgh Cohort. It cannot be taken to reflect the opinion among experts throughout Scotland but it does show a level of understanding of the wider context. The exposure of haemophilia patients to risk was clearly documented.

**11.164** The *MMWR* dated 11 January 1985 published provisional public health recommendations on screening donated blood. By way of background, it stated:

Evidence has shown that a newly recognised retrovirus is the cause of AIDS. Although this virus has been given several names ... it is referred to as HTLV-III in this discussion.

....

Epidemiologic data suggest that the virus has been transmitted through intimate sexual contact; sharing contaminated needles; transfusion of whole blood, blood cellular components, plasma, or clotting factor concentrates that have not been heat treated; or from infected mother to child before, at, or shortly after the time of birth.<sup>197</sup>

<sup>194</sup> Letter [SNF.001.4020]

<sup>195</sup> Gracie et al, 'Acquired Immune Deficiency Syndrome – An Overview', *Scottish Medical Journal*, January 1985; 30/1 [LIT.001.0829]

<sup>196</sup> Ibid [LIT.001.0829] at 0833

<sup>197</sup> 'Provisional Public Health Service Inter-Agency Recommendations for Screening Donated Blood and Plasma for Antibody to the Virus Causing Acquired Immunodeficiency Syndrome', *MMWR*, 11 January 1985 [SNB.004.9195] at 9195–6

**11.165** In the public health context in the USA, AIDS was unequivocally held to be caused by HTLV-III.

**11.166** On 9 February 1985, a letter written by Professor Arthur Bloom was published in *The Lancet*.<sup>198</sup> It was concerned primarily with clinical practice and relative risks associated with the use of concentrates but it acknowledged finally and expressly the infection of British Factor VIII with HTLV-III and the risk of transmission.

**11.167** On 3 August 1985 *The Lancet* published the Royal Infirmary of Edinburgh (RIE) preliminary study of Edinburgh haemophilia patients ('the Edinburgh Cohort') referred to in Chapter 10 *Knowledge of the Geographical Spread and Prevalence of HIV/AIDS 2*, paragraphs 10.57–10.60. This was a milestone document. The authors of the report were Professor Ludlam, Dr Tucker, Dr Steel, Professor Tedder, Dr Cheingsong-Popov, Professor Weiss, Dr McClelland, Ms Philip and Dr Prescott. The article stated:

As part of the continuing assessment of our haemophiliacs, we have now observed that sixteen of our patients acquired anti-HTLVIII during 1984; all but one of these patients had received a common batch of SNBTS factor VIII concentrate.<sup>199</sup>

**11.168** The text acknowledged that substantial evidence had accumulated that the most likely cause of AIDS was HTLV-III/LAV infection. Re-testing stored samples had demonstrated that the patients' sub-set irregularities (identified in the spring of 1983) prior to transfusion of the infected batch were not associated with HTLV-III infection. This demonstrated that the abnormal T lymphocyte subsets reported in 1983 were a result of the intravenous infusion of Factor VIII and not HTLV-III infection but it also suggested a relationship between CD4/CD8 ratios and the exposure of patients to HTLV-III infection: the lower the ratio, the greater the incidence of HTLV-III antibodies.<sup>200</sup> The absence of apparent seroconversion in a substantial number of patients was thought to be due to a range of factors including the concentration of antibodies; the immunological status of the individuals; the absence of viral infection; or replication of the lymphocyte cells.<sup>201</sup>

**11.169** The paper acknowledged the reality for Scottish clinicians and patients: HTLV-III was the most likely cause of AIDS and was transmitted by blood products. Information about these cases and contemporaneous English experience put the issue of risk to patients beyond question, as Professor Bloom's letter in *The Lancet* of February 1985 shows.

**11.170** More widely, there was further evidence. The *NEJM* of 21 February 1985 published an article by Dr Evatt and others describing research into the incidence of antibodies to HTLV-III/LAV in haemophilia patients in California, Georgia, New York and Texas by testing stored serum samples from several centres. There were no seropositive patients in the 1968 and 1969 samples and there was only one seropositive patient in 1978 in California. They also found that a seropositive response was related to the amount of Factor VIII used.<sup>202</sup>

<sup>198</sup> Bloom, 'Haemophilia and AIDS', *The Lancet*, 9 February 1985 [LIT.001.1029]

<sup>199</sup> Ludlam et al, 'Human T-Lymphotropic Virus Type III (HTLV-III) infection in seronegative haemophiliacs after transfusion of Factor VIII', *The Lancet*, 3 August 1985 [LIT.001.1669]

<sup>200</sup> Ibid, [LIT.001.1669]

<sup>201</sup> Ibid, [LIT.001.1669] at 1671

<sup>202</sup> Evatt et al, 'Coincidental appearance of LAV/HTLV-III antibodies in hemophiliacs and the onset of the AIDS epidemic' *New England Journal of Medicine*, 1985; 312:483-486, February 21, 1985

## 1986 and beyond

**11.171** Between 11 and 13 February 1986 there was a conference in Newcastle on AIDS sponsored by the Haemophilia Society. The introduction to a paper presented (by Dr Philip Mortimer, PHLS)<sup>203</sup> at the conference stated that:

There is convincing evidence available from studies involving donor-recipient pairs that the HTLV-III/LAV virus can be transmitted by the transfusion of infected blood and blood products.<sup>204</sup>

**11.172** It was also narrated that during 1984 the causative virus for AIDS was recognised as HTLV-III/LAV and that there was a significant correlation between the antibody to HTLV-III/LAV and patients with AIDS.<sup>205</sup> In his paper, Dr Mortimer said that of 4000 haemophilia patients in the UK, 25% were positive for antibodies to HTLV-III.<sup>206</sup> Only 0.006% of transfusion recipients were positive for antibodies to HTLV-III.<sup>207</sup> Blood donor screening had shown that one in 45,000 donors was positive.<sup>208</sup>

**11.173** It is clear that by this date there was general acceptance of a causal association between some infected blood products and the development of HTLV-III/LAV and AIDS in haemophilia patients.

**11.174** Between 14 and 16 April 1986, the WHO held a meeting in Geneva, on the safety of blood and blood products in relation to AIDS. A report on the meeting was prepared by the World Hemophilia AIDS Center.<sup>209</sup> Prior to the meeting, WHO officials and plasma fractionators met to discuss current LAV/HTLV-III inactivation methods. Thirty-three countries were represented at this meeting, principally by staff from blood banking or blood transfusion facilities and a large staff of participants from the secretariat of the WHO under the direction of John Petricciani, Chief of Biologicals.

**11.175** The meeting began with an overview of infection with LAV/HTLV-III virus, in which information was presented regarding the recognition and identification of two new retroviruses termed LAV-2 and HTLV-IV. The speaker representing Professor Montagnier stated that the AIDS virus was the first human lente virus (otherwise 'lentivirus') and was comparable to the visna virus in sheep.<sup>210</sup> The envelope gene in the visna virus is highly variable. The two new viruses had been termed LAV-II (isolated from two patients in West Africa) and HTLV-IV (isolated in Kakar, also in West Africa). These two viruses were not identical, although they had some cross-reactivity with LAV-1 and HTLV-III respectively. The new terminology apparently would be HIV-1 (human immunodeficiency virus 1), which was equivalent to LAV-1, to HTLV-III, and to ARV (AIDS retrovirus). HIV-2 was equivalent to LAV-2 (from West Africa). HTLV-IV remained to be classified. The phylogenetic tree (see Chapter 10, *Knowledge of the Geographical Spread and Prevalence of HIV/AIDS 2*) of the human immunodeficiency viruses was being described by amino acid homologies. There

<sup>203</sup> See Dr Foster's report of the meeting [SNF.001.4215] at 4217–9

<sup>204</sup> AIDS Conference Newcastle – 11–13 February 1986 [DHF.002.0816] at 0817

<sup>205</sup> Ibid, [DHF.002.0816] at 0818

<sup>206</sup> Report of AIDS conference [SNF.001.4215] at 4218

<sup>207</sup> Ibid, [SNF.001.4215] at 4218

<sup>208</sup> 'Outline Protocol of an Epidemiological Study of the HTLV III – LAV Virus by the Blood Transfusion Service' [SNB.012.9478] at 9479.

<sup>209</sup> Report on the World Health Organization Meeting – Safety of Blood and Blood Products in Relation to AIDS, April 14–16 1986 [DHF.002.1524]. Unredacted version of first two pages is [SNB.004.7796]. The World Hemophilia AIDS Center (WHAC), Pasadena, California, was established by the World Federation of Haemophilia during its annual congress in Stockholm in July 1983 to facilitate the collection and dissemination of data on HIV/AIDS.

<sup>210</sup> See Chapter 29 *Discovery of HIV and Development of Screening Tests* at paragraph 29.4, footnote 6 for Professor Lever's view, based on further study, that HIV does not properly belong to the lentivirus genus.

was a long discussion on the clinical safety of immune globulins. Genetic analysis had now begun to dominate scientific thought: there was little or no scope for doubt about the cause of AIDS transmission more generally.<sup>211</sup>

### *The modern view*

**11.176** As discussed in Chapter 8, *Knowledge of HIV/AIDS Now*, the modern view of the aetiology of AIDS is heavily influenced by the findings of geneticists of some fundamental characteristics of the virus. Before the identification of the first retroviruses, first in other animals and then in humans (in the form of HTLV-I), it was believed that there was a single direction of flow of information in the replication of pathogens, from DNA to RNA to protein. Then retroviruses were identified. When viruses in this group were first identified, it appeared that the genetic material within the virus particle was made of RNA but it was eventually established that when the virus entered a cell the RNA was converted backwards into DNA material. That DNA material was then inserted into the DNA of the cell so that it looked like part of the cell's own DNA. Because of that apparent reversal of the flow of genetic information from RNA back to DNA, this family of viruses came to be called retroviruses. This family includes Hepatitis B, which also goes through a DNA intermediate. The term 'retro' comes from that original observation that the flow of genetic information went backwards. When cell replication begins, the flow of genetic information goes in the normal direction again because that DNA is made into an RNA copy and into protein which, in addition to normal cell products, also produces the virus, since the instructions are now encoded into the cellular DNA.<sup>212</sup>

**11.177** Professor Lever emphasised some of the common characteristics of the natural history of virus infection generally.<sup>213</sup> On general principle, the more often a person is exposed to virus infection or the bigger the 'dose' of viral particles, the more likely is the chance of infection.<sup>214</sup> More often than not, the patient mounts an appropriate immune response, clears the infection and is then immune from further infection by the same agent: the immune system remembers the infection and prevents recurrence. Mumps and rubella were taken as typical examples. At the start of the AIDS epidemic, it was known that in the case of some chronic infections, such as Hepatitis B, while some people were relatively poor at clearing the virus and a proportion of these became chronic carriers, the majority of healthy individuals did appear to be able to clear it and develop immunity from re-infection. This experience informed the common notion at the time that exposure to infectious agents gave a level of protection against further infection by the same virus. A perception had arisen that, having been exposed to a virus, the individual would not be harmed by being exposed to the same virus again because either the immune system would have developed sufficient immunity to protect the individual completely or it would somehow help to suppress the second exposure. However, almost without precedent at the time, it was to emerge that, in the case of HIV, prior exposure to the virus gave no protection against infection on further exposure.<sup>215</sup>

**11.178** As already noted, a similar discovery was later to emerge in the case of Hepatitis C. Immunity from further infection does not follow from clearance of infection with the virus.

<sup>211</sup> See Chapter 10 *Knowledge of the Geographic Spread and Prevalence of HIV/AIDS 2* at paragraphs 10.118–10.120 for an illustration of the application of genetic analysis in tracing the source(s) of infection of batch 023110090, for example.

<sup>212</sup> Professor Lever – Day 26, pages 10–12

<sup>213</sup> Day 26, page 60

<sup>214</sup> Day 26, page 62

<sup>215</sup> Day 26, pages 60–61

## Discussion

**11.179** With the identification of AIDS in 1981, scientists and clinicians were confronted by a phenomenon, unique at that time in modern medicine: a disease of no known aetiology that was rapidly progressive and fatal. Initially it appeared to affect a small set of vulnerable individuals whose known behavioural characteristics suggested that the scope of the disease was limited to promiscuous male homosexuals. Evidence undermining that hypothesis was soon to emerge in 1982 but alternative hypotheses as to the cause of AIDS, especially alternatives that depended on an agent of transmission, could not be proved in the absence of evidence that such an agent existed. There was a period of intense research and a virus was found that provided the answer to general, though not universal, satisfaction. It is important to stress that proof of a viral aetiology was provided, in France and the USA, within about three years of the first reported cases, and within two years of the initial evidence supporting the transmissible agent hypothesis. This was a remarkably short period.

**11.180** Success was achieved against the background of controversy. The CDC, and Dr Evatt in particular, became convinced by about July 1982, by evidence of infection in haemophilia patients, that AIDS was a blood-borne disease, though there was no direct proof. As late as 4 January 1983, at the advisory committee meeting convened in Atlanta, there was a hostile reaction to Dr Evatt's arguments.<sup>216</sup> By the summer of 1983 there was continuing doubt in some segments of the haemophilia community, the blood banking industry, physicians and the FDA in the USA that AIDS was a blood-borne infection.<sup>217</sup>

**11.181** The publication in *Science* by the Institut Pasteur of the isolation of LAV did not resolve the controversy. It would be February 1984 before those results were presented to the CDC. The position changed with the publication of Dr Gallo's findings in April. However, that was dramatic progress from a state of total ignorance of the disease and its viral aetiology to convincing proof.

**11.182** This chapter has set out, at some length, the evolving discussion of the alternatives, especially in the case of haemophilia patients, as the position would have been understood to clinicians and as discussed in professional literature as well as in evidence to the Inquiry.

**11.183** The pace of development of knowledge of the disease, and the concentrated effort made within a very short time to deal with the problem presented by its sudden and unanticipated appearance are particularly remarkable. As will appear from Chapter 29 *The Discovery of HIV and the Development of Screening Tests*, the public debate among haemophilia clinicians and others referred to in this chapter was for the most part irrelevant to that progress. The scientists responsible for cutting edge research and technological progress were convinced at an early stage of the viral aetiology of AIDS and were largely untouched by the debate. In contrast, doubt concerning a viral or otherwise infectious aetiology was strongest amongst haemophilia clinicians, some of whom sought other explanations (notably 'immune overload') for as long as such explanations remained tenable. This debate was fundamental to clinical practice in the treatment of haemophilia and other coagulation defect patients.

<sup>216</sup> 'Health Officials Seek Ways to Halt AIDS', *Research News*, 21 January 1983 [LIT.001.1589]

<sup>217</sup> Evatt, 'The tragic history of AIDS in the hemophilia population 1982–1984', *Journal of Thrombosis and Haemostasis*, 2006, 4/11: 2295 – 2301, (reprint) [PEN.016.1183] at 1188

## CHAPTER 12

### HIV/AIDS: RESPONSE AND CLINICAL PRACTICE

#### Introduction

**12.1** As knowledge developed in the USA, in the UK generally, and in Scotland in particular, first of AIDS and then of HIV, it inevitably had an impact on clinical practice. Chapters 9–11 set out those developments at length and are not repeated in detail in this chapter, except where necessary to provide context. Rather, this chapter of the Report discusses aspects of the response to HIV/AIDS by haemophilia clinicians over the early and middle years of the 1980s. In particular, the question to be addressed is whether clinicians in Scotland should have adapted their treatment regimes sooner than they did, in response to the threat of AIDS.

**12.2** That is a difficult issue and the context in which it has to be addressed must take account of what was happening in the rest of the UK. Scottish haemophilia clinicians did not function in isolation from their counterparts in England and Wales. The constituencies represented by the United Kingdom Haemophilia Centre Directors' Organisation (UKHCDO) and, at that time, the Haemophilia Society, were UK-wide. It is likely that views expressed and attitudes communicated in their publications would have had an impact in Scotland, as information about AIDS was nationally disseminated. In discussing when Scottish practitioners should have reconsidered haemophilia therapy generally and whether such changes in clinical practice as did occur should have been made earlier, it is therefore appropriate to have regard to what was happening in the rest of the UK.

**12.3** Although it is necessary to take into account developing views throughout the UK, as these formed an important part of the background for clinicians as they responded to the emerging threat of AIDS, it is also important to bear in mind the degree of independence in clinical matters afforded to individual Regional Transfusion Directors (RTDs) and Haemophilia Directors at the time. As noted in Chapter 21, *Haemophilia Therapy – Use of Blood Products 1985–1987*, individual RTDs of the SNBTS and Haemophilia Directors in the UK, asserted and were accorded a high degree of autonomy in their practices.<sup>1</sup> This was not limited to clinical independence at the point of delivery of care to the patient; so far as is relevant to this chapter, it also included the selection and use of therapeutic products generally. There were significant regional differences in practice throughout the UK. In Scotland, the variations in clinical practice are illustrated by the analytical tables and figures in Chapter 21, *Haemophilia Therapy – Use of Blood Products*. These are discussed in more detail below.

**12.4** The question that naturally and understandably arises from haemophilia patients who acquired HIV infection, is why they were prescribed large-pool factor concentrates when there was, as is now known, a disproportionate risk of transmission of HIV by those products as compared to treatments such as cryoprecipitate and fresh frozen plasma which might, for some patients, have represented appropriate alternative therapies.<sup>2</sup> The question cannot be

<sup>1</sup> See also Professor Ludlam – Day 18, page 102. Closer co-operation developed from the mid-1980s.

<sup>2</sup> Cryoprecipitate was responsible for the transmission of HIV in some countries although, so far as is known to the Inquiry, not in the UK. Belgium, which used mainly cryoprecipitate from local donations for the treatment of haemophilia, had a 7% rate of HIV infection in haemophilia patients. See: Hagen, PJ *Blood Transfusion in Europe: a 'white paper'*, Council of Europe: 1994, and Dr Winter – Day 16, page 127. Professor Leikola noted that Finland used 'small-pool' cryoprecipitate during the relevant period due to a lack of locally produced concentrates and that only 2 patients were infected with HIV by that means. [PEN.013.1395] at 1397–8.

answered in a simple and straightforward way for all of Scotland, much less for the UK as a whole. Implicit in the question is an assumption that clinicians were, at the material time, in possession of sufficient evidence of disproportionate risk in large-pool concentrates such that they should have adapted treatment regimes sooner than they did. That assumption may not be valid, however, and it is necessary to distinguish the existence of risk in an absolute sense from knowledge of risk sufficient to instruct a reasoned decision on therapy. In addition, the therapeutic options available to clinicians differed across the country; even within a given region, different options were available to individual patients.

**Key issues: the debate on the aetiology of AIDS; advances in haemophilia care; and faith in the safety of the UK blood supply**

**12.5** The question is complicated by a number of fundamental issues addressed in this chapter. In the first place, for much of the period before HTLV-III/HIV was identified as the infective agent causing the immune deficiencies in patients who progressed to AIDS, there were competing theories supported by bodies of influential experts on both sides of the Atlantic. The full significance of the discovery in France of LAV<sup>3</sup> in May 1983 was not widely understood and those findings were resisted by many, particularly in the USA. Medical science did not resolve the fundamental question of the cause of AIDS, to the satisfaction of the majority of experts, until the spring of 1984. Even after the seminal publication in *Science* announcing the discovery of HTLV-III, some comments continued to be published challenging the findings that AIDS was spread by means of a virus present in blood. The history is set out in detail in Chapter 11, *HIV/AIDS Aetiology*, although, for the purposes of this chapter, a few key dates are important in discussing the timing of developments in clinical practice. Secondly, there was an acknowledgement that the development of large-pool concentrates had transformed the lives of haemophilia patients. Under such circumstances, many haemophilia clinicians, and others, appear to have been reluctant to accept evidence that those therapeutic materials might have transmitted infection to their patients. Thirdly, and perhaps linked to the last point, there was a long-held and strongly felt confidence in the safety of the UK blood supply. Early reports of AIDS infection were limited to the USA and, for those who might have been prepared to entertain the idea that AIDS was caused by a blood-borne infective agent, this confidence in the relative safety of NHS blood products may also have influenced thinking on the appropriate response to AIDS.

***Irreconcilable views on the aetiology of AIDS***

**12.6** Early reports of what came to be known as HIV/AIDS infection first emerged in the USA in 1981 and the initial debate on the disease was heavily influenced by the fact that most of the earliest reports dealt exclusively with homosexual men. The major pathological features of AIDS were very profound immunosuppression (with characteristic suppression of the ratio of helper to suppressor cells) and the development of certain otherwise rare diseases such as *Pneumocystis carinii* pneumonia (PCP) and the vascular cancer, Kaposi's sarcoma (KS). Starting in 1982 similar, if less marked, immune phenomena were identified in homosexual men who appeared healthy and, in particular, did not have overt disease characteristics of AIDS.<sup>4</sup> Also in 1982, immigrants to the USA from Haiti and intravenous

<sup>3</sup> Lymphadenopathy-Associated Virus, the name given by French researchers to the AIDS-causing virus, subsequently found to be identical to HTLV-III, the discovery of which was announced by Robert Gallo in April 1984. The virus was ultimately renamed HIV. See Chapter 11, *HIV/AIDS Aetiology*.

<sup>4</sup> Gold et al, 'Acquired Immunodeficiency Syndrome: Infection and Neoplasia in Homosexual Men and Intravenous Drug Addicts', *Proceedings of the Second International Symposium on Infections in the Immunocompromised Host*, 1983, Academic Press, London [LIT.001.3668]



drug users (IVDUs) began to present with similar immune dysfunction and, occasionally, overt disease.<sup>5</sup> In July 1982, 'opportunistic infections' characteristic of AIDS were found in three US haemophilia patients who had received frequent administration of Factor VIII,<sup>6</sup> and further reports followed.

**12.7** Irreconcilable views on the aetiology of AIDS emerged in 1982 and were expressed clearly at a workshop in Atlanta on 4 January 1983.<sup>7</sup> The 'transmissible agent' theory was supported by the American Centers for Disease Control (CDC), whose spokesman was Dr Bruce Evatt. That theory of AIDS transmission postulated that a blood-borne virus was responsible for the observed cases (including those in haemophilia patients). By contrast, the 'antigen overload' theory was supported by a body of haemophilia clinicians, whose most prominent spokesman was Dr Louis Aledort, a respected haematologist and Director of the Haemophilia Center in New York. That theory considered exposure to foreign antigens in concentrates to have caused a high degree of antigenic stimulation that wore out haemophilia patients' immune systems. Both views were strongly held and forcefully argued.

**12.8** At various points in 1983 the competing theories were supported or criticised in published papers and at conferences. At this time in Scotland, Professor Christopher Ludlam (Edinburgh Haemophilia Centre) and Professor Charles Forbes (Glasgow Haemophilia Centre) conducted studies into the phenomena of immune irregularities in haemophilia patients. Of these, Professor Ludlam's studies led more positively to the view, published in *The Lancet* on 28 May 1983, that the immune changes identified in his patients resulted from infusion of 'foreign' proteins in the therapeutic products administered to them, or a ubiquitous virus, rather than a specific AIDS virus in Factor VIII concentrates: the antigen overload theory.<sup>8</sup> These studies are referred to in more detail, in a specifically Scottish context, below at paragraphs 12.111–12.119.

**12.9** By the time of the meeting of the World Federation of Hemophilia in June 1983, Françoise Barré-Sinoussi and Luc Montagnier of the Institut Pasteur, Paris, had published the results of research suggesting that they had identified an infectious agent, which they termed LAV.<sup>9</sup> That was, however, not generally accepted as persuasive (especially in the USA) until 23 April 1984, when Dr Robert Gallo and his team announced the discovery of HTLV-III.<sup>10</sup> Later research was to demonstrate that LAV and HTLV-III were, in fact, the same

<sup>5</sup> Masur et al, 'An Outbreak of Community-Acquired Pneumocystis Carinii Pneumonia', *New England Journal of Medicine*, 305(14): 1431–1438 [LIT.001.0771]; 'Opportunistic Infections and Kaposi's Sarcoma among Haitians in the United States' *MMWR*, July 09, 1982;31:353-4, 360-1 [LIT.001.0562]

<sup>6</sup> 'Pneumocystis carinii Pneumonia among Persons with Hemophilia A', *MMWR*, July 16, 1982; 31 [SGH.008.5097]. It appears that the earliest case of AIDS in a haemophilia patient may have been identified in October 1981, although it was not reported until February 1983. Discussions between Dr Oscar Ratnoff, Cleveland, Ohio, and Professor Charles Forbes, Glasgow, at the end of 1981 were probably related to this case, undoubtedly extremely unusual and puzzling at the time. See Chapter 9, *Knowledge of the Geographical Spread and Prevalence of HIV/AIDS 1*, paragraph 9.22.

<sup>7</sup> See Chapter 11, *AIDS Aetiology*, paragraphs 11.28 et seq

<sup>8</sup> Ludlam et al, 'Disordered Immune Regulation in Haemophiliacs Not Exposed to Commercial factor VIII', *The Lancet*, 28 May 1983. A fuller report was published in 1984: Carr et al, 'Abnormalities of Circulating Lymphocyte Subsets in Haemophiliacs in an AIDS-Free Population', *The Lancet*, 30 June 1984 [LIT.001.0425]. See also: Professor Ludlam – Day 35, page 21; Professor Ludlam's Statement [PEN.015.0445] at 0448.

<sup>9</sup> Barré-Sinoussi et al, 'Isolation of a T-lymphotropic retrovirus from a patient at risk for acquired immune deficiency syndrome (AIDS)', *Science*, 1983;220:868–871 [LIT.001.0058]. See also Chapter 29, *The Discovery of HIV and the Development of Screening Tests*, paragraphs 29.5–29.10.

<sup>10</sup> Gallo et al, 'Frequent detection and isolation of cytopathic retroviruses (HTLV III) from patients with AIDS and at risk for AIDS', *Science* 1984; 224:500–503 [LIT.001.3769]; Popovic et al, 'Detection, Isolation, and Continuous Production of Cytopathic Retroviruses (HTLV-III) from Patients with AIDS and Pre-AIDS', *Science* 1984, 224. (reprint) [SNB0049457] See also Chapter 29, *Discovery*, paragraphs 29.5–29.10.

virus, later named HIV.<sup>11</sup> The position until April 1984 was summed up by Professor Lever, Professor of Infectious Diseases at Addenbrooke's Hospital, Cambridge:

Up until that time I think it's a gradation. There was gradual acceptance that it couldn't just be put down to immunological-based theories and that the epidemiology looked more and more like an infectious agent.<sup>12</sup>

**12.10** It appears that Dr Mark Winter, Consultant Haematologist at Kent and Canterbury Hospital from 1983, accepted the infective agent theory at a relatively early date<sup>13</sup> but it is not clear that, by April 1984, the 'gradation' Professor Lever described encompassed all interested parties. In this context, it is of interest to note that, in a paper detailing testing for HTLV-III that was underway in the second half of 1984, the linking of antibody-positivity to AIDS was still presented as a hypothesis, albeit one which 'strongly implicated' a transmissible agent.<sup>14</sup> Even after that point, some commentators continued to publish articles sceptical of the claim that AIDS was caused by a transmissible virus<sup>15</sup> although, increasingly throughout the period and certainly after April 1984, that scepticism appears to have involved finding alternative explanations for the considerable accumulating evidence supporting the transmissible agent theory. Given the gradual progress of developing knowledge, however, and the fundamental differences of opinion that prevailed throughout 1983 and into 1984, it was highly unlikely that a view common to all or most haemophilia clinicians would have emerged before April 1984 that accepted the infectious agent theory. It is clear from the evidence available to the Inquiry that the infectious agent theory did not prevail until at least then, with some continuing to defend alternative hypotheses for some months after that date. It also appears clear from the evidence that, throughout the period of uncertainty, some haemophilia clinicians at least found their assessment of the risk associated with blood products to some extent confounded by an appreciation of the significant benefits large-pool concentrates used in coagulation disorder therapy had brought to their patients.

### *The significance of advances in haemophilia care*

**12.11** Before it was recognised that the use of factor concentrates might present a risk of immune deficiencies in coagulation disorder patients, whether caused by an infective agent or by antigen overload, the development of factor products (including cryoprecipitate but particularly large-pool concentrates) had brought about a major advance in healthcare. The improvement in life expectancy, the reduction in morbidity and improvements in the quality of life of haemophilia patients achieved were little short of spectacular.<sup>16</sup>

**12.12** Therapy for Haemophilia A and Haemophilia B in particular had revolutionised the lives of patients. At a meeting on the Infectious Hazards of Blood Products arranged by the National Institute for Biological Standards and Control (NIBSC) on 9 February 1984, Dr Duncan Thomas<sup>17</sup> noted the improvement in life expectancy which had resulted from the use of concentrates, from 37 years in 1962 to almost normal in 1984.<sup>18</sup>

<sup>11</sup> Cheingsong-Popov et al, 'Prevalence of antibody to human T-lymphotropic virus type III in AIDS and AIDS-risk patients in Britain', *The Lancet*, 1 September 1984; 477-480

<sup>12</sup> Day 26, page 41

<sup>13</sup> See paragraph 12.51 below

<sup>14</sup> Cheingsong-Popov et al, 'Prevalence of antibody to human T-lymphotropic virus type III in AIDS and AIDS-risk patients in Britain', *The Lancet*, 1984; 477-480 [LIT.001.0417] The paper noted that '[t]he likelihood of ... AIDS being caused by an infectious agent has been apparent for some years.' It noted new evidence implicating LAV/HTLV-III but still, at that point, was not definitive in its statements: 'Even if HTLV-III is causally related to AIDS ... as is strongly suggested by the evidence.'

<sup>15</sup> See Chapter 11, *HIV/AIDS Aetiology*

<sup>16</sup> See Chapter 21, *Haemophilia Therapy – Use of Blood Products*

<sup>17</sup> Head of Haematology at the NIBSC

<sup>18</sup> Minutes of the NIBSC meeting on the infectious hazards of blood products, 9 February 1984 [SNB.004.8628]

**12.13** A significant factor in these improvements was the development of ‘home therapy’ treatment programmes. Prior to the introduction of factor concentrates, haemophilia patients who experienced bleeds would attend hospital for treatment, typically with cryoprecipitate. It was impractical for most patients to keep stocks of cryoprecipitate at home for self-administration as the packs required to be stored in large quantities in deep freezers<sup>19</sup> and, compared with factor concentrates, were difficult to prepare, requiring to be reconstituted from the frozen state in a water bath at 37°C in a clean, or ideally sterile, environment.<sup>20</sup> In addition, the potency of cryoprecipitate could not be known until the point of administration and the product was frequently associated with significant side-effects, some of which could require hospital care.<sup>21</sup> By contrast, factor concentrates could be stored in a refrigerator (requiring only to be stored at 4°C), potency was more uniform and, after training, could be more easily prepared and administered by patients (or, in the case of younger children, their parents). Side-effects, at the point of administration, were less common. Patients no longer needed to attend hospital following a bleed, an experience Dr Winter described as ‘harrowing’ and ‘a pretty dreadful experience’.<sup>22</sup> A textbook on paediatric haematology written by Dr Michael Willoughby, at the time Director of the Haemophilia Centre at The Royal Hospital for Sick Children, Yorkhill, Glasgow (Yorkhill), and published in 1977 set out the advantages of factor concentrates as compared to cryoprecipitate and noted that ‘home treatment is highly efficacious in reducing the morbidity of haemophilia and improving the quality of life’.<sup>23</sup>

**12.14** Upon taking up the post of Director of the Edinburgh Haemophilia Centre in 1980, Professor Ludlam began almost immediately to radically expand the home therapy programme, using concentrates, in that area. As discussed below, his predecessor, Dr Howard Davies, had been somewhat circumspect in relation to the use of concentrates. Although they were not infrequently used while he was Director, Dr Davies was concerned about the risks associated with large-pool products. As a result, at the beginning of 1980 only six of a total of 187 haemophilia patients registered at the Centre were established on home therapy. Professor Ludlam said he was ‘continuingly being asked’ to expand the programme for which there was ‘a lot of enthusiasm’.<sup>24</sup> By 1989, this number had grown to 47. He considered cryoprecipitate inappropriate for home therapy and was ‘not prepared to take the risk’ he saw in placing patients on home therapy with cryoprecipitate.<sup>25</sup> Dr Boulton, who began working in Edinburgh around the same time, agreed.<sup>26</sup> Professor Ludlam may have been constrained in his efforts to expand the home treatment programme due to his stated preference for locally-sourced factor concentrates.<sup>27</sup> The drive towards increasing the number of patients on home therapy led him to impress upon the SNBTS his desire to have more NHS Factor VIII concentrate.<sup>28</sup>

<sup>19</sup> As noted in Chapter 21, *Haemophilia Therapy – Use of Blood Products*, paragraph 21.73, footnote 51, various sources provide different temperatures at which cryoprecipitate required to be frozen, ranging from -70°C to -18°C and it has not been possible to specify with accuracy the storage requirements at the material time. As noted in Chapter 21, *Haemophilia Therapy – Use of Blood Products*, compared to concentrates, cryoprecipitate had to be administered in very large quantities. Professor Ludlam agreed that there was ‘quite a large storage problem’. Day 18, page 37

<sup>20</sup> Dr Winter – Day 15, page 79; Professor Ludlam – Day 18, pages 34–35

<sup>21</sup> Dr Winter – Day 15, page 79; Professor Ludlam – Day 18, pages 37–38

<sup>22</sup> Day 15, page 80

<sup>23</sup> Willoughby, MLN. *Paediatric Haematology*, 1977: Churchill Livingstone, Edinburgh, London, New York p321 [PEN.016.1062] at 1068

<sup>24</sup> Day 18, page 89

<sup>25</sup> *Ibid* page 72. Professor Ludlam also noted that, almost certainly due to the volume of cryoprecipitate required to encourage normal clotting, over a course of treatment with cryoprecipitate patients ‘not infrequently ... became jaundiced’ indicating hepatitis infection. Day 18, page 39

<sup>26</sup> Day 24, pages 13–16

<sup>27</sup> ‘My clinical decision was to delay home treatment, rather than use commercial concentrates because of the different virological spectrum of the donors.’ Day 19, page 39

<sup>28</sup> See Chapter 21, *Haemophilia – Use of Blood Products*, paragraph 21.109

**12.15** There was an obvious major benefit derived from treatment, especially with large-pool concentrates as they were developed from the early 1970s.<sup>29</sup> There was a reduction in the number of school or work days lost; patients could travel more easily, whether on holiday or for business; and patients were spared frequent ‘time-consuming and psychologically undesirable’ visits to hospital.<sup>30</sup> Professor Forbes agreed that home therapy was ‘a very popular move’, describing the relatively short period between the development of home therapy programmes and the emergence of non-A, non-B Hepatitis and AIDS as ‘the golden age’ in haemophilia care.<sup>31</sup> As discussed in Chapter 21, *Haemophilia Therapy – Use of Blood Products*, paragraphs 21.95–21.100, the development of home treatment programmes had a significant effect on the demand for factor concentrates and production of concentrates increased accordingly to meet demand. In the absence of an alternative of proven efficacy, for many clinicians ceasing to use concentrates threatened patients’ quality of life, health and even their lives.

**12.16** Professor Forbes said:

For a long time after the initial cases of AIDS was [sic] reported there was great debate about the best way of treating bleeding. It was certainly not possible to stop the use of concentrate as bleeding would have resulted in death and the general reaction of most Haemophilia Directors at that time was to continuing [sic] to treat the bleeding with concentrate.<sup>32</sup>

**12.17** In oral evidence to the Inquiry, Professor Forbes said that he thought that the 1983 decision to continue treatment with concentrates was correct.<sup>33</sup> Similar views persisted into 1984. Professor Arthur Bloom, Cardiff Haemophilia Centre, took up the theme in an article in *The Lancet* dated 30 June 1984. He commented:

In view of the immense benefits that haemophiliacs have derived from treatment physicians are naturally reluctant to abandon these agents, with their hypothetical dangers, in the absence of alternative concentrates which have been proven safer. This attitude may change as information accrues, and haemophilia treatment needs to be monitored world-wide.<sup>34</sup>

**12.18** Against this background, it is not surprising that there was a range of strongly held views. The approach of Dr Aledort at the workshop in Atlanta on 4 January 1983 reflected the position held at one extreme of that range. There were clinicians who demanded full scientific proof of an infective agent as a condition of changing from established factor concentrate therapy.<sup>35</sup>

<sup>29</sup> Dr Winter – Day 16, pages 13–14

<sup>30</sup> Willoughby, MLN. *Paediatric Haematology*, 1977: Churchill Livingstone, Edinburgh, London, New York p321 [PEN.016.1062] at 1068

<sup>31</sup> Professor Forbes – Day 17, page 58. See also Dr Winter – Day 15, page 73 – who referred to this period as the ‘golden interval’ in haemophilia care.

<sup>32</sup> Statement of Professor Forbes [PEN.015.0254] at 0257

<sup>33</sup> Professor Forbes – Day 17, pages 97–98

<sup>34</sup> Bloom, ‘Acquired Immunodeficiency Syndrome and other Possible Immunological Disorders in European Haemophiliacs’, *The Lancet*, 30 June 1984; 1452–1455 [LIT.001.0409] at 0412

<sup>35</sup> See Chapter 11, *HIV/AIDS Aetiology*, paragraphs 11.28–11.35. The demand was that the proponents of the transmissible agent theory should ‘[s]ubject [the theory] to Koch’s postulates’, a well-established protocol for demonstrating the transmission of bacterial infection.

### *Faith in the safety of the UK blood supply*

**12.19** Further to the significance of advances in haemophilia care, there was faith in blood factor products, both cryoprecipitate and concentrates, produced by UK public sector facilities that strongly influenced many (but not all) practitioners throughout the UK. From the beginning of the AIDS era until 1984, this faith had at its roots a belief that, if AIDS was indeed caused by an infective agent, it had not entered the blood donor population in the UK generally and in Scotland in particular. Accordingly, for those who subscribed to the infective agent hypothesis, it was thought that Factor VIII produced in the UK was unlikely to transmit the postulated AIDS virus. Those who acknowledged that there was a risk thought it was minor. It was deeply ingrained in the psyche of haemophilia clinicians and patients, that donated blood of UK origin was much more likely to be free of viruses than blood from the USA.

**12.20** The situation in Edinburgh illustrates this point particularly well. Professor Ludlam's predecessor as Director of the Edinburgh Haemophilia Centre, Dr Howard Davies, made almost exclusive use of locally-produced therapeutic materials. Professor Ludlam stated that Dr Davies avoided the use of imported materials as a matter of policy, believing those derived from Scottish donors would be safer. Dr Davies' argument in preference of locally sourced materials centred on the risks associated with hepatitis viruses, but appears to have had a more general basis: both Professor Ludlam and Dr McClelland stated that Dr Davies was reluctant to potentially introduce 'novel' viruses to the local population. Dr Brian McClelland,<sup>36</sup> who worked with Dr Davies early in his (Dr McClelland's) career, said that Dr Davies' policy struck him as 'eminently sensible'. In relation to imported products, he thought the policy was grounded in 'elementary biology' and that 'the further afield the blood came from, there was a certainly incalculable but reasonable grounds to expect that something new and different and unfamiliar to the indigenous population might be in that blood'.<sup>37</sup> Dr Davies also tended to avoid large-pool concentrates, preferring, where possible, to use cryoprecipitate in the belief that large pools of donations were more likely to contain transmissible viruses, whatever their source. As noted above, when Professor Ludlam succeeded Dr Davies, he quickly reversed this part of Dr Davies' policy and moved as many patients as he could to home therapy with concentrates. He continued, however, to prefer locally produced products, believing that the general population of Scotland was at the time relatively 'stable' and that the risks associated with the local donor pool were 'small'.<sup>38</sup> Dr Davies' thinking on this was, he said, for its time, 'very sensible ... [o]therwise I wouldn't have continued it'.<sup>39</sup>

**12.21** Professor Ludlam's faith in the relative safety of the UK blood supply is perhaps most clearly demonstrated in relation to a policy he adopted towards patients under his care who might require to travel. A national system in place from the 1970s ensured that all UK haemophilia patients were given a card stating their condition, its severity and details of their local Haemophilia Centre. Professor Ludlam added to this a printed statement requesting that, if a patient was treated elsewhere than their local Centre, either cryoprecipitate or NHS factor concentrates be used in preference to commercial concentrates. He stated that he had provided his patients with the additional statement

<sup>36</sup> Director of the Edinburgh and East of Scotland Blood Transfusion Service, 1979–2001

<sup>37</sup> Day 21, page 153

<sup>38</sup> Day 35, pages 21–22

<sup>39</sup> Day 19, page 126

specifically so that, if they were to require treatment away from home – and particularly in England or Wales where there was considerably less NHS material available – his patients would not be exposed to commercial concentrates.<sup>40</sup>

**12.22** Not all clinicians favoured this approach. Dr Willoughby, until he was succeeded by Professor Ian Hann at Yorkhill, had ‘what appeared to be a preference for commercially (as opposed to NHS-produced) products’.<sup>41</sup> Although, as noted above, Dr Willoughby agreed that home treatment programmes were of proven efficacy, he believed commercial concentrate was a better product for that purpose, being of higher purity, resulting in fewer adverse reactions and being easier to prepare.<sup>42</sup> At least part of his approach, however, appears also to have been based on the availability of locally produced materials: in a discussion with Professor Hann, Dr Willoughby expressed disillusionment with the health service throughout the UK generally and, in particular, that he felt let down with regard to supplies.<sup>43</sup>

**12.23** As noted below in discussion of product selection at Scottish centres, Professor Hann immediately reversed this policy upon taking up the post of Haemophilia Director at Yorkhill. Professor Hann believed that, as well as being cheaper, locally produced products would be safer because the donor pool was better. He had taken into account potential problems with this approach, including availability, but for him, ‘the lower risk of infectivity was ... paramount’.<sup>44</sup> Professor Hann did not, however, criticise Dr Willoughby’s preference. It appears clear that Dr Willoughby had exercised his clinical judgement and that he reached his conclusions for what he regarded as good reasons. Dr Willoughby had not had to face the emerging problems of non-A, non-B Hepatitis/Hepatitis C or HIV/AIDS, however, and another part of the explanation for his preference and practice may have been a belief that what he perceived as the greatest risk to haemophilia patients, Hepatitis B, was reducing and that avoiding large-pool concentrates more effectively reduced that risk, than preferring large but local donor pools.<sup>45</sup>

**12.24** The selection of therapeutic materials in the three other Scottish centres (Aberdeen, Dundee and Inverness) point clearly towards a preference for NHS products. As will be seen below in discussion of the actual products administered, use of imported commercial concentrates was very infrequent throughout the material time at Aberdeen and Dundee, while Inverness used no imported products from 1974 onwards. Practice at these centres appears to have closely followed international, government and SNBTS guidance and policy that haemophilia treatment should be on a self-sufficient basis using domestically sourced products, other than in exceptional cases.

**12.25** The existence of HTLV-III/HIV infection in haemophilia patients in the UK emerged with a dreadful suddenness, however, after the publication of the seminal article in *The*

<sup>40</sup> Day 18, pages 68–69; Day 19, pages 117–118

<sup>41</sup> Professor Hann’s Witness Statement [PEN.015.0035] at 0037; Day 21, page 27

<sup>42</sup> Day 21, page 28. Dr Pettigrew, who worked with Dr Willoughby, agreed that, at that time, NHS Factor VIII could be ‘difficult to work with’ and that the commercial alternatives were ‘much more user-friendly’. She noted that the parents of haemophilia patients at Yorkhill also tended to favour commercial products for the same reasons. Day 20, pages 17–18. Professor Ludlam also agreed that early concentrates could be difficult to ‘solubilise’, although he thought this common to both commercial and NHS concentrates. Day 18, page 43

<sup>43</sup> Professor Hann’s Witness Statement [PEN.015.0370]; Day 21, pages 28–29, pages 36–37; Day 31, page 80; Dr Pettigrew – day 20, page 18. See also: Dr Willoughby’s Witness Statement [PEN.019.1272] at 1277.

<sup>44</sup> Day 31, page 81

<sup>45</sup> Day 21, page 29; Day 31, pages 80–81. Professor Ludlam agreed that Dr Willoughby was ‘a very good, enthusiastic paediatric haematologist’ and did not criticise his approach to product selection at Yorkhill. Day 18, pages 101–102

*Lancet* on 1 September 1984 by Dr Rachanee Cheingsong-Popov and others.<sup>46</sup> The article presented strong evidence supporting the infectious agent hypothesis and gave the results of 2000 HTLV-III tests conducted in the UK. It commented that there had previously been reported only limited studies of antibody prevalence in groups at risk for AIDS, but that those studies had shown a moderately high seropositivity amongst at-risk populations such as apparently symptom-free homosexual men, haemophilia patients and IVDUs. Antibodies to HTLV-III were found in 34% of haemophilia patients studied, but the article advised caution in interpreting the results. There was perceived at that time to be a relatively low risk of acquiring HTLV-III or AIDS from blood transfusion in the UK, which was said to be regarded as a 'low-risk country'.

**12.26** In retrospect, it is difficult to understand the confidence in UK blood in its most extreme form, at least among those who accepted the transmissible agent theory in the debate over the aetiology of AIDS. By 1980 international tourism was well established, both in foreign holidays for UK residents and in holidays in the UK for foreign residents. The interchange across borders of individuals with an interest in activities that exposed them to a high risk of HIV infection, whether the risk was associated with intravenous drug use or promiscuous male homosexual activity, was known from the earliest cases of AIDS in the UK to be associated with travel.<sup>47</sup> An editorial in *The Lancet* of 22 December 1984 commented on an article by Dr Mads Melbye and others in the same edition, which noted that anti-HTLV-III seropositivity in Danish homosexual men was most strongly correlated with travel to the USA and especially New York City<sup>48</sup> and noted that, of Scottish patients studied in Glasgow, of those treated with domestically sourced product only those who had travelled abroad were HTLV-III antibody positive. It observed that contamination of local blood products with HTLV-III must only be a matter of time, effectively recognising the reality that had already emerged.<sup>49</sup>

### ***Clinical practice in the United States of America; in England and Wales; and in Scotland***

**12.27** The chronology of the emergence of AIDS has been dealt with in detail elsewhere (see Chapters 9–10). In examining the clinical response to these developments, it is appropriate in the first instance to have regard to attitudes and actions in the USA, where the first AIDS cases were identified and where it was quickly recognised that AIDS was potentially a major public health issue. The UK presented a very different picture, however, and within the UK there were significant differences in treatment regimes for haemophilia therapy as between England and Wales on the one hand and Scotland on the other. Chief amongst these was the availability of therapeutic materials derived from UK donors: in England and Wales, these accounted for only a small proportion of the required products and the importation of commercial products was correspondingly high. By contrast, Scotland was increasingly able to produce a much greater proportion of therapeutic materials from domestically sourced blood and the importation of commercial products was considerably lower. After the discussion of the clinical response in the USA, therefore, there follows discussion of opinions and reactions in England and Wales before the clinical response particular to Scotland is considered.

<sup>46</sup> Cheingsong-Popov et al, 'Prevalence of antibody to human T-lymphotropic virus type III in AIDS and AIDS-risk patients in Britain', *The Lancet*, 1984; 477-480 [LIT.001.0417]

<sup>47</sup> See Chapter 9, *Knowledge of the Geographical Spread and Prevalence of HIV/AIDS 1*, paragraph 9.37. The 'Brompton patient' was a homosexual man who was a frequent visitor to Florida.

<sup>48</sup> Melbye et al, HTLV-III Seropositivity in European Haemophiliacs Exposed to Factor VIII Concentrate Imported from the USA, *The Lancet*, December 22/29 1984; 1444-1446 [LIT.001.1702] at 1704

<sup>49</sup> 'Blood Transfusion, Haemophilia and AIDS', *The Lancet*, December 22/29 1984 [DHF.002.6016]

## Clinical response to the emergence of AIDS: The United States of America

### *Initial response*

**12.28** The initial response to the emergence of AIDS in the USA<sup>50</sup> was limited to advice on clinical practice in managing patients with diseases of the 'AIDS complex'. Clinicians were advised to treat the infections identified in patients suffering from the syndrome, so far as they were treatable. In addition to managing diagnosed disease, long-term prophylaxis for PCP was suggested as a possibility.<sup>51</sup> The focus was predominantly on patient care for those infected or suspected of having been infected with AIDS and those with AIDS-related conditions, rather than on preventative measures.

### *Haemophilia patients at risk*

**12.29** After it was reported in July 1982 that US haemophilia patients appeared to be at risk,<sup>52</sup> a wider approach was adopted generally in the USA. The US National Hemophilia Foundation (NHF) called for action to protect patients and, in collaboration with the CDC and the Food and Drug Administration (FDA), instituted a surveillance programme to determine patterns of AIDS transmission among haemophilia patients, with a view to establishing guidelines for treatment.<sup>53</sup>

**12.30** In response to the threat of AIDS some haemophilia clinicians in the USA, notably Dr Oscar Ratnoff of Cleveland, proposed that haemophilia patients should suspend the use of concentrates and revert to cryoprecipitate, prepared from pools of ten donors or fewer.<sup>54</sup> He was opposed by the pharmaceutical industry and by other haemophilia doctors. In December 1982, however, after a total of eight cases of haemophilia-associated AIDS had been reported, the first NHF directive was issued recommending that concentrates should not be introduced to those who had not previously been exposed to them, including newborn children and young children up to four years old; to newly diagnosed patients; and to patients with mild haemophilia. Cryoprecipitate and fresh frozen plasma were recommended for therapy in such patients instead.<sup>55</sup> This was an approach that appears to have been based, in those very early days of the AIDS epidemic, on caution rather than firm scientific proof of the relative risks of transmission by cryoprecipitate and concentrates.

**12.31** In January 1983, a further NHF directive recommended the use of Desmopressin (otherwise known as DDAVP, a synthetic replacement for the hormone vasopressin) for patients with mild and moderate haemophilia.<sup>56</sup> The directive also recommended delaying elective surgery. This reflected considerable suspicion that AIDS was due to a blood-borne agent but, at the time, the risk of haemophilia patients developing AIDS was perceived to be very low. The use of DDAVP, where possible, was perceived as a prudent, and conceivably safer, alternative to the use of concentrate.

<sup>50</sup> See Chapter 9, *Knowledge of the Geographical Spread and Prevalence of HIV/AIDS 1* for more detailed discussion.

<sup>51</sup> Durack, 'Opportunistic Infections and Kaposi's Sarcoma in Homosexual Men 1981', *New England Journal of Medicine*, 1981; 305:1465-1467 [LIT.001.0956]

<sup>52</sup> 'Pneumocystis carinii Pneumonia among Persons with Hemophilia A', *MMWR*, July 16, 1982 [SGH.008.5097]

<sup>53</sup> Ragni, 'AIDS and Treatment of Hemophilia Patients', *Plasma Therapy and Transfusion Technology* 1988; 9: 173-191 [SGF.001.1314]; 'Update on Acquired Immune Deficiency Syndrome (AIDS) among Patients with Hemophilia A', *MMWR*; 10 Dec 1982;31: 644-646, 652 [LIT.001.0576]

<sup>54</sup> Starr, D, *Blood* page 267 [LIT.001.2936] at 2942. Professor Ludlam – Day 19, pages 29-30.

<sup>55</sup> Medical and Scientific Advisory Council, *AIDS: Implications Regarding Blood Product Use*. 21 December 1982, National Hemophilia Foundation, New York [LOT.002.2661]

<sup>56</sup> Ragni, 'AIDS and Treatment of Hemophilia Patients' *Plasma Therapy and Transfusion Technology*, 1988;9: 173-191 [SGF.001.1314].



**12.32** In US studies reported early in 1983, it was found that patients treated with cryoprecipitate did not develop impaired cell-mediated immunity.<sup>57</sup> As against the practical problems associated with a switch from concentrate therapy to cryoprecipitate, those studies appeared to suggest that cryoprecipitate exposed recipients to less risk of immune deficiencies than risks posed by concentrates.<sup>58</sup> Professor Ludlam noted, however, that it is now recognised that, largely due to variations in individuals' immune systems generally, immune changes such as those described were not necessarily a good reflection of HIV status.<sup>59</sup> As noted at paragraphs 12.114 and 12.118, it was to transpire that many of the haemophilia patients studied in Edinburgh and Glasgow, who showed changes in cell-mediated immunity, were not in fact HIV-positive at that time.<sup>60</sup> In addition, it was to transpire that in countries which used cryoprecipitate exclusively, HIV transmission still occurred, albeit to numbers of patients considerably lower than in those countries which used concentrates.<sup>61</sup>

**12.33** The preference for cryoprecipitate, as expressed by Dr Ratnoff, was repeated in an editorial in the *New England Journal of Medicine (NEJM)* of 13 January 1983 written by Dr Jane Desforges.<sup>62</sup> She commented that, in view of the results from the Lederman<sup>63</sup> and Menitove<sup>64</sup> studies reported in that edition (noted in the preceding paragraph), current modes of treatment would have to be scrutinised and suggested that, if cryoprecipitate use reduced the risk of haemophilia patients contracting AIDS, the current home treatment programme (using concentrate) needed to be revised. This was a more radical proposal than that contained in the NHF directive. She advised physicians involved in the care of haemophilia patients to be alert to the risk and wrote that, '[p]reventing the complications of the present treatment might have to take precedence over preventing the complications of haemophilia itself'. The withdrawal of factor concentrates was mooted, though it was acknowledged that there might not be enough evidence to demand such a radical change.<sup>65</sup> Professor Ludlam noted that Dr Desforges had accepted that the number of patients involved in her preliminary study was 'too small for definitive comparison of the risks of different modes of treatment' to be made.<sup>66</sup>

**12.34** These early responses related to haemophilia therapy suggested product selection in order to reduce risk in particularly vulnerable groups, or avoiding elective procedures so that blood product therapy would not be required. More generally, concentrate therapy

<sup>57</sup> Lederman et al 'Impaired Cell-Mediated Immunity in Patients with Classic Hemophilia', *New England Journal of Medicine*, 1983; 308: 79–83 [PEN.012.0263]; Menitove et al, 'T-Lymphocyte Subpopulations in Patients with Classic Haemophilia Treated with Cryoprecipitate and Lyophilized Concentrates', *New England Journal of Medicine*, 1983; 308: 83–86 [LIT.001.0031]. See also Chapter 11, *Aids Aetiology*, paragraphs 11.48–11.50

<sup>58</sup> See, however, paragraph 12.35 below: some clinicians thought that large quantities of cryoprecipitate were as likely to transmit infection as concentrates. In Chapter 2, *Patients at Risk*, paragraph 2.48, it is noted that cryoprecipitate is a high-volume product at the point of use and that, therefore, patients requiring frequent treatment were necessarily exposed to large numbers of donors. A patient experiencing 20 bleeds in a year might have been exposed to as many as 1600 units derived from up to the same number of donors.

<sup>59</sup> Day 18, page 122. See also Dr Kernoff's article for the Haemophilia Society publication, *The Bulletin* of 1983, discussed below. This contemporaneous article notes that the 'simplest' test for AIDS – measuring the ratio of T4 to T8 lymphocytes – 'is also the least meaningful' because 'low ratios are not unique to AIDS – similar results may be found in a variety of other circumstances. So the finding of a low ratio doesn't diagnose AIDS, and there's no evidence that it predicts it, either.' [PEN.016.0595] at 0606. In the UK, 'cell-mediated immunity', measured by T4/T8 ratios was considered insufficient for a diagnosis of AIDS (see Chapters 9–10).

<sup>60</sup> See also Professor Ludlam – Day 18, page 122, page 153

<sup>61</sup> See paragraph 12.4, footnote 2 above.

<sup>62</sup> Desforges, 'AIDS and the preventive treatment in hemophilia', *New England Journal of Medicine*, 1983;308: 94–95 [LIT.001.0040]

<sup>63</sup> Lederman et al, 'Impaired cell-mediated immunity in patients with classic hemophilia', *New England Journal of Medicine*, 1983; 308:79–83 [LIT.001.1593]

<sup>64</sup> Menitove et al, 'T-lymphocyte subpopulations in patients with classic hemophilia treated with cryoprecipitate and lyophilized concentrates'; *New England Journal of Medicine*, 1983; 308:83–86 [LIT.001.0031]

<sup>65</sup> Desforges, 'AIDS and the preventive treatment in hemophilia', *New England Journal of Medicine*, 1983;308: 94–95 [LIT.001.0040]

<sup>66</sup> Professor Ludlam's Witness Statement [PEN.015.0445] at 0451

was considered unavoidable, save in the more radical proposals put forward by Drs Ratnoff and Desforges. Further proposals soon emerged in the USA but, as noted above, there was controversy over the infective agent hypothesis and possible solutions based on product selection were unlikely to be persuasive while the controversy remained unresolved.

**12.35** Realistically, however, the widespread use of cryoprecipitate as proposed by Dr Ratnoff and Dr Desforges had little prospect of success in the USA or elsewhere. Production facilities did not exist to provide the quantities of cryoprecipitate that would have been required, as indeed Dr Desforges had suggested in her article.<sup>67</sup> Other clinicians thought that because of the cumulative effect of infusing large quantities, cryoprecipitate would ultimately be as likely as concentrates to transmit disease.<sup>68</sup> Many clinicians, the blood products industry and, indeed, many patients strongly resisted switching from home therapy using concentrates to the use of cryoprecipitate, which would have ended the home therapy programme and resulted in haemophilia patients requiring to attend hospital when they experienced bleeds. Subsequently, in March 1985, Dr Ratnoff reported that of 91 patients under his care, only five had followed his advice and switched to cryoprecipitate therapy.<sup>69</sup> Professor Ludlam was not aware whether Dr Desforges had acted on her 'recommendation' and changed patients under her care from concentrate therapy to cryoprecipitate.<sup>70</sup>

### ***Statements on the prevention and control of AIDS***

**12.36** On 4 March 1983, the US Public Health Service noted that statements on the prevention and control of AIDS had been issued by the National Gay Task Force, the National Hemophilia Society, the American Red Cross, the American Association of Physicians for Human Rights and others. There was broad agreement that steps were required to reduce the potential risks but the organisations differed in the methods proposed to accomplish that goal. The Public Health Service made a number of general precautionary recommendations. So far as clinical practice was concerned, it recommended that physicians should adhere strictly to medical indications for transfusions and that autologous transfusions (whereby, in anticipation of planned surgical intervention, the patient gives their own blood in advance for use in the operation) should be encouraged. Manufacturers were encouraged to produce safer products.<sup>71</sup>

**12.37** A similar point was made in the March–April 1983 edition of the journal *Transfusion* which published a joint statement on AIDS related to blood transfusion.<sup>72</sup> The statement, which was dated 13 January 1983 and had been developed by the American Association of Blood Banks, the American Red Cross and the Council of Community Blood Centers, with both voluntary and government assistance, recommended that physicians should be educated further regarding the importance of balancing the decision to use each blood component against the risks of infection, be they well established or, like AIDS, under investigation.

<sup>67</sup> Desforges, 'AIDS and the preventive treatment in hemophilia', *New England Journal of Medicine*, 1983;308: 94–95 [LIT.001.0040] at 0041

<sup>68</sup> Starr, D, *Blood*, Page 272 [LIT.001.2936] at 2942.

<sup>69</sup> Ratnoff et al, 'Haemophilia and the Acquired Immunodeficiency Syndrome', *Annals of Internal Medicine*, March 1985 [PEN.016.1171]

<sup>70</sup> Professor Ludlam's Witness Statement [PEN.015.0445] at 0451

<sup>71</sup> 'Current trends prevention of Acquired Immune Deficiency Syndrome (AIDS): Report of inter-agency recommendations', *MMWR*, 1983;32: 101–103 [LIT.001.0568]

<sup>72</sup> The Inquiry has not yet been able to trace this statement. See *Transfusion*, 1983; 23:87-88, 'Joint statement on acquired immune deficiency syndrome (AIDS) related to transfusion'

**12.38** The Medical and Scientific Advisory Council of the NHF began to produce a series of guidelines for the treatment of haemophilia patients, developed in response to the latest scientific and medical knowledge. Some of the guidelines of this period were reflected in the approaches of international bodies. For example, on 21 December 1982 the World Federation of Hemophilia issued the recommendation that:

[C]ryoprecipitate be used to treat patients in the following groups except where there is an overriding medical condition: new born infants and children under 4; newly identified patients never treated with factor VIII concentrate; and patients with clinically mild haemophilia who require infrequent treatment.<sup>73</sup>

**12.39** It was recommended that DDAVP should be used whenever possible in patients with mild or moderate Haemophilia A. These recommendations were a close parallel of the then current US Public Health Service recommendations.

**12.40** The wish of many haemophilia clinicians to maintain the status quo remained an important factor, however. In June 1983, Dr Aledort affirmed that his position on treatment was 'business as usual'. There was, in his view, no evidence that treatment with concentrates caused AIDS and no need to change therapy.<sup>74</sup>

### *The position in the United States of America at the end of 1983*

**12.41** By the end of 1983, a number of strategies had emerged in professional literature and in national agency directives in the USA:

- Physicians should adhere strictly to medical indications for transfusions.
- Physicians should be educated further regarding the importance of balancing the decision to use each blood component against the risks of infection, be they well established or potential.
- Autologous transfusions should be encouraged.
- Concentrates should not be introduced to those who have not previously been exposed to such treatment, including newborn children and young children up to four years old, newly diagnosed patients, and patients with mild haemophilia.
- According to one extreme of opinion, factor concentrates should be withdrawn.

**12.42** Two background factors appear to have been particularly important in influencing policy at the end of 1983:

- No transmissible aetiological agent of AIDS had been isolated or identified, to the satisfaction of leading authorities in the USA,<sup>75</sup> and there was no screening test to protect the blood supply.
- Strategies to reduce hepatitis infectivity in factor concentrates were in the course of development and it was presumed that, if the transmissible agent of AIDS were a virus, similar strategies could reduce the infectivity of other agents, including a possible AIDS agent.

<sup>73</sup> 'Medical and Scientific Advisory Council. AIDS: Implications Regarding Blood Product Use' National Hemophilia Foundation, 21 December 1982, New York [LOT.002.2661].

<sup>74</sup> Douglas Starr, *Blood*, Page 293 [LIT.001.2936] at 2963

<sup>75</sup> The virus had been isolated in France by Montagnier and others but this was not generally accepted at the time, particularly by US scientists and clinicians. See Chapter 11, *HIV/AIDS Aetiology*

## Clinical response to the emergence of AIDS: England and Wales

### *The aetiology of AIDS: transmissible agent or antigen overload?*

**12.43** As noted above, the emergence of AIDS, seen at the time as a genuinely new disease with no relevant history upon which to base decisions on appropriate action, gave rise to debate as to the aetiology of the condition. This debate itself – between those who believed that an infectious agent, probably a virus, was responsible for the observed clinical signs and symptoms in AIDS patients (the transmissible agent theory) and those who believed that those signs and symptoms were attributable to the repeated infusion of foreign proteins in factor concentrates in haemophilia therapy (the antigen overload theory) – was an important factor, as guidance on the selection of therapeutic materials was developed.

**12.44** Dr Peter Kernoff<sup>76</sup> expressed the view in the Haemophilia Society publication *The Bulletin*, edition 33, No 1, January 1983, that the links between AIDS and concentrate therapy for haemophilia were ‘very tenuous’. Haemophilia patients might be at increased risk of AIDS *if* AIDS was caused by an infectious agent and *if* this agent were transmitted in blood – ‘and these are both big “ifs”’.<sup>77</sup> The idea that there was an epidemic of AIDS amongst haemophilia patients was dismissed as ‘ludicrous’. In general, he said that AIDS was just the latest item in a long list of possible risks associated with factor therapy.

**12.45** Dr Kernoff’s views were noted in the media<sup>78</sup> and by the Department for Health and Social Security (DHSS), where it was commented that the benefits of clotting factor concentrates ‘far outweigh the possible, and as yet unproven hazards of the transmission of acquired immune deficiency syndrome’.<sup>79</sup> It was still four months before the first suspected case of AIDS in a UK haemophilia patient (see paragraph 12.69 below). Though expressed in strong terms, Dr Kernoff’s views were within the range of acceptable expert opinion in January 1983.

### *The benefits of factor concentrate therapy*

**12.46** Debate on the selection of therapeutic materials for haemophilia therapy appears to have been influenced, at least in part, by the appreciation of the considerable benefits of factor concentrate therapy already noted.

**12.47** On 4 May 1983, the Haemophilia Society distributed a letter by Professor Arthur Bloom that has been referred to in other contexts.<sup>80</sup> Professor Bloom was influential: he was Chairman of the Haemophilia Centre Directors, a senior member of the Society’s own medical advisory panel and a member of the Central Blood Laboratories Authority (CBLA). He wrote that the cause of AIDS was quite unknown and that it had not been proven to result from transmission of a specific infective agent in blood products. He too supported continuing use of current therapy using concentrates and referred explicitly to the benefits of factor concentrate therapy in support of his position:

<sup>76</sup> Director of the Haemophilia Centre at the Royal Free Hospital, London

<sup>77</sup> *The Bulletin*, Edition 33 No. 1 [PEN.016.0595] at 0605–0606

<sup>78</sup> *The Observer*, 16 January 1983 [DHF.001.7108]

<sup>79</sup> DHSS memo, ‘Factor 8 and the Observer article’ [DHF.001.7111]

<sup>80</sup> Professor Bloom’s statement to the Haemophilia Society [DHF.001.4474]. The letter is set out in full in the Preliminary Report at paragraph 8.25, and has been quoted in part and discussed in Chapter 9, *Knowledge of the Geographical Spread and Prevalence of HIV/AIDS 1* at paragraphs 9.90–9.98.

Haemophiliacs, their parents and doctors have always balanced the quality of life and the dangers from bleeding against the risks of treatment. We are no strangers to infective diseases, such as hepatitis, which can be transmitted by factor concentrates ....

....

Thus whilst it would be wrong to be complacent it would equally be counter-productive to alter our treatment programmes radically. We should avoid precipitate action and give those experts who are responsible a chance continually to assess the situation.<sup>81</sup>

### ***Imported commercial blood products in England and Wales***

**12.48** Throughout the UK at this time, practitioners were confident of the safety of the domestically produced factor concentrate products and remained confident so long as there was no evidence of infection in recipients of NHS blood products. There were significant differences between Scotland and the rest of the UK that affected discussion of risk, however, which have to be borne in mind. In particular, treatment options in England and Wales were limited by the inability of the public sector manufacturer to meet the demand for Factor VIII concentrate. Scotland had more ample supplies of concentrates manufactured at the Protein Fractionation Centre (PFC, the manufacturer of NHS blood products in Scotland) and this important distinction is explored below. In the first place, however, the position in England and Wales is discussed without reference to these differences.

**12.49** In most, if not all, regions of England and Wales, Factor VIII therapy using concentrates necessarily involved the use of imported commercial products. As noted in Chapter 21, *Haemophilia Therapy – Use of Blood Products*, the distribution of NHS materials in England and Wales was provided for on a regional basis, with concentrates manufactured at the Blood Products Laboratory (BPL, the manufacturer of NHS blood products in England and Wales) distributed pro rata to the contributions from each region of plasma for fractionation. At all material times, NHS output was insufficient to meet total demand and the shortfall was met by commercial purchases, funded by regional health authorities.<sup>82</sup>

**12.50** In early 1983, the supply of NHS manufactured Factor VIII concentrate accounted for less than 30% of the demand in England and Wales. The remainder was commercial product, largely imported from the USA. As shown in Chapter 21, *Haemophilia Therapy – Use of Blood Products*, Figure 21.2, commercial Factor VIII was the main therapeutic product used throughout the 1980s in England and Wales and the use of imported products could not realistically be avoided if concentrate therapy was to continue.

**12.51** Dr Mark Winter described the state of affairs as he found it when he became Consultant Haematologist at Kent and Canterbury Hospital in 1983. The scope for choice of therapeutic products was limited. The output from the BPL was restricted by the capacity of the plant<sup>83</sup> and his centre obtained only small quantities of NHS Factor VIII concentrate. At least 90% of the concentrate available for use was commercial. This formed part of the practical background to his response to the emergence of the AIDS threat: whatever

<sup>81</sup> Professor Bloom's statement to the Haemophilia Society [DHF.001.4474]

<sup>82</sup> Chapter 21, *Haemophilia Therapy – Use of Blood Products*

<sup>83</sup> Dr Winter – Day 16, page 29; Dr Winter – Day 15, page 93

he thought of the risk, he could not discontinue the use of imported concentrates. In fact, Dr Winter said that he was convinced at a relatively early date that AIDS was caused by a blood-borne infective agent but, for him and for Haemophilia Directors with similar views, concentrate therapy was dependent on the products of US pharmaceutical companies. In time, the capacity of the production facilities in England was increased. The foundation of a new facility at Elstree, aimed at self-sufficiency, was laid on 23 March 1984. That was, however, clearly too late to make any impact on the importation of commercial concentrates while the threat of transmission of HIV/HTLV-III continued.

**12.52** In the circumstances, discussion in England and Wales tended to focus on the continuing use of imported products. Support for the status quo in coagulation therapy was forcefully expressed in the article by Dr Kernoff referred to above. In addition to supporting continued use of factor concentrates generally, he wrote that it would be premature to jump to the conclusion that commercial concentrates were more dangerous than NHS concentrates. In any event, dependence on US imports was a fact of life and he saw no reason to change current practice. His final comment was that:

For particular patients, and at particular centres, there may be reasons for preferring cryoprecipitate, but these reasons have little to do with AIDS.<sup>84</sup>

**12.53** For Dr Winter – even though his personal assessment of the situation at the time was different – that was an understandable position to adopt, having regard to the obvious benefits derived from the use of concentrates:

He is a very respected figure looking at the data and saying it is of concern, but we are talking about a product that has revolutionised the lives of patients and there is a major obvious benefit to this treatment. We will have to look at the risk that appears to be evolving. That was the situation of the day.<sup>85</sup>

### ***Recommendations and guidance***

**12.54** The approach of Professor Bloom, set out in his letter of 4 May 1983, was supported at a special meeting of the UK Haemophilia Reference Centre Directors. That meeting of 13 May 1983 at St Thomas's Hospital was chaired by Professor Bloom and was convened specifically to discuss the problem of AIDS.<sup>86</sup> There were noted to be ten cases of AIDS in homosexual males in the UK by that date and one haemophilia patient was reported as being 'suspected' of suffering from the disease. Concern was expressed at the definition of AIDS and it was advised that evidence of impaired cell-mediated immunity should not be regarded as necessarily leading to AIDS.<sup>87</sup> The consensus reached at that meeting among the Haemophilia Reference Centre Directors in attendance was set out in a letter from Professor Bloom to the Directors, including Scottish Directors, dated 24 June 1983.<sup>88</sup> Reflecting both the view that the aetiology of AIDS was as yet unknown and the appreciation of the benefits of concentrate therapy, he commented that, with the exception of some vulnerable patients:

<sup>84</sup> *The Bulletin* Edition 33 No. 1 [PEN.016.0595] at 0606

<sup>85</sup> Dr Winter Day 16, pages 13–14

<sup>86</sup> Minutes [DHF.001.4384]. By this time, Glasgow and Edinburgh had been recognised as Haemophilia Reference Centres, although they do not appear to have been represented at this meeting. On 8 August 1985, Glasgow and Edinburgh were described in DHSS correspondence as 'perhaps ... regarded more as centres of excellence than Reference Centres': [DHF.001.7665]

<sup>87</sup> Impaired cell-mediated immunity was not, at the time, sufficient alone to be officially regarded as a case of AIDS. See Chapter 9, *Knowledge of the Geographical Spread and Prevalence of HIV/AIDS 1*, paragraphs 9.102–9.104 for the 'reporting criteria' in place at the time.

<sup>88</sup> Letter [SGH.002.2175]

It was agreed that there is as yet insufficient evidence to warrant restriction of the use of imported concentrates in other patients in view of the immense benefits of therapy but the situation will be constantly reviewed.<sup>89</sup>

**12.55** General recommendations were agreed:

- For mildly affected patients with haemophilia A or von Willebrand's disease and minor lesions, treatment with DDAVP should be considered.
- It was noted that many Directors already reserved supplies of NHS cryoprecipitate and concentrates for the treatment of children, mildly affected patients and patients unexposed to imported concentrates and the recommendations suggested that it would be 'circumspect to continue that policy.'<sup>90</sup>

**12.56** At this stage, the recommendations were less cautious in the case of Haemophilia A as compared with the NHF directives in the USA, noted in paragraph 12.30 above. The NHF recommendation was that DDAVP should be used for mildly and moderately affected haemophilia patients. In relation to concentrates, in addition to children and mildly affected patients or patients not previously exposed to imported concentrates, the NHF recommended that concentrates should not be introduced to newly-diagnosed patients or to patients with mild haemophilia.

**12.57** Additional points were made after the meeting and reported by Professor Bloom in his letter of 24 June. The first of these related to the treatment of patients with Haemophilia B. He commented:

The evidence to incriminate factor IX concentrates in AIDS is even less than with FVIII and it seems logical to continue to use our normal supplies of NHS concentrate.<sup>91</sup>

**12.58** That remained the consensus view throughout the development of the AIDS crisis and it was only later that a small number of AIDS cases came to be reported in Haemophilia B patients.<sup>92</sup>

**12.59** Opinion on therapy was also developing in Europe. The Committee of Ministers of the Council of Europe adopted Recommendation No R(83)8 on 23 June 1983. It dealt with the prevention of the spread of AIDS as a result of infected blood donations. It recommended that Member States:

[T]ake all necessary steps and measures with respect to the Acquired Immune Deficiency Syndrome and in particular:

- To avoid wherever possible the use of coagulation factor products derived from large plasma pools; this is especially important for those countries where self-sufficiency in the production of such products has not yet been achieved;
- To inform attending physicians and selected recipients, such as haemophiliacs, of the potential hazard of haemotherapy and the possibility of minimising those risks.<sup>93</sup>

<sup>89</sup> Ibid [SGH.002.2175]

<sup>90</sup> Ibid [SGH.002.2175]

<sup>91</sup> Ibid [SGH.002.2175]

<sup>92</sup> See Chapter 10, *Knowledge of the Geographic Spread and Prevalence of HIV/AIDS 2*.

<sup>93</sup> Recommendation No. R (83) 8 of the Committee of Ministers to Member States [DHF.001.4550]

**12.60** The first recommendation would have restricted the use of factor concentrates manufactured in the UK as well as imported commercial products. The qualification regarding self-sufficiency would have affected England and Wales to a greater extent than Scotland, which was closer to self-sufficiency. The emphasis on large-pool products appears implicitly to have reflected the view – clearly not yet accepted by all UK haemophilia clinicians – that AIDS was spread by infected blood products, as did the emphasis on the prevention of AIDS transmission by means of blood transfusion. To that extent, it presented a challenge to those who disagreed with the Committee of Ministers to explain their position.

**12.61** In May 1983, Dr Frank Boulton<sup>94</sup> wrote to Professor Bloom.<sup>95</sup> Professor Bloom replied on 23 May and commented:

We have not laid down hard and fast regulations since the detail of treatment will depend upon local circumstances. I do not think that anyone is complacent about the situation but I think that we all agree that it would be counter-productive to ban the importation of blood products at this moment ... The Haemophilia Society have expressed concern that we are not expanding the home treatment programme with sufficient vigour ....<sup>96</sup>

**12.62** There was media comment on the views of the Haemophilia Society in the same period. On 18 May 1983 in an article with the headline 'US Gay Blood Plague Kills Three in Britain', *The Sun* reported that the Haemophilia Society had appealed to the government not to ban US blood products.<sup>97</sup> The Society was said to have claimed that without the US imports there would be a sharp rise in the number of deaths among people with haemophilia.

**12.63** On 11 July 1983, in a note on 'Factors to be considered in the Selection of Hepatitis Reduced Products for Clinical Trial – Evaluation of Residual Infectivity for Hepatitis Viruses', Dr John Craske<sup>98</sup> commented that the possibility had to be considered that Factor VIII concentrate prepared from plasma donations obtained in the USA might be contaminated with a putative infectious agent associated with the cause of AIDS.<sup>99</sup> However, he said that there was, as yet, no product which was not made from sources which were likely to carry such a risk (implicitly accepting that, if the infective agent theory were to prove accurate, there was every reason to suppose that it would enter the UK blood supply in time, if it had not already done so). On his approach, there was not much that could be done to avoid the use of coagulation factor products derived from large plasma pools, whatever their origin.

### **Contrary views**

**12.64** There were, however, contrary views. Dr Spence Galbraith of the Communicable Disease Surveillance Centre supported a temporary ban on the use of certain imported

<sup>94</sup> Dr Boulton was Consultant in Haematology and Blood Transfusion in Edinburgh, 1980–90, and Deputy Director of the SEBTS from 1982–90.

<sup>95</sup> Dr Boulton's letter has not been found. He could not remember what his recommendations were: Day 24, pages 42–45. He thought that his concerns related to England and the growing awareness of the risks associated with blood products.

<sup>96</sup> Letter [SNF.001.3711]

<sup>97</sup> *The Sun* [DHF.001.4415]

<sup>98</sup> Public Health Laboratory Service (PHLS), Withington Hospital, Manchester

<sup>99</sup> Pages 3–5 of UK Haemophilia Centre Directors Hepatitis Working Party's Annual Report for the year 1982–83: Factors to be considered in the selection of hepatitis reduced products [SNF.001.0948]



products in a paper 'Action on Aids' sent to Dr Ian Field of the DHSS in May 1983. Dr Galbraith stated in his covering letter:

I have reviewed the literature and come to the conclusion that all blood products made from blood donated in the USA after 1978 should be withdrawn from use until the risk of AIDS transmission by these products has been clarified.<sup>100</sup>

**12.65** Dr Galbraith's reasoning was based on the transmissible agent theory. It was a powerful statement of the risk as perceived by a public health specialist but it did not ultimately lead to the change in policy advocated: his advice was rejected by the Biologicals Sub-Committee of the Committee on the Safety of Medicines on 13 July 1983.<sup>101</sup> It was concluded by the Sub-Committee that withdrawal of imported products was not feasible on the grounds of supply. In addition, the perceived level of risk did not 'at present justify serious consideration of such a solution'. It was anticipated that the efforts being made to secure UK independence from foreign suppliers would reduce markedly, although not eliminate, the risks to recipients. It was noted that haemophilia doctors and patients, who saw first hand the benefits of Factor VIII over cryoprecipitate, did not wish blood products from the USA to be withdrawn.<sup>102</sup> It is apparent that the Sub-Committee shared the opinions of the haemophilia clinicians and the Haemophilia Society over the crucial issue of withdrawal of imported commercial products.

**12.66** The conclusions rejecting Dr Galbraith's recommendations were controversial for some. According to evidence provided to Lord Archer, some experts were taken aback by the decision.<sup>103</sup> Professor Christopher Bartlett, formerly of the Communicable Disease Surveillance Centre (CDSC), is reported to have said, 'I was dismayed when the Sub-Committee concluded that the risk was small, because I, like Dr Galbraith, found that the evidence was rather stronger than that ....'<sup>104</sup> Dr Galbraith was 'completely bowled over' by the Sub-Committee's decision.<sup>105</sup>

**12.67** Dr Winter commented that this stage was, in his view, another highly critical time.<sup>106</sup> He thought that everything Dr Galbraith had said in his paper was true, scientifically: in retrospect, what he proposed would have saved some lives. Clinicians and those advising them were, however, constrained by concerns about the consequences of withdrawing imported concentrates. Given the risk to patients, particularly that of exposing patients to potentially fatal cerebral bleeds, Dr Galbraith's proposal would have been met with very great reluctance by doctors and by patients.

**12.68** At this stage, therefore, in the summer of 1983, Dr Galbraith, a public health specialist, favoured avoiding imported concentrates; Dr Craske, also a public health specialist, acknowledged a risk but thought it common to all Factor VIII concentrates; and the Haemophilia Society and its advisers remained committed to the use of concentrate, including imported products, though exceptions were provided for in practice guidance.

<sup>100</sup> The Inquiry team has only a very faint copy of this paper [MIS.001.0001] at 0002. A retyped version of the letter and paper is at [MIS.001.0005].

<sup>101</sup> Minutes of the Sub-Committee on Biological Products [MIS.001.0291] at 0292. Dr Galbraith was in attendance at the sub-committee as an expert adviser [DHF.002.8865]. The meeting is discussed in more detail in Chapter 9, *Knowledge of the Geographical Spread and Prevalence of HIV/AIDS 1*, at paragraph 9.106. Professor Ludlam stated that Dr Galbraith's letter was not discussed at the UKHCDO Reference Centre Directors Meeting on 13 May 1983, probably because the proceedings of the Committee on the Safety of Medicines were confidential – Day 19, page 35.

<sup>102</sup> Summary of the Main Points from a Consideration of AIDS and Licensed Blood Products by CSM(B) 13 July 1983 [DHF.002.8865].

<sup>103</sup> The Archer Inquiry was an independent, non-statutory Inquiry on 'NHS Supplied Contaminated Blood and Blood Products' chaired by Lord Archer of Sandwell which reported in 2009.

<sup>104</sup> Archer Inquiry, Professor Bartlett – Day 8, page 8

<sup>105</sup> Ibid page 22

<sup>106</sup> Dr Winter – Day 16, page 65

### *First AIDS deaths in the United Kingdom*

**12.69** By May 1983, there had been deaths in the UK from AIDS in the male homosexual community and AIDS was suspected in a haemophilia patient in Cardiff.<sup>107</sup> By 31 July 1983, 14 cases of AIDS had been reported to the CDSC.<sup>108</sup> One of the 14 was a haemophilia patient who had received Factor VIII imported from the USA.<sup>109</sup> A second case of infection in a haemophilia patient, in Bristol, had apparently not been formally reported to the CDSC by this stage. The risk from blood products imported into Britain was considered by the CDSC to be 'very small' at that time: there were about 2167 patients with haemophilia then receiving treatment in the UK, the majority with imported Factor VIII concentrate. By September there were two well documented cases of AIDS in haemophilia patients in England and Wales and one had died of the disease.<sup>110</sup> These events did not, however, have an immediate or significant impact on treatment policy or practice.

**12.70** On 21 June 1983, the CBLA Central Committee for Research and Development in Blood Transfusion met for the first time. The Chairman, Dr Harold Gunson, outlined the problems caused by AIDS and noted that 'it appeared to be spread by blood and blood products'. However, the general feeling of the committee was reported to be that 'not enough was known about AIDS to enable any decisions to be made'.<sup>111</sup>

**12.71** The coordinator of the Haemophilia Society wrote to a government official on 15 August 1983 regarding a meeting arranged to take place between representatives of the Society and Lord Glenarthur, Parliamentary Under-Secretary of State, DHSS, on 8 September 1983.<sup>112</sup> The issues the Society wanted to discuss included the avoidance of banning the importation of concentrates from the USA unless there was definite evidence that this was necessary. An undated file copy of a letter from Lord Glenarthur to the Society sets out the points made at the meeting.<sup>113</sup> He commented that, in considering whether the import of blood products from the USA should cease, it was deemed necessary to weigh the possible risks of infection from AIDS against the obvious risks arising from inadequate supplies of Factor VIII.<sup>114</sup>

**12.72** On 10 September 1983, the UKHCDO surveillance of AIDS in coagulation disorder patients was updated. The 'Cardiff patient', reported in the CDSC bulletin of 6 May as a possible case of AIDS, remained reasonably well. The 'Bristol patient', however, had been unwell through June and July and died in August. This was considered to be the first confirmed case of death from AIDS in the UK associated with blood products. Both cases were reported to the Haemophilia Centre Hepatitis Working Party on 14 September 1983<sup>115</sup> and to a meeting of the Haemophilia Reference Centre Directors on 19 September 1983.<sup>116</sup>

<sup>107</sup> CDSC Report for week ending 6 May 1983.

<sup>108</sup> 'Surveillance of the acquired immune deficiency syndrome in the United Kingdom, January 1982–July 1983', *British Medical Journal*, 1983; 287:407–408 [LIT.001.0232]

<sup>109</sup> See reference to this case in Dr Craske's update in September 1983 [SNB.001.7556]. The case was also highlighted in a letter to *The Lancet* of 19 November 1983 [LIT.001.0413].

<sup>110</sup> 'Haemophilia Centre Directors AIDS Investigation – Surveillance of AIDS Cases in Patients With Blood Coagulation Disorders' [SNB.001.7556]. Preliminary Report, paragraph 8.48

<sup>111</sup> Minutes of Central Committee for Research and Development in Blood Transfusion, 21 June 1983 [PEN.016.1156]

<sup>112</sup> Lord Glenarthur was Joint Parliamentary Under Secretary of State at the DHSS. The identity of the recipient of the letter has been removed by redaction [DHF.001.4691].

<sup>113</sup> Letter DHF.001.4573]

<sup>114</sup> At the meeting of the Biological Sub Committee of the CSM on 13 July, it had been commented that concentrates from the USA to be used in the UK should be derived from plasma complying with the new FDA regulations of 23 March 1983, provided supply could be assured. See [DHF.002.8865] at 8866.

<sup>115</sup> Minutes of the 12th Meeting of the UK Haemophilia Centre Directors' Hepatitis Working Party held at the Oxford Haemophilia Centre on 14 September 1983 [LOT.003.5434]

<sup>116</sup> Minutes [LOT.003.2862]

**12.73** The UKHCDO Hepatitis Working Party report for 1982–83 was produced on 28 September 1983 under the chairmanship of Dr Craske.<sup>117</sup> It commented on the possible contamination of plasma by a putative AIDS-related agent as a complication. It reflected the views Dr Craske had previously expressed that, at that stage, the existence of an infective AIDS agent was considered to be unproven but, if an infective agent existed, all source material might be infected by it, as was the case for the non-A, non-B Hepatitis virus. The dilemma for clinicians prescribing therapy was expressed but not resolved.

**12.74** On 17 October 1983, the UK Haemophilia Centre Directors held their 14th meeting, in Manchester.<sup>118</sup> By then, information about one of the haemophilia patients, treated in Bristol, had been published in *The Guardian* and Dr Geoffrey Scott, from Bristol, attended the meeting. There was, therefore, first-hand information available about the patient who had died there, although the record does not disclose whether Dr Scott contributed to the meeting. Dr Morag Chisholm of Southampton raised the problem of patients refusing to take up commercial Factor VIII concentrate because of the AIDS scare and wondered whether they could revert to cryoprecipitate for home therapy. Other Directors voiced similar concerns. Professor Bloom replied to Dr Chisholm:

[T]hat he felt that there was no need for patients to stop using the commercial concentrates because at present there was no proof that the commercial concentrates were the cause of AIDS .... After discussion it was agreed that patients should not be encouraged to go over to cryoprecipitate for home therapy but should continue to receive the NHS or commercial concentrates in their usual way.<sup>119</sup>

### ***Reaction to a World Health Organization Meeting on AIDS in November 1983***

**12.75** The World Health Organization (WHO) met in Geneva between 22 and 25 November 1983 to discuss AIDS. The draft report of the meeting contained a section on the prevention and control of AIDS. In relation to blood and blood products, it stated:

AIDS cases have infrequently occurred in both hemophiliacs receiving clotting factor concentrates and in recipients of blood and blood component transfusions who do not have other apparent risk factors. Approaches to reducing the possibility of spreading AIDS by blood and blood products include: ... avoiding non-essential use of blood and blood products ... and preparing and using blood and blood products in such a way as to reduce the risk of transmitting AIDS.<sup>120</sup>

**12.76** The topic was developed in the paper:

Immunoglobulin and albumin prepared by generally accepted methods have not been implicated in AIDS and are considered safe. Coagulation factor concentrates, however, have been implicated in cases of AIDS. Although additional inactivation methods have recently been developed, it will not be possible to fully establish their effectiveness until the agent of AIDS is discovered.<sup>121</sup>

<sup>117</sup> See [SNF.001.0948]. This is labelled Appendix C. AIDS is mentioned in Appendix C(i).

<sup>118</sup> Minutes of the 14th meeting of UK Haemophilia Centre Directors held on Monday 17 October 1983 SNB.001.7517]

<sup>119</sup> Ibid [SNB.001.7517] at 7526. (Emphasis in original)

<sup>120</sup> 'Acquired Immunodeficiency Syndrome, an assessment of the present situation in the world'; draft report dated 12 December 1983 [SNF.001.2575] at 2592

<sup>121</sup> Ibid [SNF.001.2575] at 2594

**12.77** The association of factor concentrates with AIDS risk was acknowledged and unchallenged, so far as the draft report discloses, although continued use of concentrates was clearly envisaged. The alternative methods available for reducing risk were: reducing pool sizes; adopting process technology aimed at reducing contamination risks; and adopting specific donor/recipient practice, especially in the case of those newly diagnosed with haemophilia and requiring only infrequent therapy.

**12.78** On 5 December 1983, Dr McClelland, Director of the South East Scotland Blood Transfusion Service, prepared an initial report on the conference, for the Scottish RTDs' Meeting of 8 December.<sup>122</sup> He noted that the WHO meeting was chaired by Walter Dowdle and was heavily influenced by him, Dr Curran and Dr Francis, all three from the CDC. The association of factor concentrates with AIDS appeared to Dr McClelland, at the time, to have been exaggerated by them. He reported that the NIH had issued practice directions for follow-up of recipients of blood and blood products in the USA.

**12.79** In his report, Dr McClelland commented on steps that might improve safety for individual recipients of therapy, such as the use of small pool concentrates and batch dedication, in particular for those who were newly diagnosed and required only infrequent therapy. The evidence adduced at the conference was primarily related to experience in the USA. Dr McClelland's observations as a Transfusion Director indicate that there was still not unqualified acceptance of the infective agent theory in the UK by the end of 1983. Publications at the end of that year appear to confirm this.

#### *The requirement for a very high standard of proof*

**12.80** In an editorial published in the *British Medical Journal (BMJ)* of 10 December 1983, Dr Peter Jones, Newcastle Haemophilia Centre, reflected one extreme in the developing views among haemophilia clinicians of the risks associated with the therapeutic use of blood products.<sup>123</sup> The introductory paragraph set the tone:

People with haemophilia, their families, and their doctors feel threatened by the deluge of speculation about the possible side effects of treatment with blood products. Two topics hold their attention: the risk of contracting the acquired immunodeficiency syndrome (AIDS) and the risk of developing hepatitis and subsequent chronic liver disease.

**12.81** Characterising the risk of AIDS as a speculative possibility reflected the approach of Dr Kernoff at the beginning of the year and was not dissimilar to the DHSS view then prevailing. However, that view was becoming less sustainable in December, having regard to increasing knowledge of the characteristics of the disease and its prevalence.

**12.82** Dr Jones stated that the incidence of AIDS among haemophilia patients in the UK and USA was about 0.8 per thousand. He suggested as a possibility the idea that what had been seen in haemophilia patients was an entirely different disorder from that seen in homosexuals, caused by 'repeated antigenic challenge over many years' (the antigen overload theory) rather than by a transmissible agent.<sup>124</sup>

<sup>122</sup> Initial report for the Scottish Regional Transfusion Directors' meeting on 8 December 1983 [SNF.001.0552]

<sup>123</sup> Jones, 'Acquired immunodeficiency syndrome, hepatitis and haemophilia', *British Medical Journal*, 1983; 287:1737-1738 [LIT.001.0243].

<sup>124</sup> *Ibid* [LIT.001.0243] at 0244

**12.83** He posed the question: what risk is there of serious harm from haemophilia treatment? With limited exceptions, he considered that there was no justification for discontinuing the use of concentrates and that 'the risk of haemorrhage and its complications far outweighs the risk of developing AIDS'. Implicitly accepting the alternative aetiology – the transmissible agent theory – he said, in relation specifically to imported concentrates:

The commercial companies in the United States acted responsibly and quickly to exclude high risk donors, and similar action has now been taken in Britain

....<sup>125</sup>

**12.84** Dr Jones stated that, while there was anxiety about AIDS, the advice from Reference Centre Directors and the Haemophilia Society was to carry on with Factor VIII treatment.<sup>126</sup> He advised that, since no Factor VIII could be guaranteed AIDS-free, cryoprecipitate should be used to treat very young severely affected children and other options (DDAVP or porcine Factor VIII) should be used for older people with mild haemophilia or von Willebrand's disease and carriers of these disorders. The comments in the editorial reflected the view already advanced by Professor Bloom that AIDS required no significant change to therapy, save for particular groups of patients.

**12.85** Dr Jones' views were reported in *The Guardian* on 9 December 1983.<sup>127</sup> There was a further comment by Andrew Veitch, medical correspondent, relating to the two cases of AIDS in haemophilia patients that had by then been confirmed.<sup>128</sup> Mr Veitch reported the two cases and noted that the affected patients were thought to have contracted the disease from contaminated supplies of Factor VIII imported from the USA. He referred to emerging data from Germany on infection within the homosexual community, confirming fears that AIDS had arrived in Europe from the USA two years earlier. He quoted Dr Jones' comment that alternatives to concentrates should be used to treat very young, severely-affected children and older people with mild forms of haemophilia. Overall, the article reflected views somewhat less sanguine than those expressed by Dr Jones.

**12.86** On the other hand, there was a constituency of opinion among haemophilia clinicians, represented by Dr Winter at this Inquiry, which took a more pessimistic view of the risks associated with concentrate therapy but often could not practically adapt clinical practice to reflect their opinions on risk. He thought that as information of an association between factor therapy and AIDS was published, the practical necessity of using imported products induced a state of denial in some haemophilia clinicians:

[I]f you like, the clinicians didn't want to believe any of this data, because we have just been through such a very major advancement in healthcare .... In America it was the same .... There were lots of political issues around that. So none of the related agencies wanted to know this. That's why ... I'm sure, this data took some time to really hit home.<sup>129</sup>

<sup>125</sup> Ibid [LIT.001.0243] at 0244

<sup>126</sup> Ibid [LIT.001.0243]

<sup>127</sup> *The Guardian* [SGF.001.0944]

<sup>128</sup> Quoted in Chapter 9, *Knowledge of the Geographical Spread and Prevalence of HIV/AIDS 1*, paragraph 9.141

<sup>129</sup> Dr Winter – Day 16, pages 28–29. A similar view was expressed by Professor Lever – Day 26, page 111. Professor Ludlam, who himself appears to have supported the antigen overload theory longer than many others, agreed that Dr Aledort found it particularly difficult to accept the possibility of a viral aetiology, even in the face of mounting evidence supporting that theory. Day 18, page 115

**12.87** However, as noted above, he also commented that many clinicians, even if they did accept the transmissible agent theory, thought that they could not change practice, given the benefits of factor concentrate therapy.<sup>130</sup> There were fundamental practical issues relating to the choice of therapeutic product for haemophilia treatment.

**12.88** There is no basis for a view that clinicians were deliberately suppressing or ignoring data on transmission in commenting on the use of concentrate therapy. It appears, rather, that those who promoted the continuing use of imported Factor VIII could not accept the conclusions resulting from those data. The problem was possibly that noted in relation to the workshop in January 1983 in Atlanta: too high a standard of proof was set. Full scientific proof according to accepted norms was impossible.<sup>131</sup>

**12.89** The official view of the cause of AIDS, as expressed by DHSS Ministers and officials throughout 1983 and into 1984, was essentially a negative view, that there was 'no conclusive proof' or 'no conclusive evidence' that AIDS was transmitted through blood products. That is discussed in Chapter 9, *Knowledge of the Geographic Spread and Prevalence of HIV/AIDS 1*, paragraphs 9.108–9.123. So far as it is possible to understand the published statements made at the time, they are consistent with what Professor Hann agreed was a requirement for a very high standard of proof.<sup>132</sup> Such a high standard was not met by a contemporaneous observation in a DoH publication that AIDS was 'almost certainly' transmissible by transfusion of blood and blood products.<sup>133</sup> The official government view at the end of the year was expressed in a letter dated 13 December 1983 written by Lord Glenarthur to John Maples MP, who had enquired about the government's assessment in light of recent press reports. It stated that the cause of AIDS was as yet unknown and there was no conclusive proof that the disease had been transmitted by US blood products. The practical situation was set out:

[T]he Government is committed to making this country self-sufficient in blood products .... Meanwhile, in the absence of a satisfactory alternative, we shall be dependent upon imports from the USA for an adequate supply of Factor VIII.<sup>134</sup>

**12.90** Professor Lever was asked to comment, with the benefit of hindsight, on the point at which there required to be a reassessment of the risk/benefit balance involved in the use of therapeutic products.<sup>135</sup> In summary, he pointed to two factors of importance as triggers of reassessment: evidence of immunosuppression associated with therapy and evidence of death from immunosuppression.<sup>136</sup> As far as the first of those is concerned, a haemophilia patient in Cardiff had become ill with suspected AIDS by the beginning of May 1983. Profound immunosuppression in the east and west of Scotland patients had been established by the studies carried out in 1983. A fatal outcome after immunosuppression in haemophilia was known from the middle of September 1983. The scene was set for review of current therapy.

<sup>130</sup> Dr Winter – Day 16, page 30

<sup>131</sup> See Chapter 11, *AIDS Aetiology*, paragraphs 11.28–11.35 and paragraph 12.7 above.

<sup>132</sup> Professor Hann – Day 21, page 51. He described such statements as, in retrospect, 'political' and as 'intended to be ... very reassuring' but said that he 'wasn't personally very reassured.' Day 21, page 50

<sup>133</sup> Leaflet – 'AIDS and how it concerns blood donors' [SGH.002.6675] at 6676

<sup>134</sup> The Archer Inquiry Report, pages 51–52

<sup>135</sup> Day 27, pages 24–31

<sup>136</sup> Ibid page 26

### *Views of the Haemophilia Society in early 1984*

**12.91** On 9 January 1984, the Blood Products Sub-committee of the Haemophilia Society produced a paper reviewing blood products supply and related issues in England and Wales.<sup>137</sup> While the Sub-committee is likely to have had expert help, the paper illustrates the response of one interested community to scientific developments at the time. On the topic of AIDS, the paper repeated the position that no infective agent had been identified for AIDS and that there was no reliable evidence that the disease was transmitted through blood products. However it commented that if AIDS was so transmitted:

[T]he 'Mail on Sunday' reasoning – that importation of American blood products should cease<sup>138</sup> – may prove to be an over-simplification, as AIDS could still be transmitted from the British donor population. Certainly the immunological abnormalities which may be associated with AIDS are observable in haemophiliacs not exposed to commercial concentrates [e.g. in Scotland and Australia].<sup>139</sup>

**12.92** After discussion, it concluded that:

[T]here are no grounds for favouring NHS Factor VIII over commercial materials in the respects we have in the past considered relevant. In addition, of course, the marginal factors of stability and more convenient presentation favour commercial material.<sup>140</sup>

**12.93** It is of interest that the second well-documented case of AIDS, that of a patient in Cardiff, does not appear to have been acknowledged at this point. The paper reflected a view, still held by at least some haemophilia clinicians at the time and in particular by the Society's advisers, that factor concentrate therapy for haemophilia patients should continue, including the use of imported products.

**12.94** As a practical matter, with the exception of Scotland (and Northern Ireland when supplied from Edinburgh), there was no reasonable prospect of avoiding the use of imported commercial products in the UK as a whole during the first five months of 1984 if factor concentrate therapy was to continue. The Blood Products Sub-committee paper of 9 January 1984 commented on the rising trend of demand from 1975–82,<sup>141</sup> which showed no sign of levelling off. The proportion of total usage represented by NHS products fluctuated over the period but the critical factor was the use of commercial products. Never less than 54%, in the last four years of the period use of commercial products was consistently over 60% and in 1982 reached 66.6%. At that stage production at BPL was near its target of 30 million units. The paper noted:

[W]e must be somewhat doubtful that NBTS could achieve the requirement, stated by the UK Haemophilia Centre Directors, of 100 million units by the middle of the present decade.<sup>142</sup>

<sup>137</sup> Haemophilia Society Report [DHF.001.5151] The paper refers in terms to 'the United Kingdom' but the context indicates that the data referred to were not UK data.

<sup>138</sup> See Chapter 9, *Knowledge of the Geographic Spread and Prevalence of HIV/AIDS 1*, paragraph 9.85

<sup>139</sup> Haemophilia Society Report [DHF.001.5151] at 5154. Ludlam et al, 'Disordered Immune Regulation in Haemophiliacs not exposed to Commercial Factor VIII'. *The Lancet*, 1983: 1226 [LIT.001.0416]. Froebel et al, 'Immunological abnormalities in haemophilia: are they caused by American factor VIII concentrate?': *British Medical Journal*, 1983; 287:1091–109 3; [LIT.001.0215]. Rickard et al, 'Absence of AIDS in Haemophiliacs in Australia treated from an entirely Voluntary Blood donor System', *The Lancet*, 1983: 50–51 [LIT.001.0414].

<sup>140</sup> Haemophilia Society Report [DHF.001.5151] at 5154

<sup>141</sup> *Ibid* [DHF.001.5151] at 5157

<sup>142</sup> *Ibid* [DHF.001.5151]

**12.95** The Haemophilia Society's own projection of demand – 145 million units in 1985 rising to 178 million units in 2000 – was much higher than the Haemophilia Directors' estimate. On any view, the inevitable inference drawn by the paper was that the 'UK' – by which the Society must have meant England and Wales – would have to rely on imported Factor VIII 'for a very long time'.<sup>143</sup> The situation in Scotland was quite different and is discussed below, beginning at paragraph 12.124.

**12.96** The paper set out arguments in favour of imported products, covering ethical and financial factors as well as risk of infection. At that stage, there appears to have been little apprehension among those responsible for the paper that the use of imported products carried a high level of risk.

**12.97** In relation to AIDS and blood products, it stated:

The AIDS scare has given us the opportunity, which we have not yet utilised, to campaign strongly for self-sufficiency in blood products. Given, however, that the original factors in our policy no longer apply or have reduced force, and that AIDS is still a great unknown, I submit that we should not undertake such a campaign. Now is not the time to ask that all our blood-product 'eggs' should be placed in one basket. Instead, without necessarily abandoning our long-term objectives, we should take Mr Asquith's advice 'Wait and see'. When more facts emerge about AIDS we would then be in a better position to press for whatever action these facts seem to demand.<sup>144</sup>

### *Developments in 1984: the impact of HTLV-III infection*

**12.98** As noted above, on 23 April 1984 Dr Robert Gallo and his team announced the discovery of HTLV-III.<sup>145</sup> The identification of the virus is more fully discussed in Chapter 29, *The Discovery of HIV and the Development of Screening Tests*. Although it appears that some commentators remained of the view that the AIDS in haemophilia patients might be caused, not by the virus announced by Gallo and his team (or, indeed, that announced by Montagnier a year earlier), but by some other mechanism (such as antigen overload) it is reasonably clear that most accepted that the HTLV-III discovery pointed very clearly towards the infective agent theory. Professors Weiss and Tedder had been working on a screening assay for several months, using French virus obtained from Luc Montagnier,<sup>146</sup> and a prototype assay was ready for laboratory application on 4 July 1984, allowing them to begin epidemiological studies.<sup>147</sup> It took several months to develop an HIV test kit for general use, as discussed in Chapter 30, *Screening of Donated Blood for HIV*. In the meantime, however, many haemophilia clinicians had begun to submit samples to Professor Tedder.

**12.99** As noted above, in the last three months of 1984 the reality of HTLV-III infection in a significant proportion of Haemophilia A patients was brought home to clinicians, and the wider scientific and medical community, when test results became available.<sup>148</sup>

<sup>143</sup> Ibid [DHF.001.5151] at 5152

<sup>144</sup> Ibid [DHF.001.5151] at 5155

<sup>145</sup> Gallo et al, 'Frequent detection and isolation of cytopathic retroviruses (HTLV III) from patients with AIDS and at risk for AIDS', *Science*, 1984; 224:500–503 [LIT.001.3769]; Popovic et al, 'Detection, Isolation, and Continuous Production of Cytopathic Retroviruses (HTLV-III) from Patients with AIDS and Pre-AIDS', *Science*, 1984; 224. (reprint) [SNB0049457] See also Chapter 29, *The Discovery of HIV and the Development of Screening Tests*, paragraphs 29.11–29.14.

<sup>146</sup> Day 48, page 6; Letter from Professor Weiss to the Inquiry on the development of HIV screening tests [PEN.017.1261] at 1263

<sup>147</sup> Professor Tedder – Day 49, pages 15–16

<sup>148</sup> See paragraph 12.25 for the effect of publication of the Cheingsong-Popov article on 1 September 1984.



By October 1984, many Haemophilia Directors, including Professor Ludlam, Dr Winter and Dr Kernoff, had already had samples tested by Professor Tedder. Professor Forbes had samples tested by Dr Gallo. Many, if not all, Directors knew that some of their patients were infected with HTLV-III. All but one of Dr Winter's patients, about 30 in total, were infected.<sup>149</sup>

**12.100** In a letter dated 23 October 1984, Dr Craske reported that it had been confirmed that a donor who had provided plasma used in the preparation of a batch of Factor VIII concentrate had been admitted to hospital with AIDS. The letter was concerned mainly with Dr Craske's interests as a public health doctor and discussed the need for follow-up.<sup>150</sup> He referred, however, to the likelihood that any patient who had received commercial Factor VIII since 1980 had possibly already been exposed to HTLV-III.<sup>151</sup>

**12.101** A meeting of the UK Haemophilia Reference Centre Directors was held on 10 December 1984, chaired by Professor Bloom.<sup>152</sup> He introduced the meeting by referring to recent events in Newcastle and Australia 'and the continuing work on HTLV III'. The most extensive record of discussions available indicates that this was a major strategic meeting.<sup>153</sup> 'Events in Newcastle' included the death of a haemophilia patient who had contracted AIDS.<sup>154</sup> Apart from a comment attributed to Dr Ludlam, the record does not disclose a report of the cases of infection in Glasgow and Edinburgh, though from subsequent events it appears that the position in Edinburgh at least must have been disclosed.<sup>155</sup> After extensive discussion of HTLV-III antibody tests and their significance, Professor Bloom's summary was that HTLV-III antibody-positive haemophilia patients should be considered a risk but that it could not be assumed that those who were apparently HTLV-III antibody-negative were not, in fact, infective.<sup>156</sup> That appears to have set the scene for a discussion of clinical implications.

**12.102** It was anticipated that by the end of December 1984 or very early in 1985, Scotland would be self-sufficient in heat-treated concentrate. However, discussion proceeded to the availability and use of heat-treated Factor VIII more generally. It was reported that there was not a sufficient supply of NHS heat-treated concentrate to meet demand. In some circumstances the alternative to avoiding non-heat-treated concentrate would be that there would be no treatment. Professor Bloom summarised a long discussion by commenting that it was difficult to avoid the argument that non-heat-treated concentrate constituted a risk.

**12.103** According to an alternative record of the meeting, after prolonged discussion it was agreed that children should be treated with cryoprecipitate or if necessary with heat-treated Factor VIII.<sup>157</sup> New haemophilia patients should be treated with heat-treated Factor VIII. It was not proven that heat-treatment inactivated HTLV-III; nevertheless Directors felt that they should use commercial heat-treated Factor VIII in preference

<sup>149</sup> Day 15, pages 43–44

<sup>150</sup> Letter from the Public Health Laboratory Service dated 23 October 1984 and Report [SNF.001.4020]

<sup>151</sup> Letter [SNF.001.4020] at page 4024

<sup>152</sup> Records of meeting in [DHF.003.0898] and [SNF.001.3850].

<sup>153</sup> Notes of the Haemophilia Reference Centre Directors Meeting Blood Products Laboratory [SNF.001.3850]

<sup>154</sup> Record of meeting [DHF.003.0898] at 0900

<sup>155</sup> Notes of the Haemophilia Reference Centre Directors Meeting Blood Products Laboratory [SNF.001.3850] at 3853. See Chapter 33, *An Investigation into the Systems in Place for Informing Patients about the Risks*, paragraphs 33.303–33.308: It appears that details of the meeting were leaked to a journalist from *The Yorkshire Post* and that this included the report of infection in Edinburgh haemophilia patients.

<sup>156</sup> Ibid [SNF.001.3850] at 3853

<sup>157</sup> Meeting of the Haemophilia Reference Centre Directors, 10 December 1984 [DHF.003.0898]

to commercial non-heat-treated Factor VIII. Dr Jones reported to the meeting that at Newcastle all concentrate used was heat-treated commercial product. There had been no other change in therapy apart from holding back on prophylaxis for children on home therapy.<sup>158</sup> The Reference Directors agreed that heat-treated product should be given to all patients, if freely available.<sup>159</sup> The commercial products on the market were reviewed.<sup>160</sup> Most agreed to use non-heat-treated product until heat-treated product was available from BPL, although Dr Jones refused to do so, stating that all of his patients would have 'safe' heat-treated Factor VIII.<sup>161</sup>

**12.104** It was anticipated that this guidance would cause severe financial problems for treatment centres in England since the newly introduced US commercial heat-treated Factor VIII concentrate was more expensive.<sup>162</sup>

**12.105** There followed a discussion of the need to control the arrangements for the use of unlicensed products as it was felt that the rules at that time allowed companies to exploit the named patient system. In discussion of the availability and use of heat-treated Factor VIII, Professor Cash, Medical Director of the SNBTS, urged that the financial consideration be looked at seriously. Notwithstanding the small number of patients involved, the cost of imported heat-treated factor products would be high.<sup>163</sup> The regulatory bodies would also need to consider applications for variation orders on existing licences and to determine whether the products were new formulations requiring new licence applications. Commercial companies were being asked to reapply for licences for heat-treated products.<sup>164</sup> The meeting was concerned about the social attitudes being adopted towards AIDS patients and haemophilia patients. The situation was becoming very emotive and common sense was giving way to panic amongst donors, patients and contact groups.<sup>165</sup> Guidelines on treatment were to be issued by Professor Bloom after the meeting.

**12.106** The transmission of infection by the infusion of PFC Factor VIII was established in October 1984 in Edinburgh and the east of Scotland and in or about October 1984 in Glasgow and the west of Scotland. The information shared on 10 December (as summarised in the letter of 14 December referred to below) reflected acceptance of the transmissible agent theory and its association with profound immuno-suppression. Three patients with haemophilia had developed AIDS and two had died. Accordingly, the meeting on 10 December marked a further important juncture in the assessment of appropriate therapy: immunosuppression in haemophilia and its potentially fatal consequences was now definitively associated with NHS product. There was, in the event, a comprehensive reassessment of policy for the treatment of coagulation disorder patients.

**12.107** On 14 December 1984, the UKHCDO produced an 'AIDS advisory document', in consultation with Drs Lane, Cash, Gunson, Mortimer, Tedder, Craske and others.<sup>166</sup> The background information provided included data on infection. In the USA, there had been

<sup>158</sup> Ibid [SNF.001.3850] at 3853

<sup>159</sup> Ibid [SNF.001.3850] at page 3853

<sup>160</sup> Ibid [SNF.001.3850] at page 3856

<sup>161</sup> Ibid [DHF.003.0898] at 0899. By this stage the Newcastle Centre had a very high prevalence of HTLV-III infection as well as a death from AIDS.

<sup>162</sup> Notes of the Haemophilia Reference Centre Directors Meeting Blood Products Laboratory [SNF.001.3850] at 3854

<sup>163</sup> Ibid [SNF.001.3850] at 3856

<sup>164</sup> Ibid [SNF.001.3850] at 3858

<sup>165</sup> Ibid [SNF.001.3850] at 3860

<sup>166</sup> UKHCDO, 'Aids Advisory Document' [SGF.001.2388]

over 6000 cases of AIDS including 52 haemophilia patients. It was said that in the UK there had been 102 cases of AIDS with three reported cases in haemophilia patients and doubtless other cases developing. The information provided on infectivity was:

Antibody positivity probably correlates with exposure to imported concentrates but there have been two notable recent episodes concerning U.K. concentrates.

Antibody tests indicate prior infection but do not imply immunity as antibodies may not be neutralising ....

Antibody positive persons should ... be considered at risk of transmitting or developing AIDS but antibody negativity does not exclude infectivity.<sup>167</sup>

**12.108** The document described the tests available. It proceeded to discuss the inactivation processes currently in use and the processes used in the production of specific concentrates. It set out the options, in 'probable decreasing order of safety from AIDS for Haemophilia A' as:

1. Heated U.K. concentrate (note: still NANB hepatitis risk)
2. Single donor cryo. or FFP
3. Heated imported conc. (note: still NANB hepatitis risk)
4. Unheated U.K. conc.
5. Unheated imported conc – almost certain to be contaminated

...

#### RECOMMENDATIONS

1. Concentrate is still needed; bleeding is the commonest cause of disability and death.
2. Use DDAVP in mild Haemophilia A and vWd if possible.
3. For Haemophilia A needing blood products
  - a. 'Virgin' Patients those not previously exposed to concentrate, and children, use cryo or heated NHS factor VIII (if available)
  - b. Severe and Moderate haemophiliacs previously treated with factor VIII use heat treated NHS factor VIII, if available or heat treated US commercial.
4. Haemophilia B
  - a. Mild Christmas Fresh frozen plasma if possible (otherwise NHS Factor IX.
  - b. 'Virgin' Patients and those not previously exposed to concentrate use fresh frozen plasma (or NHS factor IX concentrate if essential)
  - c. Severe and Moderate Christmas Disease previously exposed to factor IX concentrate continue to use NHS factor IX.

In individual patients there may need to be a choice. In general heated concentrate appears to be the recommendation of virologists consulted but individual Directors may wish to make up their own minds. This is particularly true of unheated NHS material. The evidence that heated U.S. factor VIII is safer than unheated NHS is debateable and some Directors may wish to continue

<sup>167</sup> Ibid [SGF.001.2388] at 2388

using unheated NHS material until all supplies are heated. This is valid for carefully selected patients but must be on individual decision based on the assumption that some batches of NHS materials will be contaminated with HTLVIII. The argument that HTLV III positive patients have already been infected and could receive unheated American material is probably scientifically true but this material would pose an additional risk to staff and families and its continued use would pose logistic problems.<sup>168</sup>

**12.109** In the case of haemophilia B, Professor Ludlam summed up the position in 1984:

I had a few patients with particularly moderate Haemophilia B. That was difficult. I think there was commercial heat-treated Factor IX of unproven safety from a donor pool that was likely to have many more HIV positive donors in it, versus [non-heat-treated] NHS clotting Factor IX. We knew at that stage in December 1984 that the prevalence of anti HTLV-III positivity in Haemophilia B was very much lower than in Haemophilia A, and we presumed that that was because the virus to a large extent was excluded in the manufacturing process, excluded from the final Factor IX product. So Factor IX was seen as a much safer product from the point of view of HTLV-III, even unheated. So the national recommendation was to continue to use unheated NHS Factor IX concentrate in those who had already been exposed to it and to use fresh-frozen plasma in patients who hadn't been exposed to it, if possible. If they had severe new patients with severe haemophilia, they might anyway have to be put on to the concentrate but to use UK concentrate. So it wasn't an entirely black and white issue. It was in a sense slightly easier to not use the heat-treated commercial because the epidemiology at that stage was that patients were much less likely to get infected with anti HTLV-III.<sup>169</sup>

## Clinical response to the emergence of AIDS: Scotland

### *The aetiology of AIDS: competing theories in Scotland*

**12.110** In common with both the USA and England and Wales, as discussed above, until at least June or July 1984 it remained a common view among commentators in Scotland, representing a broad spectrum of medical and scientific expertise, that the cause of AIDS was unknown and that it had not been established, or proved, that it resulted from transmission of a specific agent in blood products. Even after that date, a small number of commentators continued to resist the transmissible agent theory. In Scotland, as already noted, two separate studies in 1983 – led by Professor Ludlam in Edinburgh and the east of Scotland and by Professor Forbes in Glasgow and the west of Scotland – attempted to determine whether the phenomenon of immune abnormalities in haemophilia patients first noted in the USA in 1982 was also occurring in Scottish haemophilia patients.

### Edinburgh research

**12.111** Professor Ludlam explained that he was prompted to conduct his research following the publication of a letter in *The Lancet* by Dr Robert Gordon, NIH, dated 30 April 1983. The letter noted that, by March 1983, eleven cases of clinical AIDS in haemophilia patients had been reported to the CDC. It presented the two principal possible aetiologies

<sup>168</sup> Ibid [SGF.001.2388] at 2389–2390. (Emphasis in original.)

<sup>169</sup> Professor Ludlam – Day 44, pages 41–42

considered at the time: the transmissible agent theory and the immune overload theory. Dr Gordon concluded by suggesting that 'the alternative hypotheses might be distinguished through a study ... among similarly treated haemophiliacs in a geographical area to which AIDS has not yet been introduced'.<sup>170</sup> Professor Ludlam said:

I thought that we were studying individuals with haemophilia who were treated with blood products in what appeared to be an AIDS-free population, and therefore perhaps the results that I was beginning to gather might be able to address the question that Dr Gordon is posing.<sup>171</sup>

**12.112** He carried out his research in the spring of 1983 and found that many of his coagulation disorder patients who were otherwise feeling well had immune abnormalities very similar to those reported from homosexual men and haemophilia patients living in North America.<sup>172</sup> As he saw it, however, it was inappropriate in mid- to late-1983 to make an assumption that the AIDS in people with haemophilia was necessarily of similar aetiology to the AIDS in the other groups. It was known that, clinically, the spectrum of AIDS-related conditions differed to some extent as between the groups and so clinicians considered the possibility that they had arisen simultaneously, or nearly simultaneously, but were of different aetiologies.<sup>173</sup>

**12.113** Professor Ludlam's view in 1983 was that, while his patients had immune abnormalities similar to those reported in homosexual and other populations in the USA, they could not have been infected with an AIDS virus and that, at least in Edinburgh, haemophilia patients' immune disturbances were not due to an AIDS-causing agent.<sup>174</sup> In a letter to *The Lancet* dated 28 May 1983, reporting on his research, Professor Ludlam expressed confidence in the local blood supply and, subsequent to this, explicitly endorsed the 'antigen overload' hypothesis as a possible explanation for the immune irregularities he had observed in his haemophilia patients:

Since there are no known cases of AIDS in our blood donor population it seems likely that the immunosuppression observed in haemophiliacs ... results from infusion of foreign proteins or a ubiquitous virus rather than a specific AIDS virus in factor VIII concentrates.<sup>175</sup>

**12.114** In due course it emerged that there were three sub-sets among the patients with lymphocyte abnormalities in the study group: those with abnormal immune systems who were subsequently shown to be infected with HIV; those with abnormal immune systems who were not infected with HIV; and those with normal immune systems who were infected but in whom changes in the immune system had not yet begun.<sup>176</sup>

<sup>170</sup> Gordon, 'Factor VIII Products and Disordered Immune Regulation', *The Lancet*, 30 April 1983 [LIT.001.0911]

<sup>171</sup> Day 19, pages 14–15

<sup>172</sup> Day 35, page 21; Chapter 11, *HIV/AIDS Aetiology*, paragraphs 11.65–11.72; Professor Ludlam's Statement [PEN.015.0445] at 0448. Ludlam et al, 'Disordered immune regulation in haemophiliacs not exposed to commercial Factor VIII', *The Lancet*, 28 May 1983 [LIT.001.0416]. Carr et al 'Abnormalities of Circulating Lymphocyte Subsets in Haemophiliacs in an AIDS-Free Population', *The Lancet*, 30 June 1984; 1431–1434 [LIT.001.0425]

<sup>173</sup> Chapter 11, *AIDS Aetiology*, paragraphs 11.42–11.43

<sup>174</sup> Day 19, page 18; Day 19, page 21; Chapter 11, *HIV/AIDS Aetiology*, paragraph 11.85

<sup>175</sup> Ludlam, 'Disordered immune regulation in haemophiliacs not exposed to commercial Factor VIII', *The Lancet*, 28 May 1983 [LIT.001.0416]

<sup>176</sup> Day 19, pages 18–20. Ludlam, et al, 'Human T-Lymphotropic Virus Type III (HTLV-III) Infection in Seronegative Haemophiliacs After Transfusion of Factor VIII', *The Lancet*, 3 August 1985 [SNB.008.3434] at 3436

**12.115** Professor Ludlam noted that there was ‘much speculation’ as to the cause of the immune irregularities observed in haemophilia patients.<sup>177</sup> In oral evidence he noted that the immune system ‘has only a number of limited ways’ of responding to ‘provocation’ and that, therefore, there were ‘lots of possible reasons why you can get these immune changes’.<sup>178</sup> The possibilities considered were: (i) that immune disturbance could have been a previously undescribed feature of haemophilia; (ii) that chronic liver disease (and many haemophilia patients had contracted hepatitis viruses by transfusion) had caused changes in patients’ immune systems; (iii) that large amounts of proteins other than Factor VIII/IX present in blood products for the treatment of haemophilia had disordered patients’ immune systems (the antigen overload theory); and (iv) that the immune changes observed could have been caused by a putative AIDS virus (the transmissible agent theory).<sup>179</sup> He stated that, at the time, he and others tended to believe that the antigen overload theory was particularly convincing, although he did not dismiss the transmissible agent theory entirely:

Of the four principal causes for immune modulation in haemophiliacs there was general agreement that it was due, at least in part, to the extraneous non-factor VIII proteins in the concentrates. Some of the immune disturbances might in addition be due to the presence of a putative AIDS virus in some patients.<sup>180</sup>

**12.116** In oral evidence, he suggested that the results of his studies ‘cast doubt over the extent of infection with a putative virus in other patients with haemophilia elsewhere in the world. That was one of the inferences from this’.<sup>181</sup> Indeed, his research supporting the antigen overload theory was to receive international attention and form part of the evidence base for international debate around the aetiology of AIDS. At a joint meeting of the World Federation of Haemophilia and the International Society on Thrombosis and Haemostasis in June 1983, discussed above, the response of US delegates to the suggestion that commercial concentrates manufactured in North America might be ‘bad news’ (implying that they might be contaminated with an AIDS-causing virus) was ‘to cite Ludlam *et al*’ and cast doubt upon the data implicating commercial products. Dr Foster, who attended the meeting, thought at the time that there was in this ‘something of an attempt to suppress AIDS “hysteria”’ but that some of the arguments put forward ‘did appear to make some sense’.<sup>182</sup>

**12.117** In oral evidence, Professor Ludlam summarised the thinking behind the antigen overload theory:

I calculated ... that in an average lifespan, you gave out a kilogramme of protein intravenously in an average severe haemophiliac. We are not designed to accept proteins in that magnitude intravenously. So one possibility was that ... maybe haemophilia as a whole was sliding into AIDS because of all the concentrate we were using. Quite separate from HIV or a putative virus.<sup>183</sup>

<sup>177</sup> Prof Ludlam – Human Immunodeficiency Virus Infection in Haemophiliacs [PEN.015.0385] at 0401; Day 19, page 18

<sup>178</sup> Day 19, page 17

<sup>179</sup> Prof Ludlam – Human Immunodeficiency Virus Infection in Haemophiliacs [PEN.015.0385] at 0401–0405. In another statement on contemporaneous thoughts on the possible aetiology of AIDS, Professor Ludlam suggested, in addition to the aetiologies noted above, that it was briefly considered that a previously identified virus (such as the Hepatitis B virus) might have mutated to cause immunosuppression; that a virus (such as CMV or EBV) already known to cause immune suppression had become more ‘virulent’; and the use of recreational drugs (such as amyl nitrate).

<sup>180</sup> Prof Ludlam – Human Immunodeficiency Virus Infection in Haemophiliacs [PEN.015.0385] at 0405.

<sup>181</sup> Day 19, page 17

<sup>182</sup> Dr Foster’s memo [SNF.001.3714]

<sup>183</sup> Day 18, page 150

## Glasgow research

**12.118** There was similar research in Glasgow, published in October 1983.<sup>184</sup> Professor Forbes' research group also found an association between the administration of large amounts of Factor VIII concentrate and the immune process, which was suppressed in many patients and presumed by the research group to be caused by something in the concentrate they were given. He thought that there was a mystery, not resolved even now; as with Professor Ludlam's group, it was to transpire, when HIV testing became available, that not all of the haemophilia patients in his group with immune irregularities were HIV-positive at the time of the initial research. His comment was:

I think it was probably accurate to say that there were abnormalities but what they meant, we didn't know, and of course, some of it probably was that they were infected with the unknown virus, HIV. So we were looking for something but we didn't know what we were looking for at the time.<sup>185</sup>

**12.119** The report of this research suggested gradual diminution of the patients' ability to resist infections or neoplasms (tumours) as a possible consequence of repeated injection. As Professor Forbes recalled, he and his colleagues 'guessed it probably was some kind of virus that we had never encountered before'.<sup>186</sup>

## A spectrum of opinion

**12.120** In Scotland as internationally, then, from the initial reports of immune irregularities in various cohorts of patients, there was a spectrum of opinion as to the aetiology of AIDS. Shortly before his appointment at Yorkhill, Professor Hann attended the Second International Symposium of Infections in the Immunocompromised Host, held in Stirling in June 1982. Despite not originally being included amongst the topics for discussion, AIDS was 'the talk of the meeting', although discussion was characterised by 'extreme' puzzlement. Various aetiologies for the new and alarming condition were presented at that conference, including cytomegalovirus infection alongside hereditary factors and amyl nitrate use.<sup>187</sup> Professor Hann noted that the proceedings of the symposium made only passing reference to the possibility of transmission by blood and blood products<sup>188</sup> but, in oral evidence, said that 'it was thought most likely that there may have been a new agent, a new viral agent, but that may well not be the only cause'.<sup>189</sup> Although he adapted practice at Yorkhill upon his appointment, at least in part due to concerns about AIDS, this appears, at least in the earlier stages of the epidemic, to have been based on precaution rather than firm scientific evidence implicating blood and blood products:

My memory ... is that it was not plainly obvious at this time [early 1983], until later that year... and I would say the second half of that year ... that this was a blood product transmitted issue in haemophilia.<sup>190</sup>

<sup>184</sup> Froebel et al, 'Immunological abnormalities in haemophilia: Are they caused by American Factor VIII concentrate?' *British Medical Journal*, 1983; 287: 1091–1093 [LIT.001.0215] See Chapter 11, *HIV/AIDS Aetiology*, paragraphs 11.73–11.75

<sup>185</sup> Day 17, page 90

<sup>186</sup> Ibid page 97

<sup>187</sup> Comments from Professor Hann on excerpts from the 2nd International Symposium of Infections in the Immunocompromised Host [PEN.015.0270]

<sup>188</sup> Ibid [PEN.015.0270] The paper in question suggested that 'blood or body secretions would appear to be potential vehicles of infection' [LIT.001.3668] at 3691–2

<sup>189</sup> Day 21, page 45

<sup>190</sup> Day 31, page 16

**12.121** According to Professor Forbes, he and his colleagues guessed that the observed immune irregularities in haemophilia patients were caused by a novel virus. For much of 1983, that remained a controversial view, however; there was, he noted, 'still a lot of doubt about it and many people didn't believe it was an infective agent'. It took time for proof of a viral aetiology to emerge and he thought that 'all this was speculation at the time'. He thought, however, that as 1983 progressed, a viral aetiology for AIDS in haemophilia patients 'rapidly' became clear and that, over the course of the year, 'most people' came to accept that AIDS was caused by transmission of an infective agent.<sup>191</sup>

**12.122** Professor Ludlam appears to have resisted the infective agent hypothesis longer than some others: neither increasing numbers of haemophilia patients exhibiting immune irregularities (in the USA, the UK and elsewhere) nor specific cases (such as 'the San Francisco child')<sup>192</sup> were, for him, 'clinching events' sufficient to prove to his satisfaction that AIDS was transmissible by blood products. Although he acknowledged the significance of these developments, he thought that the antigen overload hypothesis was 'still on the table' for much of 1983.<sup>193</sup> As early as July 1982, he had accepted that a viral aetiology 'had to be a possibility'.<sup>194</sup> In oral evidence, however, he agreed that for him it may have been as late as January 1984 that he fully accepted that the antigen overload hypothesis was 'increasingly less tenable'.<sup>195</sup> He agreed that, following the identification of LAV in May 1983, he continued to prefer the antigen overload theory. A further article on the Edinburgh research was published in June 1984, again showing a preference for the antigen overload theory. This was, however, around the same time as Gallo and colleagues announced the discovery of HTLV-III. Asked how he had reacted to the discovery of HTLV-III, which pointed clearly towards the transmissible agent theory as being correct, undermining his previously held conviction, Professor Ludlam replied:

I had no difficulty in accepting and it was very welcome news that a virus had been identified, absolutely.<sup>196</sup>

**12.123** In general, it appears that, as Dr Winter (and Professor Forbes) suggested, 1983 saw a 'gradation' of opinion and 'gradual acceptance that [AIDS] couldn't just be put down to immunological-based theories and that the epidemiology looked more and more like an infectious agent'. As noted above, even the discovery of HTLV-III was not sufficient for a minority of commentators to fully accept the infective agent hypothesis, although the discovery of HTLV-III was clearly the fundamental development in the aetiology debate for a great many interested parties.

### ***Confidence in domestic product and supply***

**12.124** Attitudes towards the choice of therapeutic materials for coagulation disorder patients in Scotland at this time appear to have reflected the confidence in NHS products and in the availability of supply of those domestically sourced products, particularly as compared with England and Wales. On 22 July 1983, the *Edinburgh Evening News* carried a report of an interview with Mr John Watt, Director of the Protein Fractionation Centre

<sup>191</sup> Day 17, page 97

<sup>192</sup> See Chapter 11, *AIDS Aetiology*, paragraphs 11.25–11.27

<sup>193</sup> Day 18, page 118–119

<sup>194</sup> Ibid page 156; 'CDC Possible transfusion-associated acquired immune deficiency syndrome [AIDS] – California', *MMWR*, 1982; 31:652–654 [SGH.008.5105] at 5108.

<sup>195</sup> Day 18, page 155

<sup>196</sup> Day 19, page 17



(PFC – the Scottish manufacturer of NHS blood products).<sup>197</sup> It was reported that Scotland was virtually self-sufficient in blood products and that only a small percentage came from the USA.

**12.125** The claim of virtual self-sufficiency was repeated in a letter to *The Scotsman* dated 14 July 1983, by Professor Ronald Girdwood, Chairman of the SNBTS. Contrasting the Scottish position with that in England, he wrote:

[T]he Scottish National Protein Fractionation Centre at Liberton ... is a very advanced non-commercial centre ....The staff are aware of the problems of the AIDS difficulties in the United States and have appropriately modified their processes here. Patients in Scotland should be reassured by the fact that, although the Elstree Centre has yet to be expanded, such development took place several years ago in Scotland and we are virtually self-sufficient.<sup>198</sup>

**12.126** Differences of opinion were to emerge as to whether these claims to self-sufficiency were accurate throughout Scotland and whether the assertion was correct that manufacturing processes had been ‘appropriately’ modified. Data on product use are discussed below. The comments clearly reflected attitudes at the time, however.

**12.127** As will be seen, there was some change in clinical practice as heat-treated commercial products came onto the market later in 1984. In the critical period between the spring of 1983 and the end of 1984, however, Scottish haemophilia clinicians were in the relatively privileged position of having available a more or less ample supply of domestically produced concentrates for therapy which, as indicated in Professor Ludlam’s letter to *The Lancet* quoted above, were considered to be free of the postulated AIDS-causing agent. Occasional use of imported products continued in some centres for a small number of patients with special clinical needs, for example where the patient could not tolerate the PFC product. That aside, Scotland was not confronted with the difficulties found by English practitioners, in having to use large quantities of imported concentrates because of a lack of supply of domestically sourced alternatives. Therefore, so far as Scottish practice is concerned, the issue, is whether use of PFC factor concentrates should have continued at all. The alternatives were those identified in England in Wales, or more amply in US practice: the use of cryoprecipitate or of DDAVP. In the first instance, however, it is appropriate to note the data on actual product use throughout the material time.

#### *Use of blood products in Scottish haemophilia therapy to 1984*

**12.128** On 21 January 1983, at a joint meeting of the Directors of the SNBTS and the Scottish Haemophilia Directors, Professor Cash referred to recent articles in the USA, and also in *The Observer* and *The Lancet*, about the problem of AIDS.<sup>199</sup> An extract from the CDC publication *Morbidity and Mortality Weekly Report (MMWR)* had been circulated with his paper. The SNBTS and the Haemophilia Directors were clearly aware of the situation developing in the USA. By then, however, there had already been movement in the choice of therapeutic products in those regions that had not previously used Scottish products exclusively.

<sup>197</sup> *Edinburgh Evening News* article [SGH.002.6717]

<sup>198</sup> *The Scotsman* article [SGF.001.0957] emphasis added

<sup>199</sup> Minutes of joint meeting of the Directors of the SNBTS and the Haemophilia Directors on 21 January 1983 [SNB.001.5160] at 5166

## The Royal Infirmary of Edinburgh

**12.129** The numerical data for Edinburgh<sup>200</sup> show that in 1980 and 1981, following the appointment of Professor Ludlam as Haemophilia Director, there was an initial increase in usage overall, mainly of cryoprecipitate and PFC Factor VIII but with commercial product usage rising in significance as output from the PFC failed to keep up with growing demand. In 1982, small quantities of two commercial products, Koate and Factorate, were used, representing about one half of one per cent of total Factor VIII usage. Use of cryoprecipitate continued to fall from its peak in 1980 to the end of the period. In the most critical part of the period, 1980–84, commercial product use was a minor element of the total Factor VIII prescribed.

## Glasgow: Yorkhill and the Glasgow Royal Infirmary

**12.130** Within Glasgow, the GRI and Yorkhill operated independently, although Dr Willoughby, Haemophilia Director at Yorkhill, referred to Professor Forbes at the GRI for advice before Professor Hann's appointment in January 1983 and Professor Hann also 'worked very closely with the adult centre' at the GRI after his appointment.<sup>201</sup>

**12.131** Dr Willoughby had favoured commercial concentrates for the home treatment of children with coagulation disorders on the ground of ease of use. Upon taking up the post, Professor Hann 'inherited' some residual stock of imported products. As noted above, however, Professor Hann regarded NHS materials as both more cost-effective and safer<sup>202</sup> and use of commercial products fell very quickly and dramatically in 1983–84. Thereafter, products supplied by the PFC were used exclusively.<sup>203</sup>

**12.132** Professor Forbes was Director of the Regional Haemophilia Centre at the GRI from 1983–87. As noted in Chapter 21, *Haemophilia Therapy – Use of Blood Products*, his account of the use of therapeutic materials at the GRI Centre was not clear. As recorded,<sup>204</sup> commercial product use at the GRI was inconsistent and without obvious pattern. From a peak in 1979, it fell to a very low level in 1982, increased in 1983, and fell again to a more or less nominal amount in 1984. Overall, a wide range of products contributed to total use, particularly Koate, Factorate, Kryobulin, Hemofil VIII and Humanate, without any apparent structured sourcing policies.

## Other centres

**12.133** In the rest of Scotland, use of Factor VIII and Factor IX concentrates was almost exclusively of PFC products.<sup>205</sup> In these circumstances there was clearly no uniform policy relating to product selection in Scotland as a whole. Until the mid-1980s each haemophilia centre operated independently: the centres carried out more or less separate institutional roles.<sup>206</sup> As matters developed, however, there was coincidentally a broad similarity of practice among Haemophilia Directors. By the spring of 1983, clinical practice in the treatment of coagulation disorder patients, with factor concentrates, was largely limited to the use of PFC products.<sup>207</sup>

<sup>200</sup> See Chapter 21, *Haemophilia Therapy – Use of Blood Products*, Table 3 and Figure 8.

<sup>201</sup> Professor Hann's Witness Statement [PEN.012.0203]; Day 21, page 14; Day 31, page 63. Professor Hann explained that this cooperation was necessary for 'transitional care' as children at Yorkhill moved to the adult centre at the GRI.

<sup>202</sup> Day 37, page 81

<sup>203</sup> See Chapter 21, *Haemophilia Therapy – Use of Blood Products*, Table 4 and Figure 9

<sup>204</sup> See Chapter 21, *Haemophilia Therapy – Use of Blood Products*, Table 5 and Figure 10

<sup>205</sup> See Chapter 21, *Haemophilia Therapy – Use of Blood Products*, Tables 6, 7 and 8 and Figures 11, 12 and 13. Inverness used no commercial products at all from 1974 onwards.

<sup>206</sup> Professor Ludlam – Day 18, page 102

<sup>207</sup> See Chapter 21, *Haemophilia Therapy – Use of Blood Products*, Table 1 and Figures 5 and 6 for aggregate product usage in Scotland.

***The production and use of therapeutic materials in early 1984***

**12.134** The production and use of therapeutic materials was discussed at a joint meeting of the SNBTS Directors and the Haemophilia Directors, held on 2 February 1984. Professor Cash produced a paper setting out the background and indicating the views held at that time about the materials required.<sup>208</sup> Details of the amount of fresh plasma processed at the PFC for Factor VIII concentrates and the pattern of issue of concentrate were said to indicate that the production level was about right. Professor Cash said that trends over the previous five years indicated that the SNBTS production of Factor VIII concentrates might be exceeding clinical demand, in that current stocks at RTCs appeared to be increasing. It was agreed at the meeting that it was desirable to maintain the current production target and that existing stocks should be held for possible sudden demands on the service and to bridge the period when the PFC would be converting to a heat-treated product. It was noted that, if a surplus of PFC Factor VIII arose, other parts of the UK could be offered the product in preference to purchasing from other sources. No wastage was envisaged.

**12.135** It was recorded that the GRI was totally satisfied with the PFC product and had intimated that it was no longer necessary to purchase commercial alternatives. Dr Hann commented that he was prepared to dispose of the 30,000 units of commercial product he had 'inherited' at Yorkhill as it was going out of date. (From the numerical data outlined above, it also appears that Professor Hann had already dramatically reduced the use of these materials.) Professor Ludlam indicated that he needed a small stock of high purity Factor VIII, which would have to be imported from commercial suppliers for a very few patients. It was noted that in Glasgow and Edinburgh children were being treated with cryoprecipitate as the preferred material and that it was recognised that, bearing in mind reports from abroad, recipients of blood could 'also' be at risk.<sup>209</sup> Professor Ludlam said that cryoprecipitate was preferred in the treatment of children at that juncture because of the new danger of AIDS. Dr Hann concurred but noted that otherwise a policy seemed to be emerging to use less cryoprecipitate for Haemophilia A patients. It was agreed that a certain minimum amount of cryoprecipitate was required and Professor Cash pointed out that in emergencies Transfusion Directors could produce it themselves.<sup>210</sup> It was accepted that given domestic production it was not necessary in general to purchase commercial products from abroad unless, exceptionally, a superior product was available and clinically necessary.

**12.136** So far as Factor IX concentrates were concerned, it was noted that some Defix (a non-heat-treated SNBTS Factor IX concentrate) was still required and its availability would be retained. Subject to the provision of data which satisfied the Licensing Authority it was hoped to introduce Supernine (an improved SNBTS Factor IX concentrate)<sup>211</sup> in 1984–85, for routine use throughout the Scottish health service. These arrangements were seen as an interim step pending the development of a heat-treated product, details of which were set out in the paper.<sup>212</sup>

<sup>208</sup> Minutes of the joint meeting of the SNBTS Directors and the Haemophilia Directors held on 2 February 1984 [SNB.001.5252] at 5253

<sup>209</sup> Information about the use of commercial products is discussed, generally, in Chapter 21, *Haemophilia Therapy – Use of Blood Products*.

<sup>210</sup> Minutes of the joint meeting of the SNBTS Directors and the Haemophilia Directors held on 2 February 1984 [SNB.001.5252] at 5253

<sup>211</sup> Supernine had been developed in the hope of reducing hepatitis transmission. It was chemically treated, not heat-treated.

<sup>212</sup> Minutes of the joint meeting of the SNBTS Directors and the Haemophilia Directors held on 2 February 1984 [SNB.001.5252] at 5254

**12.137** Other strategies were discussed, including the possibility of 'batch dedication' of Factor VIII, designed to expose patients to the lowest number of batches of concentrate in order to reduce the risk of transmission of infection. This was a major review of clinical practice and of the demands that were created for therapeutic products. There was a preference for materials produced using plasma from locally donated (that is, Scottish) blood, with cryoprecipitate and other single-donor products identified as appropriate for limited groups of recipients, in line with current practice. It appears to be clear that extending the use of cryoprecipitate beyond those groups would have involved its use in the treatment of patients other than the vulnerable groups, such as children, who were already catered for by clinical practice. That apart, the policy that emerged clearly from the discussion at this stage in early 1984 was developed around the continuing use of concentrates produced from locally collected plasma.

**12.138** The purchase of commercial heat-treated products was not discussed at the joint meeting of the SNBTS Directors and the Haemophilia Directors held on 2 February 1984, so far as the minutes disclose.<sup>213</sup> By then, however, the use of commercial Factor VIII products in Scotland had almost ceased.<sup>214</sup> Use of cryoprecipitate had dwindled by 1983 to a very small percentage of total Factor VIII replacement therapy.<sup>215</sup> With the exception of patients requiring FEIBA<sup>216</sup> and a small number for whom commercial products were prescribed as a matter of clinical judgment, the product of choice in 1983 and 1984 was PFC Factor VIII concentrate. There was no general move towards imported heat-treated products until December 1984.

### *The development of heat-treated products*

**12.139** The development of heat-treated products had been in hand for some considerable time, however. Commercial heat-treated products were licensed by the FDA on various dates in and after March 1983 but in the case of most companies licences were granted during and after January 1984.<sup>217</sup> Alpha Therapeutics' product, Profilate HT, was licensed in February 1984. Because of concern over AIDS, Dr Winter and doctors from St Thomas' Hospital and the Royal Free Hospital, London, and from Sheffield approached Alpha in February for supplies of their heat-treated Factor VIII to be prescribed on a named patient basis (which under the Medicines Act 1968 allowed products to be prescribed without the need for a licence). They received some Alpha heat-treated product in May 1984 and used it on a selective basis until more ample supplies became available later in that year.<sup>218</sup>

**12.140** On 22 March 1983, Professor Forbes agreed to trial a new heat-treated Factor VIII product then being developed at the PFC.<sup>219</sup> However, it was to be December 1984 before the PFC had an effective virally-inactivated Factor VIII product available.

**12.141** The effectiveness of heat treatment to eliminate HTLV-III could not be tested until the virus was isolated and cell systems for the reproduction of HTLV-III antigen had been developed. That step was not announced until May 1984.<sup>220</sup> Earlier heat treatment had

<sup>213</sup> Ibid [SNB.001.5252]

<sup>214</sup> Chapter 21 *Haemophilia Therapy – Use of Blood Products*, Figure 5

<sup>215</sup> Chapter 21 *Haemophilia Therapy – Use of Blood Products*, Figure 6

<sup>216</sup> FEIBA (Factor Eight Inhibitor Bypassing Activity) is a 'bypassing agent' use in the treatment of patients who develop 'inhibitors', or antibodies, to Factor VIII concentrates.

<sup>217</sup> Chapter 21 *Haemophilia Therapy – Use of Blood Products*

<sup>218</sup> Dr Winter's evidence to Lord Archer, Day 7, pages 77-79

<sup>219</sup> Day 17, Page 102

<sup>220</sup> Chapter 29, *The Discovery of HIV and the Development of Screening Tests*, paragraph 29.11

been directed towards eliminating NANB Hepatitis and the elimination of HTLV-III was an incidental benefit.

### *Developments in late 1984*

**12.142** The SNBTS and Haemophilia Directors held a meeting on 29 November 1984.<sup>221</sup> The meeting had been arranged at short notice to discuss the implications of the finding of HTLV-III antibodies in Scottish haemophilia patients, and related topics including measures being taken by the SNBTS to prevent the transmission of AIDS by blood products. The cases of infection in Edinburgh and Glasgow were discussed. Dr Perry reported that it was anticipated that all PFC Factor VIII issued from about the beginning of January 1985 would be heat-treated.<sup>222</sup>

**12.143** The meeting in Scotland was, in part, preparation for the meeting of the UK Haemophilia Reference Centre Directors due to be held on 10 December 1984 (already discussed at paragraphs 12.101–12.105 above).<sup>223</sup> Professor Cash, Professor Ludlam and Professor Forbes attended the UK Reference Centre Directors Meeting, which was chaired by Professor Bloom. In his evidence to the Inquiry, Professor Ludlam said the meeting was stressful: the decisions reached were not easy and had to be made on the basis of limited data.<sup>224</sup> The commercial companies had kept much under wraps and there was very little published information on their work. There was apprehension that changes in treatment might make things worse for haemophilia patients. As a practical matter, Professor Ludlam would return to Edinburgh to find that (only) heat-treated product was to be available from the PFC from the end of December 1984 but he did not remember knowing that before the meeting. For him, as for Professor Cash in relation to initiating heat treatment, December 1984 was a 'terrible month'.<sup>225</sup> He was coming round to the view that the product was probably safe but he continued to have reservations. He had arranged for the testing of PFC heat-treated Factor VIII product in four patients earlier in December. If they had developed inhibitors,<sup>226</sup> he would not have wanted to use the product, notwithstanding the growing consensus among senior colleagues favouring heat-treated products.<sup>227</sup>

### **Central coordination**

**12.144** At a meeting of the SNBTS Directors on 11 December 1984,<sup>228</sup> Professor Cash expressed some of the frustration of Directors at the apparent lack of apparent central coordination:

Dr Cash said that he would make further representations to the SHHD that there should be a more effectively co-ordinated UK approach to transfusion and AIDS – this had already been recommended by the Scottish Directors. The Directors noted with regret that a second meeting of this Working Group on AIDS had not been arranged and that there appeared to be no evidence of co-ordination of the many splinter groups which existed.<sup>229</sup>

<sup>221</sup> Note of Meeting of Haemophilia Directors and SNBTS Representatives on 29 November 1984 [SNB.001.5256]

<sup>222</sup> Minutes [SNB.001.5256] at 5257

<sup>223</sup> Records of meeting in [DHF.003.0898] and [SNF.001.3850].

<sup>224</sup> Professor Ludlam – Day 44, pages 8–10

<sup>225</sup> Ibid pages 10–11

<sup>226</sup> Inhibitors are antibodies to Factor VIII. Haemophilia patients who developed inhibitors faced additional challenges in terms of therapeutic practice as infusion of Factor VIII was not possible without serious risk. See Professor Ludlam – Day 18, pages 83–86 (See also footnote 216 above: FEIBA was one therapeutic material used for patients who developed inhibitors.)

<sup>227</sup> Professor Ludlam – Day 44, page 14

<sup>228</sup> Minutes of a Directors Meeting held in the BTS HQ Unit on Tuesday 11 December 1984 [SGF.001.0137]

<sup>229</sup> Ibid [SGF.001.0137] at 0139–0140

**12.145** As noted above, however, on 14 December 1984 the UKHCDO produced an 'AIDS advisory document' to which Professor Cash had contributed. The treatment options presented in the document were set out in 'probable decreasing order of safety' in terms of the transmission of AIDS and demonstrated a preference for heat-treated NHS concentrates, followed by single-donor cryoprecipitate, heat-treated imported concentrates and, finally, unheated NHS concentrates and unheated imported concentrates. Use of DDAVP in mild Haemophilia A and von Willebrand's disease patients was recommended, if possible.<sup>230</sup>

**12.146** Effective heat treatment of PFC's Factor VIII product from December 1984 put an end to the risk for Haemophilia A patients treated in Scotland. There remained a risk for Haemophilia B patients until effective viral inactivation was introduced in October 1985. Two Glasgow patients acquired HIV infection from PFC Factor IX. One patient, the date of whose last negative sample is unknown, was first positive on 15 November 1985. The second was negative on 15 October 1985 but positive on 15 July 1986.

### **Should clinicians in Scotland have adapted their treatment regimes sooner than they did in response to the threat of AIDS?**

#### *The significance of early research into immune abnormalities*

**12.147** Until Professor Ludlam's findings in the spring of 1983 and the results of the Glasgow research later in that year, there was nothing in the direct experience of Scottish clinicians (as distinct from what might have been inferred from reports of experience elsewhere) to cause a radical re-assessment of haemophilia therapy. Those research projects showed that patients receiving concentrate therapy had developed immune abnormalities that shared many of the characteristics of those identified in other patient groups at high risk of progression to AIDS and diseases of the AIDS complex. It is appropriate to consider whether the discovery by laboratory testing of alterations in patients' immune systems, attributable to the administration of concentrates, marked the beginning of a period in which the continued use of factor products should have been reconsidered.

**12.148** Each of the two aetiologies postulated – the infective agent theory and the antigen overload theory – incriminated the use of concentrates in adversely affecting the immune systems of patients. As Dr Desforges commented in the *NEJM* of 13 January 1983, whatever the cause of AIDS, whether it was transmitted by an infective agent or was secondary to multiple antigenic exposures or some other unknown mechanism, haemophilia patients treated with concentrates were being exposed to a risk of immune system abnormalities which might progress to fatal illness. The nature of that risk and the extent to which it might affect haemophilia patients remained controversial and, as observed by Professor Ludlam, the spectrum of AIDS-related conditions differed to some extent between the groups. Kaposi's sarcoma appeared to be restricted to transmission by sexual routes and was not found in haemophilia patients.<sup>231</sup> However, haemophilia patients who developed AIDS did acquire *Pneumocystis carinii* pneumonia and that was associated with high mortality.

**12.149** The view of some haemophilia practitioners in the UK that British blood was likely to be essentially free of viruses and very safe and that British-produced Factor VIII was extremely unlikely to transmit the new disorder of AIDS, does not provide an answer to the risks associated with the antigen overload theory. If the antigen overload theory

<sup>230</sup> UKHCDO, 'Aids Advisory Document' [SGF.001.2388] at 2389–2390. Emphasis in original

<sup>231</sup> See Chapter 11, *HIV/AIDS Aetiology*, paragraphs 11.42–11.43

explained the development of immune disorders associated with AIDS related diseases in a significant number of haemophilia patients, with an established and increasing risk of morbidity and mortality, the continued use of concentrates in therapy would still have had to be justified on a balance of risk and benefit that took express account of the risks of progression to serious disease.

**12.150** Retrospective testing of blood samples showed that only a small proportion of the patients with immune irregularities were, in fact, HIV-positive at the time of the initial study. The outcome of this later research provided partial vindication of the conclusions reached by Professor Ludlam in 1983 supporting the antigen overload theory (or at least rejecting the transmissible agent theory as the sole cause of immune irregularities in all of the haemophilia patients studied). Nevertheless, the 1983 research provides a particular focus on the question as to when there was information that might have led to a change in use of factor concentrates in haemophilia therapy. It was widely appreciated that patients were developing AIDS-like immune abnormalities associated with concentrate therapy. The spectrum of AIDS-related conditions may have differed from those associated with AIDS caused by an infectious agent, but knowledge that there were significant immune deficiencies developing in patients that were attributable to concentrate therapy was in itself of potential importance.

**12.151** According to Professor Forbes, it was speculated by his group that something in the concentrates suppressed the immune system of recipient patients and that this made them more likely to be infected by the virus which was then appearing in concentrates.<sup>232</sup> On his account, it became accepted by most people in the course of 1983 that AIDS was transmitted by an infective agent.<sup>233</sup> He said that, as that became accepted, most people also came to think that AIDS would undoubtedly come to the UK in the course of time.<sup>234</sup> Already, haemophilia clinicians were looking at their patients to see if they had any of the features that might be an early warning of AIDS.

**12.152** It is important to emphasise that the 1983 research findings in Edinburgh and Glasgow included patients treated exclusively with PFC factor products produced from locally sourced plasma. The development of immune disorders in Haemophilia A patients in the main centres in Scotland was not associated with the use of Factor VIII imported from the USA to the extent that the prevalence of the disorders could be attributed solely to infective imported products: Scottish products were necessarily implicated. For those who accepted the transmissible agent theory as more likely, faith in the relative safety of UK blood could not have been supported, at least to the extent it had been until that point, in light of the 1983 research findings.

**12.153** Having regard to the Scottish research alone, the earliest point at which it might be suggested that an overall assessment of therapy should have begun was the spring of 1983. The issue became irrelevant at the end of December 1984: heat treatment effective to eradicate HTLV-III/HIV from blood products, and in particular Factor VIII, was developed at the end of December and was in routine use from early 1985. There were no recorded cases of infection transmitted by PFC heat-treated Factor VIII concentrates after that development.<sup>235</sup>

---

<sup>232</sup> Statement of Professor Forbes [PEN.015.0254] at 0257

<sup>233</sup> Professor Forbes – Day 17, pages 96–97

<sup>234</sup> Ibid page 103

<sup>235</sup> See paragraph 12.146 above: viral inactivation of Factor IX concentrate was not introduced until October 1985.

**12.154** The actual importance of the biochemical data as an indicator of a need to review clinical practice is limited, however, as there was no evidence of serious clinical disease among the patients studied in 1983. The initial study examined biochemical data collected over one month from patients treated during the previous five years.<sup>236</sup> It did not report progression in immunodeficiency and could not, without further study, have supported conclusions on future progression.

***Should Scottish clinicians have elected to use cryoprecipitate in preference to concentrates?***

**12.155** A particular question that arises is whether Scottish clinicians should have changed to the use of cryoprecipitate for Haemophilia A patients already receiving concentrate therapy, given the results of research in Edinburgh and Glasgow in 1983. In addition, other research evidence published early in 1983 reported that patients treated with cryoprecipitate did not develop impaired cell-mediated immunity (see paragraph 12.32 above). On the other hand, some clinicians thought that large quantities of cryoprecipitate were as likely as concentrates to transmit infection. Professor Ludlam noted that impaired cell-mediated immunity was not in itself a reliable indicator of HIV infection, as retrospective studies of patients exhibiting such abnormalities later confirmed. Furthermore, it was later to transpire that cryoprecipitate was, in fact, responsible for the transmission of HIV, albeit at greatly reduced rates and not in the UK, so far as is known to the Inquiry.<sup>237</sup> As against the practical problems associated with a switch from concentrate therapy to cryoprecipitate discussed below, however, contemporaneous evidence suggested that cryoprecipitate exposed recipients to less risk of immune deficiencies than concentrates. Some clinicians did advocate a switch on that basis, with limited success (resulting in few patients making the switch). It is important to note the recorded use of cryoprecipitate, as background to the discussion of the question.

**Use of cryoprecipitate in Scotland**

**12.156** There was extensive use of cryoprecipitate in many regions of Scotland. Recorded use over the period 1981–85, so far as the Inquiry's researches have shown, is as follows:

**Table 12.1: Use of Cryoprecipitate (units): Scottish Haemophilia Centres 1981–85**

	1981	1982	1983	1984	1985
RIE	720,160	612,000	341,700	139,000	127,680
GRI	56,650	40,950	136,550	121,100	223,990
Yorkhill	29,200	7050	30,500	32,340	27,930
Aberdeen	86,480	20,510	10,710	9030	10,300
Dundee	48,800	1370	4240	2560	0
Inverness	0	0	1540	0	0

<sup>236</sup> Carr et al, 'Abnormalities of Circulating Lymphocyte Subsets in Haemophiliacs in an AIDS-Free Population', *The Lancet*, 30 June 1984; 1431–1434 [LIT.001.0425]

<sup>237</sup> A 1990 study reached the conclusion that the transfusion of HIV-1 positive blood or blood products of any type (including cryoprecipitate) infected 90% of recipients: Donegan et al, 'Infection with human immunodeficiency virus type 1 (HIV-1) among recipients of antibody-positive blood donations', *Annals of Internal Medicine*, 1990; 113; 733-739. It appears that the relatively low rate of HIV transmission by cryoprecipitate was a result of the smaller number of donors (sometimes single donors and sometimes 'small pools' of 10–20 donors) contributing to the preparation of that product, particularly as compared to large-pool concentrates where many thousands of units of blood were used. Accordingly, cryoprecipitate was apparently responsible for the transmission of HIV in several countries which used only, or mainly, cryoprecipitate in the treatment of haemophilia patients (although not, so far as is known to the Inquiry, in the UK) albeit at a significantly reduced rate.



**12.157** Inverness used almost no cryoprecipitate over that period; PFC Factor VIII was used almost exclusively. Dundee used cryoprecipitate in 1981, as the centre had in previous years. In that year and later, however, it accounted for only a small percentage of total therapy which, as noted above, was based on almost exclusive use of PFC Factor VIII. Neither centre had a case of HIV transmission. In Aberdeen, use of cryoprecipitate fell over the period and the use of PFC Factor VIII grew proportionally.

**12.158** In Edinburgh, use of cryoprecipitate was reduced following Professor Ludlam's appointment. It remained high, in absolute and relative terms, however, throughout the period of maximum exposure of coagulation disorder patients to HIV. Cryoprecipitate was used in Edinburgh for vulnerable groups, including children. A change of practice would have affected older children and adults, many of whom would have been on home treatment programmes. Throughout that period, Professor Ludlam used considerably more cryoprecipitate than Professor Forbes, both absolutely and, taking into account that the GRI had a consistently higher number of registered patients than Edinburgh over this period, also as a ratio of their haemophilia patient populations.

**12.159** The position at the GRI is less easy to describe. Professor Forbes thought that the use of cryoprecipitate at the GRI might explain the low prevalence of HIV infection in his patients, but his evidence on this point is not supported by the analysis of the actual use of therapeutic materials in his centre. Professor Forbes' recollection of detail had clearly suffered with the passage of time. Cryoprecipitate was indeed used at the GRI but Professor Forbes' evidence on its use was less precise and it is not possible to define sub-groups with any degree of certainty. The recorded use, based on the materials available to the Inquiry, is preferred as evidence of practice at the GRI.

**12.160** The regime at Yorkhill changed after Professor Hann was appointed, reflecting both his previous interest in immunocompromised patients and his faith in the quality of the UK blood supply. Early reports of what became known as HIV infection were related to sexual behaviour and intravenous drug use but – partly through a 'corridor discussion' at the Stirling conference on immunocompromised patients in June 1982 – at an early stage Professor Hann considered it a 'possibility' that haemophilia patients would come to be affected.<sup>238</sup> By late 1983, Professor Hann said that he was 'becoming more convinced that this was a blood product transmissible disease' and that he had to do everything he could to minimise that risk.<sup>239</sup>

**12.161** He defined a 'difficult interim period' in therapy between May 1983, when the discovery of LAV (later proved to be identical to HTLV-III) was published, and late 1984, when the HTLV-III virus had been isolated and some of the patients were found upon testing to have antibody to the virus.<sup>240</sup> Although the development of tests was important, Professor Hann noted that there were still unresolved questions. The sensitivity and specificity of the tests was not clear and, more fundamentally, 'we didn't know what positivity meant'.<sup>241</sup> It was not clear whether positivity was transient or permanent and it was not known what proportion of those testing positive would progress to AIDS.<sup>242</sup>

---

<sup>238</sup> Day 21, page 46

<sup>239</sup> Day 31, page 105

<sup>240</sup> Day 21, Pages 68–9

<sup>241</sup> Day 31, page 21

<sup>242</sup> Ibid pages 21–2

**12.162** Professor Hann shared the concerns of many Haemophilia Directors about the use of cryoprecipitate, discussed below, particularly as this would have affected home therapy programmes. Nevertheless, he said that cryoprecipitate treatment may have been recommended as the first option for newly diagnosed patients in that period.<sup>243</sup> He believed that, in relation to a child who was already receiving Factor VIII concentrate in late 1983, he would have offered the possibility of ceasing concentrate therapy and returning to cryoprecipitate<sup>244</sup> and he was almost certain that in late 1983 he did change some patients over to cryoprecipitate and continued others for longer than he would have done previously.<sup>245</sup> Professor Hann's patients at Yorkhill were children, however: in due course Yorkhill patients were transferred to the GRI for treatment in their teens and as adults. He was not therefore confronted with the problem of changing the treatment regime of adults already settled on concentrate therapy and, in particular, the home therapy programme widely agreed to be advantageous.

**12.163** With the exception of Yorkhill, the picture that emerges overall, is that clinicians used cryoprecipitate on a selective basis, distinguishing children and other vulnerable groups from those settled on concentrate use and doing so on a broad precautionary basis rather than because they were committed to the infective agent theory of transmission.

#### The decision not to switch to cryoprecipitate use generally

**12.164** Dr Jones' editorial in the *BMJ* of 10 December 1983 provides a reference point in English practice.<sup>246</sup> Against the background of a view that there was no evidence that any product, 'commercial or volunteer', was free from the risk of transmitting AIDS, he commented that, for the moment, it would be sensible to treat very young severely affected children with cryoprecipitate, and that DDAVP or porcine material should be used in mildly affected haemophilia patients, von Willebrand's disease patients and carriers of those disorders. His advice was not significantly different from that observed in Scotland and favoured a discriminating approach to product selection.

**12.165** A similar approach was reflected in discussion at the Reference Centre Directors' meeting on 10 December 1984, at the end of the period. The AIDS Advisory Document of 14 December 1984 set out clearly the Reference Centre Directors' recommendations on therapy. The use of heat-treated imported concentrate was recommended after heat-treated UK concentrate and cryoprecipitate and fresh frozen plasma. Until imported heat-treated concentrates became readily available, that aspect of the advice would have had little practical effect, especially in England and Wales. Dr Winter and those of his colleagues who had no alternative to the use of commercial concentrates were in the vanguard of clinicians seeking to use heat-treated concentrates from May 1984. They were not able to obtain sufficient supplies for general use until later in the year. From a practical point of view, cryoprecipitate and fresh frozen plasma had become preferred alternative products for most clinicians and would remain so for some time, notwithstanding reservations about their use.

**12.166** The Haemophilia Reference Centre Directors' recommendations comprised a turning point in guidance. Until then there was no authoritative statement in the United Kingdom favouring cryoprecipitate for general use. There was a minority view held by

<sup>243</sup> Day 21, page 68

<sup>244</sup> Day 31, Page 25

<sup>245</sup> Ibid Page 27; Day 21, page 68

<sup>246</sup> Jones, 'Acquired immunodeficiency syndrome, hepatitis and haemophilia', *British Medical Journal*, 1983; 287: 1737-1738 [LIT.001.0243]

some clinicians, led by Dr Ratnoff in the USA and echoed by Dr Galbraith in the UK, that current therapy regimes should have been radically reviewed as soon as there was evidence of a possible association between factor concentrates and infection with a presumed agent of transmission of AIDS; that use of concentrates should have been abandoned or suspended; and that patients generally should have been prescribed cryoprecipitate.

**12.167** That view received limited support from Dr Desforges' editorial in the *New England Journal of Medicine* of 13 January 1983.<sup>247</sup> It was opposed by Dr Kernoff in his article 'AIDS and Haemophilia', in the Haemophilia Society's publication *The Bulletin*, edition 33, No 1, January 1983.<sup>248</sup> On 17 October 1983, Professor Bloom's advice in answer to Dr Chisholm of Southampton was that patients should not be encouraged to go over to cryoprecipitate for home therapy but should continue to receive the NHS or commercial concentrates in their usual way.<sup>249</sup> In December 1983, Dr Jones wrote that cryoprecipitate should be used to treat very young, severely affected children. Professor Bloom repeated his views at a meeting of the UKHCDO held in December 1983. There was a large body of informed opinion that rejected the Ratnoff/Galbraith approach.

**12.168** The question whether clinicians should use cryoprecipitate was discussed in these exchanges in terms of the selection of appropriate forms of therapy for specific groups of patients. One might suggest, in the light of later knowledge, that the decisions taken and the advice tendered were to the disadvantage of some NHS patients. It would, however, be impossible to criticise them as wrong decisions, either on the basis of the information taken into account or on the basis of the conclusions drawn from that information. Having regard to the published statements of leaders among the haemophilia clinicians, Professor Hann in Scotland and Dr Winter in England were very much in the minority in adopting the infective agent theory at an early stage in the AIDS epidemic and adapting their treatment programmes accordingly, so far as they were able to do so. Moreover, it is important to emphasise the extent to which cryoprecipitate was in fact used elsewhere: the advice on product selection was generally reflected in clinical practice.

### The impact on home therapy programmes

**12.169** The patients who would have been affected by a general switch to cryoprecipitate would be those already established on concentrate therapy, often on a home treatment basis, and those requiring frequent or heavy doses of concentrate. There was a widely held view in the UK that cryoprecipitate was not suitable for home treatment.<sup>250</sup> It was also limited in supply.<sup>251</sup>

**12.170** Under those circumstances, haemophilia patients would have required to attend hospital for all treatment. Beyond the inconvenience that would be caused by moving patients from home treatment with concentrates to hospital treatment with cryoprecipitate, there were clinical reasons for resisting such a move. Even under home treatment programmes using concentrates, cerebral bleeding was still, at the material time, the leading cause of death amongst haemophilia patients: in the UK, between 8 and 19 patients died annually from cerebral bleeds before they could attend hospital in this way. Professor Ludlam considered it inevitable that such deaths would have increased, were patients required to attend hospital for cryoprecipitate treatment. Moreover, as cerebral

<sup>247</sup> Desforges, 'AIDS and the preventive treatment in hemophilia', *New England Journal of Medicine*, 1983;308: 94–95[LIT.001.0040]

<sup>248</sup> *The Bulletin*, Edition 33 No. 1 [PEN.016.0595] at 0605–0606

<sup>249</sup> Minutes of the 14th meeting of UK Haemophilia Centre Directors Held on Monday 17 October 1983 [SNB.001.7517] at 7526

<sup>250</sup> Dr Winter – Day 16, page 25; Professor Hann – Day 31, page 27; Dr Pettigrew – Day 20, page 21

<sup>251</sup> Dr Winter – Day 16, page 26

bleeds were often 'spontaneous', by the time a patient arrived at hospital for treatment, 'very severe brain damage ... often occurred'. Finally, the increased morbidity associated with delayed treatment at hospital would not have been limited to cerebral bleeds: haemarthroses, left untreated until admission to hospital, would result in 'excruciating and protracted pain' and bed rest for around 10 days. As a consequence of the disuse of the joint and bed rest, 'there would be atrophy of the muscles ... and the weakened muscles would predispose to further haemorrhage'.<sup>252</sup> Professor Ludlam noted that patients under Dr Ratnoff's care had in fact resisted his proposal to switch to cryoprecipitate use, 'despite the apparently much higher risk in the USA of haemophiliacs developing AIDS in the early-mid 1980s'. In oral evidence he recalled that, of around 90 patients under his care, only five followed Dr Ratnoff's advice.<sup>253</sup> Professor Hann noted that, principally because of the inevitable impact changing from home therapy to hospital-based cryoprecipitate therapy would have on patients and their families – a point the Haemophilia Society 'repeatedly made' during the period – the majority of families declined the offer to switch to cryoprecipitate use at Yorkhill.<sup>254</sup>

**12.171** There was clearly conflicting evidence. Professor Hann found that some of his patients were willing to switch to cryoprecipitate, or remain on it for longer than would have been normal. His patients were children, however, and his background had been in infections in patients with immune deficiencies and leukaemia and cancers associated with immune deficiencies. He offered his patients a choice, as Professor Ratnoff had done in Cleveland. Professors Ludlam and Forbes, along with the rest of the Scottish clinicians, did not do so and continued using concentrates for the majority of their patients. Although they had both carried out studies into immunological abnormalities, neither study reported *progression* in immunodeficiency and neither clinician knew what the findings of their studies meant. Due to the unstructured, preliminary character of those studies, a full research programme following up on them would have been required if reliance was to be placed upon their conclusions in instructing any changes in the approach to therapy.

### Practical issues

**12.172** The narrative of the evidence indicates that there would also have been practical problems if there had been an attempt to revert to more or less exclusive use of cryoprecipitate. That was the view, for example, of the Sub-Committee on Biological Products of the Committee on the Safety of Medicines on 13 July 1983 (see paragraph 12.65 above). Professor Ludlam considered that it would have been necessary to invest considerable sums of money to purchase equipment such as centrifuges and fridges.<sup>255</sup> Dr Galbraith's proposal that concentrates manufactured in the USA from blood donated after 1978 should be withdrawn from use was held to be not feasible in the UK on the basis of supply.

<sup>252</sup> Professor Ludlam's Witness Statement [PEN.015.0445]; Dr Pettigrew noted three relevant case histories, one a case of a child with haemophilia, insufficiently treated at a local hospital when he experienced a bleed, who died of intracranial bleeding; and two cases of severely affected boys with haemophilia who sometimes required more than one visit daily to treat bleeds. Day 20, page 13

<sup>253</sup> Day 19, pages 29–31. See Ratnoff et al, 'Hemophilia and the Acquired Immunodeficiency Syndrome', *Annals of Internal Medicine*, 1985; 102(3)[PEN.016.1171]. In his statement, Professor Ludlam wrote: 'The suggestion that patients should be switched from concentrate to cryoprecipitate would have resulted in their attendance at hospital for all treatment (ie abandoning home therapy). Where this was recommended in Cleveland, USA, it was not accepted by the patients (despite the apparently much higher risk in the USA of haemophiliacs developing AIDS in the early-mid 1980s). The proposed increase in use of cryoprecipitate, instead of concentrate, in the USA did not find favour amongst patients, and it was also associated with very significant HIV infection.' Professor Ludlam's Statement [PEN.015.0445] at 0448

<sup>254</sup> Day 31, page 27

<sup>255</sup> Professor Ludlam's Statement [PEN.015.0445] at 0454

**12.173** Those were factors that clinicians and others were entitled to have regard to but it is questionable whether they would have been conclusive, or even material, if it had been understood that the relative risk of transmission of HIV infection by use of concentrates was so high that their continued use exposed patients to serious morbidity and mortality risks when an alternative – the use of cryoprecipitate – was available and could have been used notwithstanding the difficulties involved. In other words, in a question of patient safety, the decision of the Sub-Committee on Biological Products of the Committee on the Safety of Medicines was hardly credible unless the risk that was implicitly accepted was of such a low order as to be dismissed. Difficulties in process change would have been real, but those difficulties would have had to be addressed if the difference made was a real reduction in the perceived overall risk to patients.

*Should Scottish clinicians have made greater use of DDAVP?*

**12.174** Dr Winter noted that ‘a good number’ of mildly affected haemophilia patients and von Willebrand’s disease patients in the UK contracted HIV through contaminated blood products; he considered that switching mildly affected patients to DDAVP might have prevented this, ‘[o]ne wonders why they were ever treated with concentrate. Because they would have been suitable for DDAVP treatment’.<sup>256</sup>

**12.175** It is appropriate to consider this issue, not least because advice regarding the use of DDAVP appeared regularly in guidance on the selection of therapeutic materials in the USA, in the UK generally and in Scotland.<sup>257</sup>

**12.176** As noted at paragraph 12.31, Desmopressin, otherwise known as DDAVP, is a synthetic replacement for the naturally-occurring brain hormone called vasopressin. As it is not derived from human blood, it was not capable of transmitting HIV. Administered to patients with mild Haemophilia A and von Willebrand’s disease, it releases Factor VIII from the lining of blood vessels, allowing normal clotting to occur. It is important to note, however, that not all such patients are responsive to DDAVP and that, while it is an important and useful drug for those patients who are responsive, it is ineffective in patients with moderate or severe haemophilia and those mildly affected patients who do not respond to it.<sup>258</sup> Professor Ludlam said that, at the point of diagnosis, his practice was to give a ‘test dose’ of DDAVP to determine whether a mildly affected haemophilia or von Willebrand’s disease patient was responsive to the drug.<sup>259</sup> Professor Lowe said that the same practice applied at the GRI.<sup>260</sup>

**12.177** DDAVP is not generally considered useful in response to a spontaneous bleed of any real severity: more immediate treatment is usually required than DDAVP can provide. Professor Forbes stressed that DDAVP was principally used for elective procedures, such as minor operations or tooth extractions, and that it was rarely used to treat bleeds.<sup>261</sup> Professor Ludlam, who had a long-term clinical and research interest in DDAVP,<sup>262</sup> generally agreed but noted that DDAVP could be useful in treating some minor bleeds (giving a nose bleed as an example) or prophylactically in advance of minor operations (again, such

<sup>256</sup> Dr Winter – Day 16, pages 56–57

<sup>257</sup> See the US guidance at paragraphs 12.31 and 12.38–12.39 above. See the UK guidance at paragraphs 12.54–12.55 and 12.107–12.108 above.

<sup>258</sup> Dr Winter – Day 16, page 56; Professor Forbes – Day 17, pages 108–109

<sup>259</sup> Day 18, page 52

<sup>260</sup> Day 54, pages 69–70

<sup>261</sup> Day 17, page 109

<sup>262</sup> Day 18, page 15; Professor Ludlam’s Witness Statement [PEN.015.0445] at 0453

as tooth extraction) but not for bleeding into joints.<sup>263</sup> He noted that at his centre, 'it was standard practice to use DDAVP if that was suitable'.<sup>264</sup>

**12.178** In addition to the relatively limited number of patients for whom DDAVP was suitable, its use was also associated with side-effects and it had to be used with care. Professor Forbes noted that DDAVP is 'not without its own problems' and that 'it could not therefore be used routinely'.<sup>265</sup> In oral evidence, he stated that 'we did use it but with some caution'.<sup>266</sup> In particular, the therapeutic use of DDAVP is associated with fluid retention and changes in blood pressure. This did not constitute a general contra-indication for therapeutic use, as such problems as noted would only become apparent, if they arose, after administration. In his statement he noted that, at the GRI:

We were ... very aware of the possibility of using DDAVP in patients with mild disease who were having small traumas or small surgery. This we widely accepted, and was really very successful for a day or two's treatment only, for example one or two teeth or a very small procedure. During this time we also became aware of the other long term implications of DDAVP particularly fluid and electrolyte retention so it was used with some caution.<sup>267</sup>

**12.179** Professor Lowe agreed, stating that at the GRI '[t]he policy was to treat patients with mild Haemophilia A preferentially with DDAVP, where appropriate and tolerated'.<sup>268</sup> He added that DDAVP had only a short-term effect and that its effectiveness decreased with repeated administration:

It has a short-term effect. And usually after about 48 to 72 hours, if you are giving a daily or twice daily injection, you observe a phenomenon called tachyphylaxis, which is a reduced response, and this is because you are trying to stimulate release of the patient's own Factor VIII [or] von Willebrand factor complex .... [T]here is individual variation, but usually, after four doses of desmopressin, you don't get any more bang for your buck. So you have to bear in mind that limited situation.<sup>269</sup>

**12.180** Professor Hann stated that, from his appointment in January 1983, Yorkhill operated a policy whereby mildly and moderately affected Haemophilia A and von Willebrand's disease patients were treated preferentially with DDAVP (where a response to its use had been demonstrated). He noted that shortly after his arrival at Yorkhill, he made these policies 'explicit' and 'spent the first few months of my job writing them down' in a specific set of protocols. He stressed, however, that this approach 'was not always feasible or appropriate' – DDAVP is not considered safe for very young children (under one year of age) and was contra-indicated in those with fluid retention or neurological problems (in whom it can cause convulsions). Like Professor Lowe, he pointed to the problem of tachyphylaxis, making it inappropriate in many surgical settings, and to the fact that some patients do not respond at all to DDAVP.<sup>270</sup>

<sup>263</sup> Professor Ludlam – Day 18, page 51

<sup>264</sup> Day 55, page 46

<sup>265</sup> Professor Forbes' Witness Statement [PEN.015.0254] at 0261

<sup>266</sup> Day 17, page 109

<sup>267</sup> Professor Forbes' Witness Statement [PEN.012.0411]

<sup>268</sup> Professor Lowe's Witness Statement [PEN.016.1250] at 1252

<sup>269</sup> Day 54, page 67

<sup>270</sup> Professor Hann's Witness Statement [PEN.015.0370] at 0373

**12.181** Professor Ludlam also agreed with the reservations regarding DDAVP use. Asked whether this meant that DDAVP was a drug which had to be used with great care, he replied:

With a degree of circumspection, yes. Great care in small children, and particularly if you want to give repeated doses, because of the water retention. And also in patients who have atherosclerosis ....

So, although it's a very useful drug, it is not without its contra-indications.<sup>271</sup>

**12.182** Professor Lowe was the lead author of a letter to *The Lancet* in 1977,<sup>272</sup> the first to note the problem of progressive water retention associated with the use of DDAVP and which recommended that water intoxication should always be considered a potential side-effect, particularly after repeated administration. In oral evidence, he said:

I think the point I'm making is that desmopressin is not the panacea. It had a very useful place – let's not underestimate it – during the 1980s, in sparing many patients with haemophilia and von Willebrand's disease around the world from getting virus infections. So it has its place, but it's not the panacea. And you have to assess every patient individually across the whole spectrum of haemostatic agents, not only in this period of time that we are talking about, concentrates versus cryoprecipitate or fresh-frozen plasma ....<sup>273</sup>

**12.183** The numerical data on the use of DDAVP suggests that its use varied among Haemophilia Centres in Scotland. At Edinburgh, it is recorded as having been used in small amounts (between 6 and eleven international units) between 1984 and 1987, but not at any other time.<sup>274</sup> At Yorkhill, it was used in 1989 only (20 international units).<sup>275</sup> Aberdeen and Dundee used no DDAVP at all in the material period.<sup>276</sup> Inverness used varying amounts (between 4 and 108 international units) beginning in 1987 but used none before that date.<sup>277</sup> Glasgow Royal Infirmary was the centre which made most use of DDAVP. Although none was used in 1980, 1983 or 1984, in every other year between 1979 and 1987, use ranged between 229 and 978 international units. From 1988–1991, use ranged from 1210 to 1548 international units.<sup>278</sup>

**12.184** Ultimately, however, the most important point for this Inquiry to make in relation to the use of DDAVP is that, so far as the data available to the Inquiry show, no mildly affected haemophilia patient in Scotland contracted HIV from concentrate therapy. The comment made by Dr Winter in paragraph 12.174 above does not therefore apply in Scotland.

### *Use in Scotland of imported commercial products*

**12.185** Until commercial products imported from the USA were heat-treated to inactivate HIV, American Factor VIII posed a relatively high risk of transmission of infection. The experience at Yorkhill, where Dr Willoughby favoured the use of commercial concentrates until he was succeeded by Professor Hann, is persuasive evidence of the risk associated

<sup>271</sup> Day 19, page 38

<sup>272</sup> Lowe et al, 'DDAVP in Haemophilia', *The Lancet*, 17 September 1977

<sup>273</sup> Day 54, pages 69–70

<sup>274</sup> See Table 3 in Chapter 21, *Haemophilia Therapy – Use of Blood Products*

<sup>275</sup> See Table 4 in Chapter 21, *Haemophilia Therapy – Use of Blood Products*

<sup>276</sup> See Tables 6 and 7 in Chapter 21, *Haemophilia Therapy – Use of Blood Products*

<sup>277</sup> See Table 8 in Chapter 21, *Haemophilia Therapy – Use of Blood Products*

<sup>278</sup> See Table 5 in Chapter 21, *Haemophilia Therapy – Use of Blood Products*

with older generations of product. Patients registered at the hospital numbered between 70 (1980) and 108 (1985). Twenty-one HIV infections in an average population of 90, just over 23%, exceeds by a considerable margin the experience elsewhere in Scotland. Excluding Yorkhill, the average for the rest of Scotland was just over 8% (39/480).

**12.186** On Dr Winter's evidence, the safety of the American product changed in 1984 with the adoption of effective heat treatment. Heat-treated product manufactured by Alpha Therapeutics was obtained in May 1984 and used on a named patient basis in Kent, St Thomas' Hospital and the Royal Free Hospital, London and in Sheffield. Dr Jones moved to exclusive use of commercial heat-treated Factor VIII at Newcastle before 10 December 1984, the date of the meeting of the UK Haemophilia Reference Centre Directors at which treatment policy was widely discussed. That was, however, too late for many patients at both the Kent and Newcastle centres where seropositivity was high. On 14 December 1984, the UKHCDO 'AIDS Advisory Document' summarised recommendations on treatment options and preferences. At this point, as events were to prove, PFC was on the threshold of routine production of heat-treated Factor VIII concentrate that, as with the commercial product, was in time found to be effective in inactivating HIV.

**12.187** The record of the meeting of 10 December reflects the dismay and deep uncertainty of the professional community, desperate to find a solution to a problem that had not been anticipated but which went to the very roots of their management of patients. It might suggest that more positive action could have been taken in the last quarter of 1984 to obtain US heat-treated products for all patients, as Dr Jones had done by December of that year. It is not likely that supplies could have been obtained earlier. Dr Winter, who had a long history of use of commercial products, initially had difficulty in sourcing sufficient quantities for all of his patients. Dr Jones' determination to use the products suggests that he would not have delayed in his efforts to obtain them. It remains a matter of speculation when commercial heat-treated products would have been available in sufficient quantities to meet total demand in the UK as a whole, or in Scotland in particular. It could not, however, have been earlier than late 1984.

**12.188** It is reasonably clear that a switch to imported heat-treated products would have been of little advantage to Scottish patients. Early in December 1984, the PFC began distributing its first heat-treated product to haemophilia centres. The product was despatched by carrier to Belfast, Aberdeen, Dundee and Inverness around 10 December. At the same time, the PFC itself delivered heat-treated product to Glasgow and Edinburgh.<sup>279</sup> In each case, the quantity delivered was about one month's supply. Full scale production of heat treated product took over from the beginning of 1985.

**12.189** There is no evidence available to the Inquiry to suggest that the UK or Scottish demand for heat-treated factor VIII concentrate for haemophilia therapy could have been met at any time during 1984 wholly from American pharmaceutical companies. The Haemophilia Reference Centre Directors recommendation on 10 December was that heat-treated product should be given to all patients, '*if freely available*'.<sup>280</sup> The market position remained uncertain at that date, when the PFC was already issuing a domestic heat-treated product.

<sup>279</sup> Arrangements set out in Dr Perry's letters to Haemophilia Directors [SGH.002.6506]. On 11 December, Dr Mitchell acknowledged receipt of product [SNB.007.4669].

<sup>280</sup> Notes of meeting [SNF.001.3850] at page 3853 (emphasis added)



### *The ethics of medical practice*

**12.190** The ethics of medical practice in this field are discussed in Chapter 32, *An Investigation into Systems in Place for Informing Patients about the Risks – Ethical Context*. In short, prior to 1988 there were no rules, relevant to such a situation as described in this chapter, requiring clinicians to consult their patients about potential changes in therapy. Furthermore, the approach of both Professor Forbes and Professor Ludlam throughout the 1980s was consistent with the advice that was to be provided by UKHCDO in mid-December 1984.

### **DISCUSSION**

**12.191** Sixty patients with bleeding disorders acquired HIV infection from treatment in Scotland (see Chapter 3, *Statistics*, paragraph 3.296). The infection of all but one of these patients can be associated with specific centres: Edinburgh, 23; GRI, 12; Glasgow Yorkhill, 21; and Aberdeen, 3. The remaining patient is known to have been infected in Scotland, probably at a hospital that was not a haemophilia centre. At least 18 NHS patients are known to have acquired HIV/AIDS transmitted by blood or blood component transfusion (see Chapter 3, *Statistics*, paragraph 3.321).

**12.192** All of the patients with bleeding disorders acquired their infection from blood factor concentrates. There is no recorded case in the UK of transmission of HIV related to the use of cryoprecipitate. The UKHCDO did not record relevant data of cryoprecipitate use, however, and it is not possible to be totally confident that transmission by infusion of infected cryoprecipitate did not happen. Transmission of HIV by cryoprecipitate certainly did occur in other countries. However it seems appropriate to proceed on the basis that, if there were any cases, they would be very few, and that cryoprecipitate generally was not responsible for transmitting HIV in the UK generally or Scotland in particular.

**12.193** Leaving aside the multiple infections of the Edinburgh Cohort,<sup>281</sup> there is no evidence of transmission of HIV to groups of patients in Scotland by use of SNBTS large-pool concentrates. On the evidence available to the Inquiry about the chemistry of plasma processing, the pool of plasma prepared for processing would be more or less uniformly affected by a component donation that was infected by a virus. On that basis, the pooling of plasma from the donations of many hundreds of individuals clearly created a risk that an infected donation might infect large numbers of recipients. The experience of the Edinburgh Cohort demonstrates that the risk was real. Most members of the Cohort have been shown by genetic analysis to have acquired the virus from a single source. The Inquiry has not recovered similar evidence for other infected individuals. Cryoprecipitate was pooled in general application at the point of administration: the dose for an adult patient might require 10–20 bags. An infected donation would still reach one recipient only, however. Had cryoprecipitate been used exclusively in the treatment of coagulation disorder patients throughout the AIDS period – roughly 1981–85 – then the risk of transmitting HIV infection would have been arithmetically reduced: the number of patients potentially infected could not have exceeded the number of infected donations.<sup>282</sup>

<sup>281</sup> A group of 18 RIE haemophilia patients infected with HIV by NHS products, discussed in Chapter 10 *Knowledge of the Geographical Spread and Prevalence of HIV/AIDS 2*.

<sup>282</sup> There is a theoretical risk that the use of mini-transfusions in neo-natal cases might have increased the risk, as happened in Italy but there was no evidence of similar practice in Scotland.

**12.194** In relation to risk, it is important to bear in mind that, untreated, haemophilia carries a high rate of serious and potentially fatal illness. The life expectancy data noted in this chapter provide one measure of the risk of fatal illness: bleeding was the most frequent cause of death before concentrate therapy was introduced. It is against that risk that the risks associated with therapy had to be balanced. The studies carried out by Professors Forbes and Ludlam suggested that profound immunosuppression occurred in patients treated with PFC Factor VIII. Those studies were of a preliminary nature and did not provide evidence of progression in immunodeficiency. More significantly, however, it became widely known in the autumn of 1983 that a haemophilia patient treated with concentrates had died of AIDS. Once it was apparent that immunosuppression could progress to fatal illness the risk/balance assessment changed: the risk of death from bleeding then had to be measured against the risk of death from HIV/AIDS. Decisions on therapy had to take account of a different context.

**12.195** The only alternatives at this stage were to cease entirely the use of blood products in haemophilia therapy or to endeavour to switch all Haemophilia A patients to cryoprecipitate. In relation to the period from autumn 1983 to December 1984, the point when heat-treated product began to be issued in Scotland, it is not possible to conclude that a general cessation of use of blood products should have occurred. Given the uncertain state of knowledge of AIDS and the risks posed by untreated haemophilia, it was reasonable for general treatment policy to continue to include the use of blood products, provided these were used on a more discriminating basis. The advice formulated at the Reference Centre Directors meeting of 13 May 1983 appears sound – that it was circumspect to continue to reserve NHS concentrates for children and mildly affected (adult) patients, rather than using concentrates imported from the USA. More specifically, the advice contained in Dr Jones's editorial in the *BMJ* in December 1983 that cryoprecipitate should be used for children and other options, such as DDAVP, considered for older patients, was prudent; one might have expected similar points to have been made by Professor Bloom at the UKHCDO meeting on 17 October 1983, rather than his seemingly unqualified endorsement of concentrate therapy.

**12.196** In relation to the suggestion that all Haemophilia A patients should have been switched to cryoprecipitate from around autumn 1983 onwards, several points need to be borne in mind. As with the proposition dealt with in the preceding paragraph, the general uncertainty surrounding the proportion of patients who would develop the profound immunosuppression being observed, and the proportion of that group who might not survive, was relevant. To be balanced against these unquantifiable risks were the known dangers of untreated haemophilia, as noted above. As Professor Lever put it, 'the risk-benefit ratio of being infected versus not receiving concentrates was not clear cut'.<sup>283</sup> Treatment was necessary and therapy with concentrates was well established. Clinicians and patients favoured concentrates rather than cryoprecipitate for understandable reasons, a preference also strongly supported by the well respected Haemophilia Society. In addition, it cannot be concluded that a mass switch to cryoprecipitate would have been practically possible.

---

<sup>283</sup> Professor Lever's Report [PEN.015.0517 at 0522

**12.197** Cryoprecipitate appears to have been utilised for particular groups of patients; on all of the evidence available to the Inquiry, that appears an appropriate general course. Issues concerning information given to individual patients, and the choices they were offered in relation to their own treatment, are dealt with in Part 5 of this Report.

## Conclusions

**12.198** Professor Lever's evidence is accepted: reassessment of the risk/benefit balance in the use of factor concentrates in haemophilia therapy became necessary when evidence of two factors was present: (i) the association of profound immunosuppression in patients with infusion of factor concentrates and (ii) death from immunosuppression.

**12.199** Independent of the cause of the immunosuppression in coagulation defect patients treated with factor concentrates, knowledge that there was an association between established therapy and immunosuppression in patients was a potential trigger for a reassessment of clinical practice. The studies reported in Edinburgh in May 1983 and in Glasgow in October 1983 were preliminary in nature: they demonstrated immunosuppression in patients treated with factor concentrates but did not, and could not, report *progression* in immunodeficiency. At that point, there had been no report of a UK haemophilia patient having died of AIDS. Nevertheless, published guidance and letters in journals at the time, as well as the records of materials used, suggest there was a general awareness of the importance of a discriminating approach to product selection in light of incomplete information.

**12.200** The association of immunosuppression in patients with haemophilia treated with factor concentrates and a potentially fatal outcome was established in the UK by the autumn of 1983. The general approach to the use of blood products in haemophilia therapy was reassessed and appropriately modified, insofar as references were made to the need to protect children and mildly affected patients in particular.

**12.201** The transmission of infection by infusion of PFC Factor VIII was established around the end of October 1984 in Edinburgh and the east of Scotland and in or about October 1984 in Glasgow and the west of Scotland. A further general reassessment of coagulation defect therapy was therefore necessary and took the form of the meeting and guidance issued in December 1984. The response in autumn 1984 of the Haemophilia Reference Centre Directors to emerging knowledge was appropriate and is not open to criticism.

**12.202** The use of imported heat-treated products was not an issue in Scotland so long as there was no evidence that the PFC product transmitted HTLV-III infection and so long as there was no evidence that the immunosuppression found in coagulation defect patients might progress to fatal illness.

**12.203** Having regard to the timing of the discovery that PFC materials transmitted infection, and the imminence of production of a safe product by PFC, the failure of Scottish practitioners to import and use US heat-treated products is not material.



## CHAPTER 13

### KNOWLEDGE OF VIRAL HEPATITIS NOW

#### Introduction

**13.1** This chapter provides an account of what is known now, in 2014, about Hepatitis C virus (HCV) infection, in particular in relation to the two affected groups with whom the Inquiry is concerned: blood disorder patients receiving therapy and people infected by blood transfusion in the course of medical or surgical procedures. Very little of what is described in this chapter about HCV was known, or could have been known, until well into the 1990s and much, indeed, has been understood only in the past few years.

**13.2** The information set out in this chapter is intended, particularly, to inform and illuminate the accounts provided by patients and their relatives of experiences of HCV infection narrated in Chapters 4 and 6 of the Report.

**13.3** As further background to an understanding of those accounts, this chapter also discusses the investigative procedures and forms of drug therapy associated with the diagnosis and treatment of HCV infection, with particular reference to the side-effects of treatment.

#### Background

**13.4** At the date of the Inquiry's Preliminary Report (2010), the group of hepatitis viruses had not been finally defined but it was thought there were six, viruses A to E and G, as described in a standard textbook of 2007.<sup>1</sup> The current view is that virus G is not a hepatitis virus in humans. Now known as GBV-C and a member of a family of flaviviruses, it causes hepatitis in marmosets but humans who are infected do not develop liver disease.<sup>2</sup> However, it cannot be assumed that the class is now closed: research continues. Equally, the signs, symptoms, natural history and complications of viral hepatitis, generally and for each specific disease, have been and are the subject of ongoing research and have not been finally resolved. Inevitably, expert perception and understanding of the manifestations of the diseases have changed over time. The natural history of each disease has some features that are generally recognised and are increasingly understood, however. In this changing environment, the Inquiry is particularly grateful to Professor Howard Thomas, Emeritus Professor of Hepatology, Imperial College, London, and Professor Peter Hayes, Professor of Hepatology and Honorary Consultant Gastroenterologist at the Royal Infirmary of Edinburgh (RIE), for their contribution to the understanding of the present state of knowledge of viral hepatitis.

**13.5** All five of the human hepatitis viruses currently recognised, A to E, are from different families of the virus kingdom. The viruses are grouped together because they all replicate in the liver and cause inflammation and fibrosis (scarring) in that organ.<sup>3</sup> Two of them, Hepatitis A virus (HAV) and Hepatitis E virus (HEV), are enterically transmitted, through the digestive system, and generally cause a self-limiting infection.<sup>4</sup> Rarely, HAV and HEV may cause fulminant (rapidly progressing) liver failure and a small proportion of patients die

<sup>1</sup> Hepatitis G was described at paragraph 2.10 of the Preliminary Report. The standard text was *Schiff's Diseases of the Liver*, 10th edition, 2007

<sup>2</sup> Professor Thomas – Day 52, pages 9–11

<sup>3</sup> Preliminary Report, paragraphs 2.5 and 2.6

<sup>4</sup> Preliminary Report, paragraphs 2.8 and 2.9

from this complication. In general, however, after two or three months the patient's liver function tests and the architecture of their liver return to normal. The virus is eradicated and the person will have protective immunity for the rest of their life against the virus causing the infection.

**13.6** Hepatitis B and C viruses (HBV and HCV, respectively) are parenteral, blood-borne infections,<sup>5</sup> transmitted by the introduction of infected material through the skin or mucosal surfaces.<sup>6</sup> They may cause acute, clinically significant hepatitis. A proportion of those infected go on to develop chronic infection. The definition of the 'chronic' condition is statistically based and internationally agreed.<sup>7</sup> In Hepatitis B and C an infection is considered to be chronic if it continues for longer than six months after identification of the virus or antibodies to it.<sup>8</sup> 'Acute' hepatitis is defined as a self-limiting illness lasting less than six months. Estimates of clearance rates for Hepatitis C within the first six months vary from 20% to around 30–40%.<sup>9</sup> The remaining 60–80% of patients progress to chronic infection.

**13.7** In Hepatitis B and C cases, many acute infections remain unidentified: they may be asymptomatic. If there are symptoms, they tend to occur in the first few months after infection, whether acute or chronic, and tend to be more severe in a patient with acute infection. These symptoms can include flu-like symptoms, jaundice, loss of appetite and abdominal pain. In the case of an acute self-limiting infection, the level of liver enzymes in the patient's blood, most commonly alanine aminotransferase (ALT), peaks typically at about three months and falls to a persistent normal level at about six months. If HCV is cleared in the earlier stages of developing fibrosis, either spontaneously or as a result of treatment, then the liver will ultimately remodel and go back to normal and the patient will have been cured both of the presence of the virus and of the liver disease.

**13.8** In chronic infection, after the initial three-month peak, ALT levels continue to fluctuate, often above the upper limit of normal. Chronic infection puts the individual at risk of 'progressive liver disease', the risk that fibrosis will develop to cirrhosis and this, in the case of cirrhotic patients, in turn creates the greatest risk of developing complications.<sup>10</sup> Progression to cirrhosis indicates that not only is there significant fibrosis but also that the normal architecture of the liver has changed to include structurally abnormal nodules.<sup>11</sup> At that stage the process is probably irreversible: while a patient may manage to clear HCV permanently, the cirrhosis will remain with its potential complications.<sup>12</sup>

**13.9** The complications of cirrhosis may be very serious and life-threatening. Two of the main complications of cirrhosis are hepatocellular carcinoma (HCC, primary cancer of the liver cells) and bleeding from oesophageal varices (varicose veins in the stomach and gullet).<sup>13</sup>

<sup>5</sup> Strictly speaking a parenteral infection is one spread by a means other than by the introduction of a pathogen to the gastrointestinal tract and, in this general way, does not refer only to blood-borne infections. Medical literature of the time, however, used the term parenteral, at least as regards hepatitis, to mean 'blood-borne' and this usage is retained here.

<sup>6</sup> Hepatitis D, referred to in the Preliminary Report at paragraph 2.11, is also a parenterally transmitted RNA virus which affects those already infected with Hepatitis B. It is not relevant to the NHS patients discussed in this Report.

<sup>7</sup> Professor Thomas – Day 52, pages 72–75; Professor Thomas' report on Hepatitis C [PEN.017.1071] at 1076

<sup>8</sup> Professor Thomas – Day 52, page 12 and pages 72–73

<sup>9</sup> Thein et al, 'Prognosis of hepatitis C virus-infected Canadian post-transfusion compensation claimant cohort', *Journal of Viral Hepatitis*, 2009; 16:802-813 [LIT.001.4184] at 4187; Professor Thomas – Day 52, page 13 and pages 56–57; Professor Thomas' report on Hepatitis C [PEN.017.1071] at 1074

<sup>10</sup> Professor Thomas – Day 52, pages 58–59. Increasing fibrosis is measured on the Ishak scale. The scale runs from 1 (no fibrosis) to 6 (cirrhosis) at which stage the individual is at risk of hepatocellular carcinoma.

<sup>11</sup> Professor Hayes – Day 78, pages 83–4

<sup>12</sup> Professor Thomas – Day 53, page 58

<sup>13</sup> Professor Thomas – Day 52, pages 8–12, generally

Further complications of cirrhosis, encephalopathy (damage to the brain characterised by confusion, cognitive impairment and lethargy) and ascites (the accumulation of fluid in the abdomen), are signs of liver failure.<sup>14</sup> A person with cirrhosis of any cause has a risk of developing a hepatocellular cancer of 2–3% a year.

**13.10** In general, the progression to End Stage Liver Disease (ESLD) encompasses all of the stages mentioned. The march of events is: acute infection, failing to resolve, leading to chronic infection and then cirrhosis, and then on to the risks of liver cancer and/or liver failure.<sup>15</sup> With very few exceptions, only those HCV-infected individuals who have developed cirrhosis are at risk of liver cancer. In a very small proportion of cases, HCC may develop at an earlier stage.<sup>16</sup> In chronic HBV, too, HCC develops after cirrhosis is established. However, in those infected with HBV in infancy, a pattern of infection found more commonly in the Far East and Africa, HCC may also develop in the non-cirrhotic liver.<sup>17</sup>

**13.11** The prevalence of these diseases varies across the world and that is frequently due to causes that are at best indirectly relevant for present purposes. Worldwide, some 350 million people have chronic Hepatitis B, three-quarters of whom were infected at birth. Most of these individuals live in China.

**13.12** Worldwide, 170 million people are estimated to have Hepatitis C.<sup>18</sup> Causes of high prevalence of HCV vary. In Bolivia it may be due to tribal scarification practices and in Egypt, which has the highest prevalence of HCV infection in the world, it is probably related to a programme of injection to treat the endemic parasitic disease schistosomiasis from the late 1950s to the early 1980s, which involved the use of unsterilised equipment. There is twice the prevalence of Hepatitis C infection in the general population of the USA when compared with the UK.

**13.13** In the UK as a whole, chronic Hepatitis B (now generally a smaller problem than Hepatitis C) has its highest prevalence in first-generation migrants from the Far East, Africa or the Mediterranean where prevalence of the disease is high. The low prevalence of the disease in the general public in the UK was attributed by Professor Thomas to the introduction of universal standards within, and provision of sterile equipment throughout, the National Health Service.<sup>19</sup> In Scotland, while the true prevalence of Hepatitis C in the population as a whole remains unknown,<sup>20</sup> the number of known cases continues to increase with improved and wider ascertainment. A great many of both new infections and newly discovered infections occur amongst intravenous drug users (IVDUs), past or present.

## Biology of HCV

**13.14** In Hepatitis B the genetic information for the virus is contained in deoxyribonucleic acid (DNA). In Hepatitis C the genetic information for the virus is contained in ribonucleic acid (RNA): it is an RNA virus. HCV exhibits considerable sequence variation, or genetic

<sup>14</sup> Professor Hayes – Day 78, pages 88–89

<sup>15</sup> Professor Thomas – Day 53, page 59

<sup>16</sup> Thein et al, 'Prognosis of hepatitis C virus-infected Canadian post-transfusion compensation claimant cohort', *Journal of Viral Hepatitis*, 2009; 16: 802–813 [LIT.001.4184] at 4187. Cf Professor Thomas – Day 53, page 59 et seq. His evidence was that HCC did not occur without prior development of cirrhosis.

<sup>17</sup> Sherlock S. & Dooley J *Diseases of the Liver and Biliary System*, 9th edition 1993, pages 504–505

<sup>18</sup> Professor Thomas – Day 52, page 16

<sup>19</sup> Ibid page 48

<sup>20</sup> See, however, Chapter 3, *Statistics*.

heterogeneity.<sup>21</sup> There are six major genotypes, with additional differences between the strains (or 'quasi-species')<sup>22</sup> found within a single genotype. The biological behaviour of the different genotypes is encoded by the genetic structure of the virus<sup>23</sup> and there are major biological differences between the genotypes which have a bearing on treatment. Treatment of Genotype 1 virus infection with Interferon and Ribavirin (the first two forms of drug therapy for Hepatitis C which became available) cures a lower proportion of cases than the same treatment of Genotypes 2 and 3.<sup>24</sup> An individual, and particularly an individual with haemophilia, may have been infected with more than one genotype of HCV and may be co-infected with Hepatitis B. In such cases the replication of one virus may interfere with the replication of the other or others, which become apparent only when the first is cleared.<sup>25</sup>

**13.15** As with each of the hepatitis viruses, the different genotypes of HCV are not distributed uniformly. The description of the distribution noted in the Preliminary Report remains valid.<sup>26</sup> In the UK as a whole about 50% of HCV is Genotype 1, with Genotypes 2 and 3 making up the other half. In the USA, Genotype 1 predominates, in particular in the haemophilia population, with Genotype 3 coming into play later.<sup>27</sup>

**13.16** HCV RNA is detectable in acute, self-limiting, cases up to about six months but not thereafter, since the body will have dealt with the virus. In chronic HCV infection the virus RNA may continue to be detectable indefinitely and is the signature of the chronic condition.<sup>28</sup> The level of viraemia (virus in the blood) probably affects the severity of liver disease.<sup>29</sup>

**13.17** The likelihood of developing a self-limiting acute infection is related to an individual's genetic make-up and, in particular, the immune system's recognition proteins (haplotype (HLA type) proteins). A person's HLA type is genetically determined and does not change. Certain HLA types confer a stronger possibility of leading to clearance of the virus after infection. The individual's HLA type forms a significant component in the risk matrix, generally and in relation to the risk of re-infection following clearance. If an individual is infected and clears the virus spontaneously, the same outcome is likely to follow a subsequent infection.<sup>30</sup>

**13.18** The sequelae of infection with HCV (the complications associated with the disease) appear to vary among populations in different geographical areas. For example, infection can be associated with a risk of non-Hodgkins B cell lymphoma in southern Europe but is rarely so associated in the UK. Care is therefore needed in applying information from different geographical areas of the world to the UK generally and, within the UK, to Scotland in particular. Understanding of some consequences of infection is still developing.

<sup>21</sup> Professor Thomas' report on Hepatitis C [PEN.017.1071] at 1072–3; Professor Thomas – Day 52, pages 38–39

<sup>22</sup> Professor Hayes – Day 78, page 98

<sup>23</sup> Professor Thomas – Day 52, page 40

<sup>24</sup> 'Cure' in this context is the permanent eradication of the virus from the patient which, in pre-cirrhotic individuals, allows the liver to return to normal. See paragraphs 13.97–13.101 below for further information on current treatment for each of the main genotypes, which takes account of these factors.

<sup>25</sup> Professor Thomas – Day 52, pages 60–61. In practice, Professor Hayes stated that it is very rare to find in clinical practice an individual with more than one genotype, as distinct from quasi-species of a single genotype: Professor Hayes – Day 78, page 98.

<sup>26</sup> Preliminary Report, paragraph 2.21

<sup>27</sup> Professor Thomas – Day 52, page 49

<sup>28</sup> Professor Thomas – Day 52, page 73; Professor Thomas' report on Hepatitis C [PEN.017.1071] at 1075–76. After 20–30 years viral DNA may no longer be readily detected in up to 10% of chronically infected patients. See Watanabe et al, 'Spontaneous elimination of serum hepatitis C virus (HCV) RNA in chronic HCV carriers: A population-based cohort study', *Journal of Medical Virology*, 2003; 71: 56–61 [LIT.001.4198]

<sup>29</sup> Professor Thomas – Day 52, page 58

<sup>30</sup> Ibid pages 57–58; Day 53, pages 61–62



For example, impaired cognitive function ('brain fog') and depressive mood disorders, which occur in some cases, are now thought to be causatively related to HCV infection.<sup>31</sup> Evidence for these sequelae strengthened with the discovery that, independently of the severity of liver disease, virus recovered from the brain of infected patients had a structure in common with that found in peripheral blood lymphocytes but different from the structure of the virus in the liver. The causal connection is now probably established.<sup>32</sup>

### Hepatitis C: Identification of the virus

**13.19** The discovery of HCV was announced by Chiron, a US pharmaceutical company, in May 1988.<sup>33</sup> Scientific details were published in April 1989.<sup>34</sup> In the same month details were also published of an enzyme-linked immunosorbent assay (ELISA) to detect antibodies to HCV.<sup>35</sup> The background to the discovery is discussed in more detail in Chapter 16, *Knowledge of Viral Hepatitis 3 – 1986 Onwards*. Chiron's work was a significant, and inventive, development in the knowledge of HCV infection. It laid the foundation for research into the genetic structure of the virus set out above and in much of the remainder of this chapter. In the context of transfusion-related transmission and blood product therapy-related transmission, post-transfusion HCV infection now appears to explain most if not all cases of what was once termed 'non-A, non-B Hepatitis' (NANB Hepatitis) virus infection.<sup>36</sup>

**13.20** Since the announcement of Chiron's discovery, research into the genomic composition of the Hepatitis C virus has identified variations which now support an increasingly sophisticated system of sub-classification. At the Inquiry's oral hearings, Professor Thomas noted that Japanese researchers had succeeded in growing the virus culture in one particular cell line within the previous five years.<sup>37</sup> There remain problems of easy and reliable replication. These problems affect the application of developing knowledge in the testing of new treatments and the preparation of a vaccine, for example. Research continues and it appears likely that much remains to be discovered before a complete description of the virus in its many sub-types, its sequelae and the most effective means of protection against and treatment for it can be attempted.

### The reproductive process of HCV

**13.21** During an episode of acute hepatitis in which the virus is eliminated, the body mounts an effective immune response, engaging the CD4 T-helper and CD8 cytotoxic cells. In general, the stronger the response the more likely the patient is to recover. Individuals who become jaundiced have a lower frequency of viral persistence than those who do not: the jaundice is a reflection of the immune system killing infected liver cells.<sup>38</sup> The

<sup>31</sup> Professor Thomas – Day 52, pages 61–64; Professor Thomas' report on Hepatitis C [PEN.017.1071] at 1075. See also: Weissenborn et al, 'Hepatitis C virus infection and the brain', *Metabolic Brain Disease*, 2009; 24:197 – 210 [LIT.001.4204]

<sup>32</sup> Professor Thomas – Day 52, pages 64–68. See also: Weissenborn et al, 'Hepatitis C virus infection and the brain' *Metabolic Brain Disease*, 2009; 24:197-210 [LIT.001.4204]

<sup>33</sup> Ezzell, 'Candidate Cause Identified of Non-A, Non-B Hepatitis', *Nature*; 19 May 1988 [SGH.002.8036]

<sup>34</sup> Choo et al, 'Isolation of a cDNA Clone Derived from a Blood-Borne Non-A, Non-B viral Hepatitis Genome', *Science*; 1989, 244: 359-362 [LIT.001.0629]

<sup>35</sup> Kuo et al, 'An Assay for Circulating Antibodies to a Major Etiologic Virus of Human Non-A, Non-B Hepatitis' *Science*, 1989; 244: 362 [LIT.001.0629] at 0632

<sup>36</sup> As noted in Chapter 14, *Knowledge of Viral Hepatitis 1*, paragraph 14.67, the expression 'non A, non B Hepatitis' (frequently abbreviated to 'NANBH' or 'NANB Hepatitis') was coined in the mid-1970s as a collective term for hepatitis from which, at that time, Hepatitis A and Hepatitis B, as well as cytomegalovirus (CMV) and Epstein-Barr virus (both of which can cause liver inflammation), had been excluded.

<sup>37</sup> Professor Thomas – Day 52, page 38

<sup>38</sup> Ibid pages 68–69

'price' of clearing the HCV completely and spontaneously from the body is often a more severe acute clinical illness. In patients developing persistent infection, the CD4 and CD8 responses are less strong, though still detectable, and clinical manifestations at the acute stage are often trivial or absent.<sup>39</sup>

**13.22** Where the virus persists, it must replicate. In order to replicate, a virus needs to use many of the enzymes within a living cell. It must, therefore, enter a cell which has a suitable point of entry on its surface. Liver cells have a surface receptor which normally transports fat into the cell, among other functions, and the envelope in which the Hepatitis C virus is contained has the appropriate physical configuration to bind onto the liver cell receptor. HCV gains entry to the liver by docking with the liver cell: the virus 'piggy-backs' its entry onto the normal receptor process.<sup>40</sup>

**13.23** When the virus enters the liver cell, it 'hijacks' the replication mechanism of the host cell: the RNA of the virus enters the protein-synthesising machinery of the cell, immediately making use of the apparatus of the cell to make more copies of itself. New viral particles of positive strand RNA are manufactured and then self-assemble in the cell: they 'encode' for a polyprotein comprising all of the structural and non-structural proteins of the virus. The new viral particles follow the same pathway through the cell as fat. The fat globules passing through the liver therefore incorporate virus particles.<sup>41</sup> The virus particles are then excreted from the cell, by the same structures that are normally used to get rid of fat from the liver cell and exit from the liver to circulate in the blood stream.<sup>42</sup>

**13.24** HCV does not damage or kill liver cells directly. Rather, the liver cells suffer because of the body's immune response to the virus: small protein molecules called cytokines are released to both shut down virus replication and kill the infected cells.<sup>43</sup>

**13.25** There are two highly variable proteins on the surface of the HCV envelope and the new virus particles produced are, in turn, highly variable, although the variability does not extend to shifting the virus from one genotype to another. Rather, HCV creates a swarm of quasi-species: every virus particle in the patient is slightly different in its RNA sequence.<sup>44</sup> Even within an individual infected with a single genotype the genetic sequence of each virus particle is different and changes over time as the virus comes under various selection pressures. Many of the different variations, the quasi-species, produced in replication will be non-viable (unable to replicate). Otherwise they are targeted, initially by the host's immune response and, in more recent times, by potentially therapeutic drugs such as the protease and polymerase inhibitors.

**13.26** The patient's antibody response may neutralise most of the virus particles that are viable. As virus neutralising antibodies are made by the host's immune response, new variants of the virus, which existing antibodies do not immediately neutralise are selected.<sup>45</sup> There will be a small number of quasi-species that have antigens (epitopes) that are not targeted by the patient's immune system and, because they are not neutralised, these become dominant and provide the virus with an advantage until the system adapts to find

<sup>39</sup> Professor Thomas' report on Hepatitis C [PEN.017.1071] at 1075

<sup>40</sup> Professor Thomas – Day 52, pages 42–46

<sup>41</sup> Ibid page 44 and 50

<sup>42</sup> Ibid pages 53–54; Professor Thomas' report on Hepatitis C [PEN.017.1071] at 1073

<sup>43</sup> Professor Thomas – Day 52, page 56

<sup>44</sup> Ibid page 41

<sup>45</sup> Technically 'selected for'.

antibodies to them.<sup>46</sup> After a significant new antigen appears, it takes about 10 days for the immune system to produce an antibody.<sup>47</sup>

**13.27** HCV exhibits greater genetic diversity than most other viruses and this is a major contributor to the high rate of chronicity, the difficulty in producing a vaccine and the rapid emergence of virus strains that are resistant to new treatments such as protease, polymerase and NS5a inhibitors.<sup>48</sup>

**13.28** There are continuing issues relating to HCV infection. Professor Hayes commented on the changing understanding of the natural history of Hepatitis C over time.<sup>49</sup> In the early 1990s people did not know how aggressive the condition was and there is still considerable debate on this point. When a test for HCV infection became available, instead of confirming the diagnosis of NANB Hepatitis in the small number of people who had been so labelled, clinicians here and abroad found that large numbers of people who had not been suspected of having NANB Hepatitis were infected with HCV. In the UK the prevalence of HCV is low, at less than 1%. How the disease would impact on people's lives nevertheless became a major issue. The risk of progression to cirrhosis was originally estimated at 20% but the natural history of the disease is still unclear and is complicated by other major factors such as alcohol consumption and obesity. It is now thought that a large number of HCV-infected patients will go on to develop major complications, including cirrhosis and its sequelae.<sup>50</sup>

**13.29** As understanding of the characteristics of HCV has developed, it has become increasingly clear that advances in knowledge are dependent on the science of genetics and on the application of technology that was quite unknown at periods when exposure to risk, at least via transmission by blood or blood products, was greatest and the response to infection was least effective.

**13.30** Overall, the circumstances in Scotland were very similar to those described above for the UK as a whole, subject to some variation in percentages.<sup>51</sup>

### **Risk of transmission of HCV by blood, blood components and blood products**

**13.31** It is important to note that the risk of transmission of Hepatitis C by transfusion of blood or blood components, or the infusion of blood products, has greatly diminished following the introduction, in current practice, of highly developed testing procedures which are rigorously applied. Separate samples are taken at the time of blood donation to be tested for blood group (ABO, Rhesus and sometimes more minor groups) and microbiology markers (syphilis, HIV, HCV, HBV, and HTLV-I and II by serology and HIV, HBV and HCV by nucleic acid testing). All platelet donations are tested for bacterial contamination.<sup>52</sup> Apart from HCV, serology tests also look for patients with antibodies to infections. Nucleic acid testing is based on polymerase chain reaction, which amplifies RNA or DNA and is highly sensitive. Currently, donations are tested by both techniques.<sup>53</sup> Discretionary tests are carried out for other pathogens.

<sup>46</sup> Professor Thomas – Day 52, pages 41–42 and 69–70

<sup>47</sup> Ibid page 49

<sup>48</sup> Professor Thomas' report on Hepatitis C [PEN.017.1071] at 1071–72

<sup>49</sup> Professor Hayes – Day 78, page 78; Professor Hayes' report on Hepatitis C [PEN.018.0240]

<sup>50</sup> Professor Hayes – Day 78, pages 78–80

<sup>51</sup> 'Surveillance of known hepatitis C antibody positive cases in Scotland: results to 31 December 2003,' *SCIEH Weekly Report*, 2004; 38: 150–155 [LIT.001.4176]

<sup>52</sup> Professor Turner's statement on practices in Scotland in respect of the collection, testing, processing and distribution of blood [PEN.002.0452] at 0455

<sup>53</sup> Professor Turner – Day 7, pages 24–25

**13.32** New forms of screening are rigorously trialed. A test must be sensitive enough that it is going to be worth doing in the first place but has a specificity level that is manageable without unnecessarily deferring large swathes of people.<sup>54</sup> When screening large numbers of healthy people, the false positive group far outweighs the true positives, so the positive predictive value (the number of true positive results amongst the 'positive calls') of the initial screening test is very poor from that point of view. Normally, there should be at least one kind of confirmatory assay, based on a different platform or technology to the original test, since otherwise there would be no way of sorting out the false positives and the true positives. In addition, legally the test has to be CE marked,<sup>55</sup> under the In Vitro Diagnostics Directive<sup>56</sup>, which means it can be marketed in the European Union and, therefore, in this country.<sup>57</sup>

**13.33** Samples which are initially reactive on screening are subjected to a hierarchy of very sensitive further tests. This series of tests is made as sensitive as possible to avoid missing people with infection. The aim is to achieve a low false negative result. That, in turn, creates a risk of more false positives. So, typically, in the modern screening, with third or fourth generation tests reflecting much refinement of technology over the last 10 or 20 years, about two per cent of donations have been found to be reactive on initial screening for one or other marker. These samples are withdrawn prior to use. The sample is then tested again twice using the same assay. About 90% of those are repeat reactive negatives, pointing to a system problem in the initial test. Perhaps only about 0.02% are repeat reactive positive at the second stage. It is not concluded even then that the patient has the infection. Rather, at that stage the donation is quarantined for much more detailed examination; samples are sent to a reference laboratory, where a whole series of different tests, based on different kinds of platforms and technology, are applied to try to establish whether or not there is a true positive result. Again, in general terms, around 10% of those repeat reactive samples turn out to be true infections and the other 90% tend to be technical artefacts (an artificial effect introduced by the technology used). The procedure, as described, now ensures that donors are informed of an infection only when the SNBTS is absolutely certain that the diagnosis is correct.<sup>58</sup> The procedure described protects the patient recipients of blood or blood products without exposing the donor to unnecessary anxiety.

**13.34** This highly sophisticated system has developed rapidly over the last 20 years. Throughout the material part of the reference period, however, the technology underlying the screening tests available was both less sensitive and less specific. There is no basis in the evidence for concluding that, in general, the best available methods of screening were not used as they became available but it is important to note the steps that have been taken to avoid transmission of infection in the course of modern transfusion practice and the treatment of coagulation disorders.

### *Transmission of Hepatitis C and risk of repeat infection*

**13.35** From 1991, when screening of blood became universal practice in the UK, transfusion of blood and blood components and the infusion of blood products have not been associated with the transmission of Hepatitis C to any material extent. In the

<sup>54</sup> 'Sensitivity' is a function of the test's ability to capture all cases of infection with the target pathogen. 'Specificity' is a function of the test's ability to identify only the target pathogen.

<sup>55</sup> CE marking is a manufacturer's declaration that a product meets the requirements of relevant EU directives.

<sup>56</sup> 98/97/EC of October 1998

<sup>57</sup> Professor Turner – Day 7, page 28

<sup>58</sup> Ibid pages 26–27

case of blood products used to treat coagulation disorders, largely retrospective research demonstrated that there had been almost 100% infection with the concentrates that were available before effective virus inactivation began in the mid-1980s, whether commercial materials or the products of the UK public service (NHS) fractionators were used.<sup>59</sup>

**13.36** In the case of blood products, the risk of transmission of blood-borne viruses was related to the number of infective donors contributing to a particular batch and to the severity of the patient's condition requiring coagulation factor therapy and therefore the number of infusions required. The very large number of donors contributing to the plasma pools made the prevalence in the general population almost irrelevant.<sup>60</sup>

**13.37** Other means of transmission raised different issues, such as the relevance of the level of concentration of virus in the source blood and the risk of sexual and neonatal transmission.<sup>61</sup> Hepatitis B is much more readily transmitted sexually than Hepatitis C. Similarly, Hepatitis B is more easily transmitted in the course of surgical procedures, through the perforation of gloves for example. In each case this is due to the concentration of virus in the source blood. The levels that are typically found in Hepatitis B are around  $10^7$  to  $10^8$  (10 million to 100 million) virus particles per millilitre. At those levels, neonatal and sexual transmission is seen fairly frequently. In a normal HCV infection a typical concentration may be  $10^5$  (100,000), or  $10^6$  (a million) virus particles per millilitre. At those levels, it is unusual for either sexual or neonatal transmission to occur.<sup>62</sup> The figure cited in the literature for sexual transmission is 5%. However, Professor Thomas did not think that, in testing spouses, he had ever found a positive case, with the exception of cases of co-infection with HIV where the rate of HCV replication was higher (by one or two logs) and the level of viraemia was relatively high. (The Inquiry identified one such case, the witness given the pseudonym 'Laura'. See Chapter 6, paragraphs 6.228–6.277.)

**13.38** Comparison with Hepatitis A and Hepatitis B gave rise to misconceptions about NANB Hepatitis/HCV which were only dispelled during the 1990s when knowledge of the biology and immunology of HCV developed. Patients who had an attack of Hepatitis A or an acute attack of Hepatitis B and recovered, as indicated by the normalisation of liver enzymes (ALT levels), and the appearance of antibodies indicating immunity (anti-HAV, anti-HBV), had cleared the virus from their bodies and would not be infected again. So when, after a putative attack of NANB Hepatitis, the patient's ALT fell to within the normal range, it was initially assumed that the person had cleared the virus, had acquired immunity and would not be infected again. This turned out to be wrong for two reasons. First, many patients with 'indolent' (apparently benign) NANB Hepatitis/HCV infection had intermittently normal liver enzyme levels but were still harbouring the virus and could still develop significant ill health from it. Secondly, it was realised after the discovery of the HCV antibody that, unlike anti-HAV or anti-HBV, anti-HCV did not indicate immunity to further HCV infection, particularly by HCV with a different genotype. Professor Thomas described this as 'an anomaly in virology'.<sup>63</sup>

<sup>59</sup> Professor Thomas – Day 52, page 76; Professor Thomas' report on Hepatitis C [PEN.017.1071] at 1077. And see, for example: Yee et al, 'The Natural History of HCV in a cohort of haemophilic patients infected between 1961 and 1985', *Gut*, 2000: 47: 845–851 [LIT.001.4318].

<sup>60</sup> Professor Thomas – Day 52, pages 84–85 and pages 89–90; Fletcher et al, 'Non-A, non-B hepatitis after transfusion of factor VIII in infrequently treated patients', *British Medical Journal*, 1983; 287 [LIT.001.0239]; Kernoff et al, 'High Risk of Non-A Non-B Hepatitis After a First Exposure to Volunteer or Commercial Clotting Factor Concentrates: Effects of Prophylactic Immune Serum Globulin', *British Journal of Haematology*, 1985; 60: 469–479 [LIT.001.0800]

<sup>61</sup> See comments on mini transfusion of neonatal infants below at paragraph 13.72.

<sup>62</sup> Professor Thomas – Day 52, page 77

<sup>63</sup> *Ibid* page 83. (See also Chapter 8, *Knowledge of HIV/AIDS Now*, paragraph 8.23 – exposure to HIV does not provide subsequent immunity to that virus either).

**13.39** So, during the 1970s and 1980s, when an individual haemophilia patient was found to have a 'second infection' (often merely a period of months during which ALT levels in the blood became elevated), haemophilia doctors thought that it was probably caused by a second, quite different virus, when in fact it was often the original HCV infection resurfacing in the form of raised ALT levels. It is now also believed that the same individual can acquire second, third and further infections after recovering from a first infection with Hepatitis C. In some haemophilia patients several genotypes and subtypes of HCV have, albeit rarely, been identified in the same individual.<sup>64</sup>

### **Developing perception of the severity and natural history of NANB Hepatitis/Hepatitis C liver disease**

**13.40** Despite significant developments in knowledge, the natural history of HCV is still unclear and tends to be complicated by other factors.<sup>65</sup> The changing perceptions of the severity of NANB Hepatitis/HCV over time are traced in greater detail in Chapters 14–16, *Knowledge of Viral Hepatitis 1–3*. In this chapter it is necessary only to identify some milestones along the way as markers that may be of assistance in interpreting the statements of patients and their relatives.

**13.41** Until the end of the 1970s, the generally accepted view was that NANB Hepatitis was, clinically, relatively unimportant. By 1981 Professor Sheila Sherlock would write in the sixth edition of her highly respected textbook, *Diseases of the Liver and Biliary System*, that the prognosis of NANB Hepatitis was 'uncertain but probably benign'.<sup>66</sup>

**13.42** However, at the time of publication of the sixth edition of Professor Sherlock's book, Dr May Bamber and others, including Professor Sherlock and Professor Thomas, were already engaged in studies based on biopsy findings which demonstrated that patients with chronic NANB Hepatitis had disease that covered the whole spectrum of acute and chronic hepatitis, including cirrhosis.<sup>67</sup> That study was also published in 1981. In retrospect, it marked the beginning of a significant change in expert opinion. US research published in 1982 pointed in the same direction.<sup>68</sup>

**13.43** Research into the progression to serious liver disease in Hepatitis B, relying on biopsy findings, had enabled the development of prognostic indicators relating to the pattern of inflammation observed in the liver tissue. Chronic persistent hepatitis, considered to have a very benign prognosis, was related to inflammation in the portal tracts. Inflammation that extended out into the periportal area – chronic active hepatitis – was associated with the risk of subsequent development of cirrhosis. Inflammation spread evenly in the hepatic lobule (chronic lobular hepatitis) was associated with a benign prognosis. Bridging fibrosis, in which fibrous tissue was found between the portal tracts and the central veins, or between the portal tracts themselves, was an indication of the onset of cirrhosis.<sup>69</sup>

<sup>64</sup> Professor Thomas – Day 52, pages 83–84

<sup>65</sup> Professor Hayes – Day 78, pages 79–80

<sup>66</sup> Sherlock, S. *Diseases of the Liver and Biliary System*, 6th edition 1981

<sup>67</sup> Bamber et al, 'Clinical and histological features of a group of patients with sporadic non-A non-B hepatitis', *Journal of Clinical Pathology*, 1981; 34: 1175–1180 [LIT.001.0759]

<sup>68</sup> Koretz et al, 'Non-A, non-B post-transfusion hepatitis: disaster after decades?', *Hepatology*, 1982; 2: 687 [LIT.001.3738]; Professor Thomas' report on Hepatitis C [PEN.017.1071] at 1079–80

<sup>69</sup> Professor Thomas – Day 52, pages 116–118

**13.44** It was initially assumed that the prognostic indicators for NANB Hepatitis/HCV infection were the same as for Hepatitis B.<sup>70</sup> In the early biopsies carried out in patients with NANB Hepatitis, the findings were of chronic persistent or chronic lobular hepatitis and the supposition was that they were unlikely, as a matter of probability, to progress to serious sequelae. Initially, biopsies were performed on putative NANB Hepatitis patients who had biochemical indications of a steep rise in ALT before it returned to normal.<sup>71</sup> It was on the basis of indications from these procedures that it was inferred initially that NANB Hepatitis was a benign prognostic disease, partly because, as already noted at paragraph 13.7, these were the minority of individuals who were likely to recover fully and not develop chronic illness.<sup>72</sup> In retrospect, the widely held supposition that chronic persistent and chronic active hepatitis would follow the same clinical course in Hepatitis C as in Hepatitis B, was wrong.<sup>73</sup>

**13.45** A Sheffield study by Dr David Triger and others in 1978 showed cases of cirrhosis in haemophilia patients infected with NANB Hepatitis. There was case selection towards the adverse end of the disease spectrum, however, confounding the picture that emerged.<sup>74</sup> Additionally, the basic characteristic of biopsy, that it targets a minute piece of the liver, gave rise to sampling errors.<sup>75</sup> Further, there were other factors that might have contributed to the progression of disease, such as age at infection, the duration of infection, obesity and alcohol use, which were not necessarily reflected in biopsy findings or properly understood at that time.<sup>76</sup>

**13.46** The 1981 study by Bamber and colleagues related to 12 patients, both transfusion patients and patients without a transfusion history, who were diagnosed on serological grounds as having NANB Hepatitis infection. No haemophilia patient was involved. Some patients had cirrhosis; some had chronic active hepatitis with piecemeal necrosis; one had portal-systemic encephalopathy associated with cirrhosis and severe liver dysfunction. There was evidence of fatty change and bile duct damage. The findings were an affirmation of the work of Dr Triger's Sheffield group, which had previously been controversial.<sup>77</sup> By the 8th edition of her book in 1989, Professor Sherlock had changed her stance: she wrote in that edition that 20% of infected individuals would develop cirrhosis over 20 years and that after 30 years the proportion would increase progressively.<sup>78</sup>

**13.47** Professor Thomas emphasised that doubt remained:

[S]ome would say, even now, we do not really know the factors that determine the rate of progression and, for instance, in Italy Hepatitis C has a much worse prognosis to what you see in northern Europe ... and ... that's arguably related to all the other factors ... how much alcohol you take, the genetic factors, whether there is co-infection with other viruses, all manner of things.

So I don't think this uncertainty about the natural history that was prevalent between 1978 and 1985 has changed massively. I think we are still wondering:

<sup>70</sup> Ibid page 117

<sup>71</sup> Professor Thomas' report on Hepatitis C [PEN.017.1071] at 1079; Professor Thomas – Day 52, pages 120–121

<sup>72</sup> Professor Thomas – Day 52, pages 117–118

<sup>73</sup> Ibid page 119

<sup>74</sup> Preston et al, 'Percutaneous liver biopsy and chronic liver disease in haemophiliacs', *The Lancet*, 1978; (ii): 592–594 [LIT.001.0387] Day 52, pages 121–122

<sup>75</sup> Ibid page 136–137. See sections below on these 'aggravating factors'.

<sup>77</sup> Professor Thomas – Day 52, page 129; Bamber, Sherlock et al, 'Clinical and histological features of a group of patients with sporadic non-A non-B hepatitis', *Journal of Clinical Pathology*, 1981; 34: 1175–1180 [LIT.001.0759]

<sup>78</sup> Professor Thomas – Day 52, pages 129–131

is it 20 per cent or 40 per cent that will develop cirrhosis? All we can deduce from these studies is that some people in the context of normal life ... where we eat and drink ... some people have severe liver disease. But how many, that's an open question still, because none of the studies ... are statistically significant. There isn't a large enough sample of unselected cases.<sup>79</sup>

**13.48** As noted above, once a patient already has cirrhosis, it does not disappear even when the causative viral infection is cured. The risk of progression to hepatic decompensation (liver failure) and possible HCC is reduced, however, and the patient is no longer infectious. Cirrhosis does put the patient at risk of liver cell cancer, however. There are patients who had cirrhosis prior to treatment who have undergone a sustained viral response and are cured, virologically speaking; some of them have nonetheless gone on to develop primary liver cell cancers.<sup>80</sup> In current practice, once a person has been identified as having cirrhosis, he or she will be monitored by ultrasound and an alphafetoprotein test every six months in the hope of identifying tumours when they are small and more treatable.<sup>81</sup> The patient will also be regularly monitored for varices by upper gastro-intestinal endoscopy. In this group clinicians do not anticipate a cure of the patient's overall condition because they are still at risk of severe complications.

**13.49** The position of a haemophilia patient is complicated by his primary condition. Thus, in terms of the overall effects of their underlying illness on quality of life metrics, the starting Quality of Life score would be unlikely to be the score typical for a member of the general public because of the clinical manifestations of haemophilia itself and possible associated psychological factors. There will also be continuing concern whether the condition has been dealt with.<sup>82</sup> Professor Thomas said:

[I]t's a very complicated situation really. There is the pre-treatment problems. They may have additional problems, other worries, financial worries, you know, and doctors tend to find reassurance, since they are making very difficult decisions ... if there is something objective they can measure, which is the presence or absence of the virus by techniques which are exquisitely sensitive really. And if, when you do that, you come up with a logic, something that you can understand -- when the virus goes down the patient feels better; when it goes up again, he feels unwell -- all that reassures the doctor that he is probably measuring something that's relevant.<sup>83</sup>

**13.50** By contrast, he suggested, Quality of Life measures – before and after 'successful' treatment for HCV in haemophilia patients – are much more complex.

**13.51** Now, over 20 years after the identification of HCV as the 'culprit' for almost all NANB Hepatitis infections, perceptions have changed. It has recently been estimated that, in the USA at least, the cohort of HCV-positive individuals (the total HCV-positive population) peaked around 2001 and will decline slowly over the following 20 years. Recently, Dr Gary Davis and colleagues observed that, bearing in mind that the prevalence of HCV infection in the population increased very quickly in the 1970s and 1980s (the first part of the HCV 'cohort'), by 1989 cirrhosis is thought to have occurred in about 5%

<sup>79</sup> Professor Thomas – Day 52, pages 138–139

<sup>80</sup> Professor Thomas – Day 53, page 58

<sup>81</sup> Professor Hayes – Day 78, page 88

<sup>82</sup> Professor Thomas – Day 53, pages 70–72

<sup>83</sup> Ibid pages 72–73



of all cases of chronic Hepatitis C, in 10% of all cases by 1998 and 20% by 2006. It was projected to have risen to 25% in 2010 and to be likely to rise to up to 37% in 2020 and 45% in 2030.<sup>84</sup>

### Clinical and other features of Hepatitis C infection

**13.52** This section notes clinical and other features associated with Hepatitis C infection in the UK. That excludes some complications found elsewhere. Marked geographical differences occur. For example, as noted above at paragraph 13.18, there is a high prevalence of HCV-positive patients in Mediterranean countries with non-Hodgkin's B Cell Lymphoma (a cancer of the lymphoid system) but there is no epidemiological evidence for the virus being involved in non-Hodgkin's B Cell Lymphoma in northern Europe.<sup>85</sup>

**13.53** In the early 1970s, jaundice was thought to be an important diagnostic feature of hepatitis generally and, from the mid-1970s, of NANB Hepatitis in particular. However, jaundice is rare in Hepatitis C infection.<sup>86</sup> Fulminant (rapidly progressing) hepatitis, indicative of liver failure, is very rare. Less than a fifth of cases involve jaundice. Professor Thomas emphasised that the rareness of jaundice was quite important because of the impact it had on the early lack of understanding of the infection. (See Chapters 13–15, *Knowledge of Viral Hepatitis 1 to 3.*)

**13.54** Two factors contribute to the severity of HCV infection. The first is the size of the inoculum (the amount of virus with which the patient is initially infected) and, resulting from that, the rate of spread of infection through the liver and the number of liver cells infected. The second is the speed of response of the immune system. If the immune response is very quick, there is rapid clearance of the infected liver cells, faster than the rate at which liver regeneration can replace the infected cells, and severe and more acute symptoms follow.<sup>87</sup>

**13.55** Clinical features common in acute hepatitis include influenza-type symptoms with malaise, myalgia (muscle pain), arthralgia (joint pain), anorexia (loss of appetite) and nausea and there may be mild pyrexia (elevated temperature). These may be followed by the biochemical features of hepatocyte necrosis (liver cell death) as the immune system attempts to clear the virus-infected liver cells. Transaminases (liver enzymes) increase in the blood as they are released from dying liver cells. An increase in serum bilirubin (described below) may occur. In such cases, the patient's urine becomes dark, stools become pale, and the patient may become jaundiced and develop itching.

**13.56** Where jaundice does occur in Hepatitis C, it lasts usually one to four weeks and heralds improvement in most cases, though a feeling of malaise and of being generally unwell may last many months.<sup>88</sup> Jaundice occurs when the liver cell mass is reduced, so that bilirubin can no longer be excreted. Bilirubin is a product of the red blood cells of the body, formed from broken-down haemoglobin. It is excreted through the liver and, because of reduced liver cell mass and also the fact that the liver cells swell, inhibiting the passage of the bilirubin into the bile ducts, there is obstruction of bile flow and cholestasis

<sup>84</sup> Davis et al, 'Aging of Hepatitis Virus (HCV)-infected Persons in the United States: a Multi-cohort Model of HCV Prevalence and Disease Progression', *Gastroenterology*, 2010; 138: S13 – S21 [LIT.001.4046]

<sup>85</sup> Professor Thomas – Day 53, pages 74–75

<sup>86</sup> Professor Thomas' report on Hepatitis C [PEN.017.1071] at 1080.

<sup>87</sup> Professor Thomas – Day 53, pages 10–12

<sup>88</sup> Professor Thomas' report on Hepatitis C [PEN.017.1071] at 1080

occurs: bile cannot flow from the liver to the duodenum, the first portion of the small intestine. Both factors, reduced liver functioning cell mass and reduced ease of flow of bilirubin into the bile ducts, contribute to a rise in bilirubin in the blood, and the eyes, and sometimes also the skin, become yellow.

**13.57** Jaundice does not happen in most cases of Hepatitis C because the initial 'insult' (damage) to the liver is less severe than, for instance, in Hepatitis A or B, when a larger proportion of the liver cells is infected and destroyed by the immune system as the infection is cleared.<sup>89</sup> Post-transfusion screening for jaundice therefore picked up only a small proportion of cases of NANB Hepatitis/HCV infection. This led to differing perceptions among doctors. While transfusionists in Scotland around 1980 believed that post-transfusion NANB Hepatitis was rare, on the basis of low reporting of jaundice, haemophilia centres saw persistent mild liver blood test abnormalities as very common, but probably of little importance.

**13.58** There are also extra-hepatic manifestations of infection.<sup>90</sup> The most readily understood of these are renal and dermatological and related to 'cryoglobulinemia', a condition in which the Hepatitis C virus forms an immune complex with associated antibodies and circulates in a patient's blood. When the blood cools in circulation, the complex precipitates out of suspension and this 'cryoprecipitate' can stick in small blood vessels, particularly in the kidney, which sometimes results in renal dysfunction.

**13.59** Dermal complications can be related to those immune complexes being deposited in the capillaries or small arterioles in the skin, often on the lower limbs, leading to the formation of small, painful and uncomfortable black nodules: a condition known as cryoglobulinaemia.<sup>91</sup> The nodules look like purpura but are actually thrombosed blood vessels, where the cryoglobulins, the immune complexes, have become stuck in the small blood vessels of the leg. The lower leg is more likely to be affected because, as the circulation is slower there, the lower legs are colder than the upper limbs or trunk and precipitation is more likely.

**13.60** Other dermatological features of HCV infection are associated with the problem called 'lichen planus' which manifests in rashes on the skin. Professor Thomas thought there was really no idea, as yet, as to why the infection should be associated with lichen planus.<sup>92</sup>

**13.61** Many of the flu-like signs and symptoms, which arise both in acute hepatitis (when the body naturally produces interferon) and in the course of treatment with Interferon for chronic infection, were noted in a 2006 study by Dr Mark Wright and others (including Professor Thomas).<sup>93</sup> This gave rise to a question as to whether the symptoms were caused by treatment rather than by HCV itself.

**13.62** Professor Thomas thought that some auto-immune diseases found in association with HCV infection, such as rheumatoid arthritis and autoimmune thyroiditis, were likely

---

<sup>89</sup> Professor Thomas – Day 53, pages 4–5

<sup>90</sup> Ibid pages 73–76

<sup>91</sup> Ibid pages 76–77

<sup>92</sup> Ibid page 74

<sup>93</sup> Ibid pages 34–36

to result from a genetic predisposition common to those conditions rather than a causal connection with HCV, but agreed that treatment would exacerbate those conditions in those with a genetic predisposition to them.<sup>94</sup>

**13.63** Using validated methods to assess mental and physical wellbeing, it has been shown that Hepatitis C patients have generally reduced mental and physical wellbeing, of a comparable level to what might be seen in diabetes (another chronic disease), for example.<sup>95</sup> Since such neurological and psychological difficulties may occur without serious liver disease, attributing a cause for such symptoms can be difficult in an individual case. Severe liver disease may be the cause, since with liver failure there may be an accumulation of nitrogen compounds derived from the gut which leads to hepatic encephalopathy (confusion, cognitive impairment and lethargy). In some patients, mental acuity is blunted by past use of recreational drugs. If those two are excluded, the third case, what is called 'mental fog' in the USA, represents infection of the central nervous system with HCV.<sup>96</sup>

**13.64** Although the association of HCV infection with some of these features of quality of life and brain function is based on 'soft' evidence, these are precisely the symptoms and signs that many patients have complained of in statements provided to the Inquiry. Such symptoms have been under-appreciated in the past but the bulk of evidence now strongly supports an association. Dr Karin Weissenborn and colleagues have recently characterised the well-documented neuropsychological effects of HCV infection on the brain as follows:

A reduction in health related quality of life, chronic fatigue, depression and cognitive decline are characteristic complaints of HCV-infected patients even in the absence of significant liver disease.<sup>97</sup>

**13.65** In chronic hepatitis, the measure of severity is related to the rapidity of progression but Professor Thomas' evidence revealed that there is still some uncertainty about causal relationships. He thought that the rapidity of progression (as well as the severity of the infection, as noted in paragraph 13.54) would be related to the size of the initial inoculum but the picture was complicated by that the interaction of other variables, such as co-infection with HIV, immunosuppression due to medication and the rate of reproduction of the virus.<sup>98</sup> In relation to the rate of progression of the disease, he said:

In chronic hepatitis C the presence and quantity of virus in the blood stream is determined by reverse transcriptase polymerase chain reaction (rt-PCR). Levels fluctuate from month to month and tend to be higher in immunosuppressed people such as those infected with HIV. The level of viraemia in HCV does not appear to determine the rate of progression to liver cirrhosis in the non-immunosuppressed. Levels of transaminases also fluctuate over time. The presence of normal transaminases does not exclude significant liver fibrosis. The rate of progression to cirrhosis varies among individuals chronically infected with HCV. Different sub-groups of patients progress at different rates. Major risk factors have been identified: male gender, excess alcohol and age [over] 50 at acquisition.<sup>99</sup>

<sup>94</sup> Ibid pages 75–76

<sup>95</sup> 'Life score metrics' may be made more complex by background issues affecting the patient which, in the opinion of neurologists, make it difficult to evaluate residual symptoms after an acute illness.

<sup>96</sup> Professor Thomas – Day 53, pages 7–9

<sup>97</sup> Weissenborn et al, 'Hepatitis C virus infection and the brain', *Metabolic Brain Disease*, 2009; 24: 197-210 [LIT.001.4204] at 4215

<sup>98</sup> Professor Thomas – Day 53, pages 12–14

<sup>99</sup> Professor Thomas' Report on Hepatitis C [PEN.017.1071] at 1082

## Factors which influence the outcome of HCV infection

**13.66** Professor Thomas agreed generally with the conclusions of the *Bassendine Review of Natural History of HIV Infection* relating to HCV infection.<sup>100</sup> The Review stated:

The proportion of patients who develop chronic HCV infection may be determined by many factors. These include age at time of infection, gender, ethnicity, presence of symptoms during the acute infection, genotype, immunosuppression and HIV.<sup>101</sup>

**13.67** Professor Thomas expanded on some of these matters.<sup>102</sup> There is consensus that certain factors do influence outcome. Others are postulated but are not confirmed or sustained by other studies. Some factors are not confirmed because they are not direct determinants: they are correlates of something that is a direct determinant. Male gender indicates a more severe outcome in chronic infection, in all studies. Ethnicity plays a role. That is now known to be related to the frequency in which the IL28 genetic polymorphism is found in different ethnic groups. Most people are offered treatment and the mechanism of the response rate to Interferon, which will determine whether the patient does well after infection, has a different frequency in different ethnic groups, again due to differences in the prevalence of the immune system's recognition proteins.

### *Age at time of infection*

**13.68** Age at the time of infection is agreed to be a contributory factor in the progression of HCV infection. Above about 50–60 years of age, there is a deterioration of the body's capacity to regenerate, whether it is to replace scar tissue resulting from a simple cut or to replace liver cells killed by the immune response to HCV infection. There is a change in the gradient of the curve measuring progressive liver damage. If an individual is infected after this change, progression is more rapid. After discussion with Professor Oliver James, Medical Assessor to the Inquiry, Professor Thomas said:

[B]oth with Hepatitis B and Hepatitis C, if you get an acute hepatitis in your later years, let's say 60, then there is a syndrome called "failure to regenerate". You ... have a wave of destruction of liver cells, which is essential for part of the recovery process because the cells contain the virus, you have to destroy them to get rid of them, you are then producing antibody to stop the virus moving into the neighbouring cells, but in addition, the neighbouring cells have to regenerate to replace the ones that have been killed.

So there are four components, if I could summarise it. There is the number of infected cells; there is how quickly they are being destroyed, which is dependent on the cellular immune response; there is the production of antibody, which is going to be important to stop the virus released from the destroyed cells to infect the cells next door; and the last thing is you are down on the number of liver cells that you have, because of the ones that have been destroyed, so you are dependent on the liver regenerating. So if any of those components result in a situation of a [reduction] in liver cell mass, then you will ultimately enter liver failure.<sup>103</sup>

<sup>100</sup> Professor Thomas' report on Hepatitis C [PEN.017.1071] at 1084

<sup>101</sup> 'Reviewing the Natural History of Hepatitis C Infection', ('The Bassendine Review') – Annex 4 to the *Skipton Fund Review of the support available to individuals infected with Hepatitis C and/or HIV by NHS-supplied blood transfusions or blood products and their dependants* [PEN.017.1968] at 2013; Professor Thomas – Day 53, page 15

<sup>102</sup> Professor Thomas – Day 53, pages 15–17

<sup>103</sup> *Ibid* pages 27–28

**13.69** The Inquiry heard evidence from a number of witnesses who added to its understanding of the relevance of age. Dr Graeme Alexander, Consultant Haematologist at Addenbrooke's Hospital, Cambridge, drew on information from the national HCV look-back study<sup>104</sup> of which he was Chairman. He said that the majority of people who were young at the time of infection did not progress to cirrhosis at all.<sup>105</sup> In the case of patients who were relatively young at the date of infection who did progress to cirrhosis, the period from that stage to the development of end stage liver disease would be of the order of 10 years or more. Both the period of evolution from infection to cirrhosis and the period of evolution from cirrhosis to death were shorter in people who were older when they were first exposed to HCV.<sup>106</sup> Publications drawing attention to the importance of age first began to appear in about 1997; before that time, the natural history of Hepatitis C in older patients had been misunderstood. Most clinical experience had been based on an understanding of NANB Hepatitis in patients, most of whom died from the disease that had led to intervention in the first place. A diagnosis of NANB Hepatitis was simply the identification of abnormal liver test results that arose after transfusion, for which there were many possible explanations. The view of what NANB Hepatitis did to patients was artificially skewed. It was not until the introduction of testing for HCV in 1991 that it began to be realised that there were many people who had a disease that was very different from the disease as previously understood. In the clinical context there was not much that could be done. The report on Mr Laing, referred to the Inquiry in Term of Reference 6, provides clear evidence of a high rate of progression in an older man with no aggravating factors. (See Chapter 7.)

**13.70** Other evidence supported the view that, among younger patients infected with HCV with no other aggravating factors, progression may be slow and with a mild outcome for considerable periods of time. Long-term follow-up studies over a period of 35 years have been reported of Italian children given HCV-infected 'mini-transfusions' from a single donation at or about the time of birth.<sup>107</sup> In Italy, during the 1960s, mini-transfusion of blood or plasma was a frequent treatment of under-weight or pre-term newborn children. Transfusions of blood from a single donor later found to be HCV-infected were given to 31 children, all of whom were 35 years of age at the date of the report. At enrolment into the study in 1998, 18 were found to have HCV antibody and 16 were HCV-RNA positive. Eleven of the viraemic patients had liver biopsies. Nine of the 11 biopsies showed no fibrosis or mild portal fibrosis, and two had either discrete (Ishak's stage 3) or marked (Ishak's scale 4) fibrosis. None of the individuals was aware of having been transfused during the first weeks of life and none reported a history of jaundice or had signs or symptoms of hepatitis. For all practical purposes, the infections had been silent for 35 years.

<sup>104</sup> The purpose of look-back was to trace NHS patients who had received blood, blood components or blood products derived from donations by donors who tested positive for Hepatitis C antibodies after 1 September 1991, when screening was introduced, and who had previously donated blood which was found by retrospective testing also to have been infective. See Chapter 36, *An Investigation into the Steps Taken to Identify the Individuals Who Were Infected*.

<sup>105</sup> Day 4, pages 35–36

<sup>106</sup> *Ibid* page 36

<sup>107</sup> Casiraghi et al, 'Long term outcome (35 years) of Hepatitis C after acquisition of infection through mini transfusions of blood given at birth', *Hepatology*, 2004; 39: 90–96 [LIT.001.4027]

**13.71** Dr David Mutimer (Consultant Hepatologist, The Queen Elizabeth Hospital, Birmingham) described his experience with relatively young people in the Birmingham area.<sup>108</sup> His data had been derived from a large population of patients who were infected with Hepatitis C. The median time from infection to cirrhosis was thought to be about 30 years: half of the patients had developed cirrhosis at 30 years after infection and the other half had some lesser degree of liver damage at that stage. What distinguished the people who progressed more quickly to cirrhosis was only partly understood. Some factors had been identified but others were not known. The study showed that men progressed more rapidly than women. It had also been established that alcohol would accelerate the progression to cirrhosis. In that cohort it was very rare to see cirrhosis within 10 years of infection in that cohort and it was uncommon to see it within 20 years of infection, unless there were aggravating factors.

### *Duration of infection*

**13.72** Duration of infection is a factor. In the USA, much Genotype 1 infection occurs after blood transfusion, where the onset of infection is known and therefore doctors can work out the duration of the infection, sometimes 20 years later. In Genotype 3, infection occurs mainly in the Asian population and there, in large group studies, it is apparent that a great many of the patients are infected in infancy and the infection turns out in later life to be apparently more severe than Genotype 1. That is probably related to the fact that the reference point at which people present with significant liver disease is 40 years after the onset rather than perhaps 15 or 20 years. Assessing the role of genotypes is frequently confounded by being unable to determine the time when infection was acquired, hence the duration of infection also remains unknown. Immuno-suppression and HIV infection are well documented as being associated with more severe HCV disease. In the haemophilia population, that has clearly been evident, in that those with co-infection have, in the main, had a higher liver-related mortality than those who have had Hepatitis C alone.

**13.73** Haemophilia patients present particular problems of analysis. The level of virus might have been constantly topped up by successive infusion of infected coagulation factor concentrates, as indicated by the observation that some patients had several genotypes of the virus present. In their cases, as distinct from transfusion patients, there was the problem that the date when the first infective dose was administered might be the 'unknown variable'.<sup>109</sup> Successive biopsies over a period of years gave data of developing fibrosis on which clinicians could project the progression of the disease and advise on the need for treatment in the case of an individual patient, essentially to stop progression before Ishak's stage 6 (cirrhosis) but the pattern was variable and generalisation difficult.<sup>110</sup> Furthermore, multiple biopsies in haemophilia patients are hazardous and seldom indicated.

### *Infection with more than one genotype of HCV*

**13.74** The possibility of infection with more than one genotype of HCV raises a question whether that factor of itself increases the rate of progression of disease. Professor Thomas did not know of any data to suggest that but thought that confronting a wider range of infection might well present a greater challenge to the immune system.<sup>111</sup>

---

<sup>108</sup> Dr Mutimer – Day 1, pages 110–112

<sup>109</sup> Professor Thomas – Day 53, pages 18–19

<sup>110</sup> Ibid pages 19–22

<sup>111</sup> Ibid pages 29–30

## *Aggravating factors*

### Alcohol

**13.75** There are some well-recognised aggravating factors that affect the outcome of HCV infection, though the evidence available to the Inquiry was not uniform. In particular there were conflicting views relating to alcohol. Professor Thomas took the more extreme view of the damaging effects of alcohol in patients with Hepatitis C. He contrasted Hepatitis B and Hepatitis C and his evidence was that alcohol affects the progression of Hepatitis C but not Hepatitis B. Data on liver damage seen in Hepatitis B cases where there is evidence of consumption of alcohol suggests that the liver damage found is the summation of the damage due to alcohol and what is due to the disease: the alcohol does not 'synergise' with Hepatitis B. He said that it is now accepted that alcohol increases the level of replication of Hepatitis C and, as a consequence, the liver damage seen in a patient with Hepatitis C who is, in addition, taking significant amounts of alcohol is greater than the sum of the damage due to the alcohol and the Hepatitis C: the two factors are synergistic in HCV but not in HBV.<sup>112</sup>

**13.76** In Professor Thomas's view, the synergistic effect of alcohol was established around 2004–05 as a result of studies by Dr Ralf Bartenschlager, using a system of cells which supported replication of a model of HCV. In looking at a variety of factors that altered the effectiveness of replication, the synergistic effect of alcohol was observed.<sup>113</sup> Lifestyle advice, particularly relating to alcohol consumption, had long been common but was given added emphasis as a result of this finding. On this approach, the risk of accelerated liver damage in chronic HCV infection may be associated with quite moderate consumption: it is not limited to groups commonly recognised as alcoholics or those who would be described popularly as 'drunks' or who exhibit functional deficiencies in their ordinary lives.<sup>114</sup>

**13.77** For this reason, Professor Thomas said:

[B]efore we had ways of treating patients with Hepatitis C, one important thing to say was that you can slow down the progression of your Hepatitis C if you reduce your alcohol intake, and the ideal scenario would be that you would be abstinent from alcohol.<sup>115</sup>

**13.78** Professor Hayes adopted a different stance. In his unit, patients were generally advised to abstain entirely from alcohol if they had cirrhosis, but if their liver disease was short of cirrhosis then drinking within sensible limits of 21 units a week for a man and 14 units for a woman was considered safe (the same recommended safe limits of alcohol as advised for members of the public generally).<sup>116</sup> He did not think that advice based on that view had changed much over time.<sup>117</sup> He was examined on the advice contained in the Scottish Intercollegiate Guidelines (2006) on the management of Hepatitis C that:

Even moderate amounts of alcohol (within government recommended guidelines) have been associated with increased liver fibrosis compared to those who abstain.

....

<sup>112</sup> Professor Thomas – Day 52, pages 17–18

<sup>113</sup> Professor Thomas – Day 53, page 42

<sup>114</sup> SIGN 92: Management of Hepatitis C (2006) paragraph 8.4; [PEN.018.0298] at 0317 (Repeated in SIGN 133: *Management of Hepatitis C* (2013) paragraph 9.4 [LIT.001.5550] at 5574)

<sup>115</sup> Professor Thomas – Day 52, page 18

<sup>116</sup> Professor Hayes report [PEN.018.0240] at 0243

<sup>117</sup> Professor Hayes – Day 78, page 69

Patients with [chronic Hepatitis C] should be advised that drinking alcohol (even in moderation) can accelerate progression of liver disease.<sup>118</sup>

**13.79** He thought it debatable whether drinking alcohol in moderation created a risk of progression of chronic Hepatitis C in the mild and moderate categories.<sup>119</sup> He had never been persuaded by the evidence and it had not been drawn to his attention that drinking within the recommended limits would accelerate liver disease.<sup>120</sup>

**13.80** Dr Mutimer's experience in Birmingham provided a practical indication of the impact of alcohol. In his experience, the majority of patients with Hepatitis C requiring liver transplants had been infected in their late teens or early twenties and many would have had a history of significant alcohol consumption. He did not suggest that dependency, or the excesses associated with alcoholism, were prerequisites.<sup>121</sup> The average age at which liver transplant was necessary was 55. Dr Andrew Bathgate's findings in that respect were broadly consistent with Dr Mutimer's broadly based investigations.<sup>122</sup>

**13.81** It is not yet possible to resolve completely the issue of the extent to which alcohol consumption affects progression of HCV-related liver disease. The scientific basis for Professor Thomas's evidence is strong. Professor Hayes' clinical experience is extensive. Dr Mutimer's evidence correlated advanced liver disease at a relatively early age with significant alcohol consumption in the late teens or early twenties. In general terms it would appear not unreasonable to conclude that the consequences of consumption of alcohol would depend on a range of factors, including the quantity consumed, the regularity of the practice, the duration of the practice and the patient's liver disease profile.

## Smoking

**13.82** The *Bassendine Review* listed smoking tobacco as an aggravating factor.<sup>123</sup> Recent studies have suggested that heavy smoking generally increases both liver fibrosis and inflammatory activity in chronic HCV infection, supporting the Bassendine finding.<sup>124</sup> Initially, French researchers suggested that smoking cannabis might also stimulate fibrosis. It is now known that there is indeed a mechanism by which cannabis causes fibrosis: some cells have cannabinoid receptors to which the cannabis molecule binds and the cells which stimulate fibrosis also have those receptors.<sup>125</sup>

## Obesity

**13.83** Obesity is an aggravating factor. Professor Thomas said:

[I]t's becoming increasingly the case that three things are operating adversely in many patients. One is Hepatitis C itself. Second is, as we have mentioned, alcohol, and whether there is obesity, which is associated with deposition of fat in the liver. So what's becoming clear with all of these so-called insults to

<sup>118</sup> SIGN 92: Management of Hepatitis C (2006) paragraph 8.4; [PEN.018.0298] at 0317 (Repeated in SIGN 133: Management of Hepatitis C (2013) paragraph 9.4 [LIT.001.5550] at 5574)

<sup>119</sup> Professor Hayes – Day 78, page 112

<sup>120</sup> Ibid page 113

<sup>121</sup> Dr Mutimer – Day 1, page 112

<sup>122</sup> Medical Report on Mr Victor Tamburrini [TAM.001.2380] at 2382–83: Dr Bathgate – Day 1, page 25

<sup>123</sup> 'Reviewing the Natural History of Hepatitis C Infection' ('The Bassendine Review') – Annex 4 to the *Skipton Fund Review of the support available to individuals infected with Hepatitis C and/or HIV by NHS-supplied blood transfusions or blood products and their dependants* [PEN.017.1968] at 2015

<sup>124</sup> Tsochatzis et al, 'Smoking is associated with steatosis and severe fibrosis in chronic hepatitis C but not B', *Scandinavian Journal of Gastroenterology*, 2009; 44: 752–59; [LIT.001.4418] Hezode et al, 'Impact of smoking on histological liver lesions in chronic hepatitis C', *Gut*, 2003; 52: 126–129 [LIT.001.4100]

<sup>125</sup> Professor Thomas – Day 53, pages 31–32



the liver is that the accumulation of fat, which ultimately may burst the liver cells, is bad news in terms of creating a risk of fibrosis.

... .

And those three things that I have mentioned, alcohol and obesity and certain genotypes of Hepatitis C, all cause an accumulation of fat in the liver. And the genotype that is most involved in the accumulation of fat is genotype 3.<sup>126</sup>

### Co-infection with Hepatitis B

**13.84** Co-infection of Hepatitis C with Hepatitis B is a significant complication. The risks associated with HBV infection vary with age. Children infected at birth, or up to about two years of age, have a 95–100% risk of becoming chronically infected, with a risk of progressive liver disease. In contrast, after two years of age, right through the middle and later years of adult life, 95% of individuals who are infected develop an acute, self-limiting infection and only 5% develop chronic infection. Of those who have a chronic infection and proceed to develop cancer, 30% (almost all of whom acquired infection in early childhood) will develop a cancer before the stage of cirrhosis, and 70% will already have had cirrhosis before the cancer is developed.<sup>127</sup> Increasing knowledge of the pattern of developing disease as understood from time to time has an important bearing on patient care, and the need to provide treatment before a cirrhotic stage is reached. In co-infection with HBV and HCV the viruses interact with each other and affect immune response. HCV may inhibit HBV replication and vice versa. Combined chronic Hepatitis B with Hepatitis C leads to more severe liver disease and an increased risk of development of HCC.<sup>128</sup>

### *Do symptoms persist after successful treatment?*

**13.85** A question arose whether there could be 'occult hepatitis', a persistence of symptoms, or 'extra-hepatic manifestations', after the patient had a negative polymerase chain reaction (PCR) test, showing that the virus had been cleared. Professor Thomas explained the position.<sup>129</sup>

**13.86** He said that there could be situations at or within a few months after the end of a period of treatment when the virus could not be detected in the circulating blood but might be present in the liver or in a cell. That had been described in the case of Hepatitis B.<sup>130</sup> However, the extra-hepatic manifestations he had discussed, the renal and dermatological signs and non-Hodgkin's lymphoma,<sup>131</sup> arose without exception where there was continuing viraemia detectable by HCV RNA PCR test systems. In the case of 'brain fog', the majority of the virus was being produced in the liver and the patients had viraemia. Low physical and mental wellbeing scores were not indicative of continuing infection in the absence of viraemia. After a demonstrable sustained viral response (where more than six months after the end of treatment viraemia is undetectable by the most sensitive HCV RNA tests), residual cognitive or other abnormalities are often associated with non-viral related problems: they are not attributable to a continuing 'occult' presence of the virus.<sup>132</sup>

<sup>126</sup> Ibid page 49

<sup>127</sup> Professor Thomas – Day 52, pages 13–14

<sup>128</sup> Crockett and Keeffe, 'Natural history and treatment of hepatitis B virus and hepatitis C virus coinfection', *Annals of Clinical Microbiology and Antimicrobials*, 2005; 4:13 [LIT.001.4034]

<sup>129</sup> Professor Thomas – Day 53, pages 68–70

<sup>130</sup> Ibid pages 65–66

<sup>131</sup> As noted in paragraphs 13.18 and 13.52, non-Hodgkin's lymphoma is not associated with HCV infection in northern Europe, but it is relevant to Professor Thomas' opinion.

<sup>132</sup> Professor Thomas – Day 53, pages 69–70

## Investigation and Treatment

**13.87** Up-to-date knowledge of the natural history of HCV infection is clearly necessary for a proper understanding of the witnesses' evidence. In order fully to understand the evidence of patients and their relatives, however, it is necessary to have regard also to some significant developments in the investigation of the infection and in the treatments available.

### *Investigation*

**13.88** From about 1978 doctors used blood tests to monitor haemophilia patients' ALT levels more or less as a matter of course, although it is not clear whether they had a well-developed understanding of why they were doing so. Biopsy changed the course of investigation. As indicated in paragraph 13.42, by 1981 experts, including Professor Sherlock and Professor Thomas, were already engaged in studies of NANB Hepatitis infection based on biopsy findings.

**13.89** Once established in research practice, histology (microscopic examination of samples of tissue) obtained by conventional liver biopsy was thought to be the most reliable way of monitoring the severity of liver disease. The degrees of necro-inflammation (grade) and fibrosis (stage) were key to interpretation and consequent clinical decision-making regarding treatment.<sup>133</sup>

**13.90** Generally, the standard method for performing a liver biopsy is to introduce local anaesthetics to the skin overlying the liver, insert a needle into the organ and remove a small core of liver tissue. An alternative method of removing a tissue sample involves inserting a long needle through a vein in a patient's neck to their liver, with the benefit of ultrasound examination. Professor Hayes described a method used in patients with haemophilia in Edinburgh in the late 1980s which involved inserting a small telescope into the abdomen and then inserting gas to give a view of the liver. This allowed the doctor to see the liver directly and so see the part of the liver from which the biopsy was taken. Although originally biopsies were taken during these procedures, it later became the practice for the liver to be inspected without removing tissue.

**13.91** Liver biopsy carries with it a risk of haemorrhage and even death, the latter risk being about 1 in 10,000. These risks are significantly increased in patients with haemophilia. Liver biopsy of a patient with haemophilia is not straightforward and there are a few examples of fatal outcomes from the standard method.<sup>134</sup> Occasionally a blood transfusion may be required following haemorrhage. The standard method of liver biopsy causes variable pain but it can be extremely painful.<sup>135</sup> The narrative of the experiences of patients illustrates the impact of these biopsy procedures. More recently the non-invasive procedure FibroScan, using transient elastometry to measure liver stiffness, is employed to assess the degree of fibrosis of the liver.<sup>136</sup>

**13.92** Other investigative procedures include endoscopy, used to examine and monitor the patient for upper gastro-intestinal varices. Many patients find the procedure uncomfortable.

<sup>133</sup> Professor Thomas' report on Hepatitis C [PEN.017.1071] at 1081; Professor Thomas – Day 53, pages 9–10

<sup>134</sup> Professor Thomas – Day 52, page 116

<sup>135</sup> Professor Hayes – Day 78, pages 56–58

<sup>136</sup> SIGN 133: *Management of Hepatitis C* (2013) paragraph 8.2 [LIT.001.5550] at 5571

## Treatment

**13.93** Brief comments on treatment are contained in paragraphs 2.39–2.44 of the Preliminary Report. An excellent national clinical guideline, *Management of Hepatitis C*, has recently been updated by the Scottish Intercollegiate Guidelines Network (SIGN).<sup>137</sup> The oral evidence, particularly the evidence of Professors Thomas and Hayes, has increased the Inquiry's understanding of the topic. An account of progress in the management of patients and in therapy is contained in Chapters 14–16 *Knowledge of Viral Hepatitis 1 to 3*. At this stage it is sufficient to note a few significant developments.

**13.94** Initially, it was remarkably difficult to treat a condition with an unknown cause. After the Chiron discovery, Alpha Interferon was the first drug that looked promising, though some early trials look less than convincing by contemporary standards.<sup>138</sup> It was used by Professor Thomas and his colleagues from about 1989. In terms of sustained viral response, rates varied between 12% and 15%.<sup>139</sup> This proportion may have been even lower among haemophilia patients.<sup>140</sup> The use of Alpha Interferon in a clinical research setting in 1989 was the first step in England in what would be a lengthy process of controlled trials leading to a licence and approval for use; a licence was granted in November 1994 for Alpha Interferon to be used in the treatment of chronic Hepatitis C. Professor Hayes had no recollection of treating anyone with Interferon before 1991. He treated the first few patients in Scotland in 1991 and 1992.<sup>141</sup> He also found that the drug appeared to be effective in clearing HCV in a minority of patients.<sup>142</sup> It was, however, to be some years before the technology was developed that demonstrated benefit even in those patients.<sup>143</sup>

**13.95** The next significant development was the use of recombinant Interferon with Ribavirin, around 1995–96, and then of pegylated Interferon, a longer acting form of Interferon.<sup>144</sup> From the mid-1990s to the early 2000s access to newer treatments was not available outwith clinical trials until the treatments had been approved and licensed.<sup>145</sup> With each stage in development effectiveness improved, from the base level of 10–20% with monotherapy.<sup>146</sup>

**13.96** Professor Hayes also pointed out that, to be eligible to participate in a trial at that period, a patient had to agree to liver biopsy before and after treatment since liver histology was deemed the 'gold standard' by which to measure the effect of treatment on the liver. It was a regulatory requirement.<sup>147</sup> Because of the hazards of liver biopsy in haemophilia, very few haemophilia patients entered the studies and thereby benefited from early access to more effective treatment.<sup>148</sup> Clinically, biopsy was considered not to be a sensible risk for haemophilia patients to take unless it was required in clinical practice.<sup>149</sup> Whilst not being included in a trial might well have been a source of frustration for a patient who was

<sup>137</sup> SIGN 133: *Management of Hepatitis C* (2013) [LIT.001.5550]

<sup>138</sup> Professor Hayes – Day 78, pages 49–50

<sup>139</sup> Professor Thomas – Day 53, page 40

<sup>140</sup> Professor Hayes – Day 78, page 52

<sup>141</sup> Ibid page 51

<sup>142</sup> Ibid page 51

<sup>143</sup> Ibid pages 61–62

<sup>144</sup> Professor Hayes' Report on Hepatitis C [PEN.018.0240] at 0242

<sup>145</sup> Professor Hayes – Day 78, pages 54–59, especially Page 54

<sup>146</sup> Professor Hayes' report on Hepatitis C [PEN.018.0240] at 0245; Professor Hayes – Day 78, page 93

<sup>147</sup> Professor Hayes – Day 78, page 60

<sup>148</sup> Ibid pages 54–55

<sup>149</sup> Ibid page 57

aware of a potential new treatment, Professor Hayes considered that not being included in a trial was not 'a major disadvantage'.<sup>150</sup> He gave two reasons for this. First, even if a patient was included in a clinical trial it did not necessarily mean that he received the new treatment, as half of those participating in a trial received the standard treatment and half the new treatment. Secondly, it took about two to four years for a treatment to become available following a trial and Professor Hayes considered that a wait of that duration was not a major disadvantage since the natural history of the condition from the time of infection until it caused symptoms is measured in decades rather than years.<sup>151</sup>

### **Current guidance**

**13.97** The current SIGN guidelines (see paragraph 13.93, above) for therapy adopt an evidence-based hierarchy, with treatment based upon HCV genotype.<sup>152</sup>

**13.98** For Genotype 1 patients, all 'treatment naïve' patients (those who have not previously undergone antiviral treatment) with Genotype 1 should be considered for treatment with pegylated Interferon and weight-based Ribavirin, with the addition of a protease inhibitor as triple therapy. The same treatment should be considered for those who have failed previous antiviral treatment.

**13.99** For Genotype 2 and 3 patients, standard treatment is pegylated interferon and weight-based Ribavirin for 24 weeks. Non-cirrhotic patients with Genotype 2 or 3 who achieve a 'rapid viral response', in which HCV RNA is undetectable, indicating the efficacy of therapy at week four, should be considered for a shortened duration of therapy of 12–16 weeks.

**13.100** For patients with Genotypes 4, 5 and 6, standard treatment is 48 weeks of pegylated interferon and weight-based ribavirin.

**13.101** In general, a sustained viral response can now be achieved following treatment based upon the above regimes in almost 80% of patients able to tolerate and complete the prescribed courses of treatment. Full details can be found in SIGN 133: Management of Hepatitis C (2013) along with references to the relevant research literature and analysis.<sup>153</sup>

**13.102** HCV particles have a relatively short half life in circulation (that is, the virus particles decay quite rapidly in the bloodstream). In contrast, infected liver cells have a relatively long half life (decay is considerably longer). In patients whose treatment is likely to be successful, the initial rate of disappearance of HCV RNA during interferon therapy is rapid and viraemia does not return. This is reflected in the shortened period of therapy noted at paragraph 13.99 above. In patients whose treatment is likely not to be successful, initial clearance is followed by a second phase of less rapid clearance which may reflect the presence of an interferon-resistant second site of HCV infection within or outside of the liver.<sup>154</sup> If HCV RNA is still positive at the twelfth week of therapy, treatment is usually stopped because the chance of a sustained viral response is insignificant.<sup>155</sup>

<sup>150</sup> Ibid pages 54–55

<sup>151</sup> Ibid pages 55–56

<sup>152</sup> SIGN 133: *Management of Hepatitis C* (2013) [LIT.001.5550] at 5577–82

<sup>153</sup> SIGN 133: *Management of Hepatitis C* (2013) [LIT.001.5550] at 5577–82

<sup>154</sup> Professor Thomas' report on Hepatitis C [PEN.017.1071] at 1082–83

<sup>155</sup> Professor Thomas – Day 53, page 51

**13.103** In the case of patients treated after they already have cirrhosis, Hepatitis C is unlikely to be cured (partly because they have been infected for so long and partly because they find it harder to tolerate treatment).<sup>156</sup> Cirrhosis does not disappear even when a positive response is achieved and the condition puts the patient at continuing risk of liver cell cancer. In this group clinicians should not be talking about a 'cure' of a patient's overall condition because they are still at risk of this severe complication. However, in these patients the risk of progression to hepatic decompensation and possible HCC is reduced and they are no longer infectious: they have a 'viral cure'.<sup>157</sup>

**13.104** The use of the term 'cure' was the subject of questioning during the oral hearing. The expression that had been commonly used was 'sustained viral response' (SVR), meaning undetectable HCV RNA six months after the end of treatment. Professor Thomas thought that it was now appropriate to speak of treatment 'curing' the patient, provided that treatment was given before the patient had developed cirrhosis.<sup>158</sup> He explained that until there had been many years of long-term follow-up showing that viral relapse was a very infrequent occurrence, clinicians were conservative about translating 'SVR' into the word 'cure'. It was not simply a matter of virological 'cure': one wished to know that, if there was sustained viral response, then fibrosis regressed and scarring was re-absorbed.<sup>159</sup> Generally, if HCV RNA were to reappear, it would be within the first few months after the end of treatment. For those who have SVR before the onset of cirrhosis, the liver should ultimately go back to normal. Professor Thomas emphasised the word 'should': there had been only a few years of observation and it might take longer than that period to progress to normal in terms of scarring of the liver; it is an evolving field of investigation. In relation to haemophilia patients it had not been possible to do frequent biopsies. However, non-invasive techniques, using fibro-elastography technology, are now available to subject the liver to an ultrasound wave and measure how much the organ wobbles. The stiffness of the liver is related to the scarring in it and that stiffness should reduce in somebody with an SVR. The evidence now available shows that it does indeed reduce. It may be several years before the liver actually goes back to normal and to date there has not been a large enough cohort of patients to enable clinicians to state definitively that the liver will go back to normal. However, 'cure' is now held to be an appropriate description in non-cirrhotic cases.<sup>160</sup>

**13.105** This is an important development for people who, perhaps encouraged by stories spread around patient groups, may have resisted treatment on the grounds that Hepatitis C was not curable and that treatment might not be effective and would have serious side-effects.<sup>161</sup> Professor Hayes commented that there are still some patients who seem to have fairly benign disease and who are happy to have no treatment, despite the fact that treatment is improving.<sup>162</sup> People who do not have Genotype 1 are strongly encouraged to go for treatment.<sup>163</sup> About 20% of individuals do not manage to complete treatment, principally due to side-effects.<sup>164</sup>

<sup>156</sup> Professor Hayes – Day 78, page 87

<sup>157</sup> Professor Thomas – Day 53, page 58

<sup>158</sup> Ibid pages 56–58

<sup>159</sup> See also Professor Hayes – Day 78, pages 52–53

<sup>160</sup> Recent analysis carried out for SIGN 133 suggests that occult Hepatitis C may persist in macrophages or lymphocytes in a small number of patients who have achieved SVR. There may be a small chance of relapse in this event.

<sup>161</sup> Professor Hayes – Day 78, pages 94–95

<sup>162</sup> Ibid page 95

<sup>163</sup> Ibid page 96

<sup>164</sup> Ibid page 97

### *Side-effects of treatment*

**13.106** Interferon alone produced flu-like symptoms and, taken three times a week, it made patients feel awful.<sup>165</sup> Pegylated Interferon is taken once a week with proportionately better impact, although some people still find it debilitating. The side-effects that most concern clinicians are depression and occasional suicidal ideation (thoughts about or preoccupation with suicide). Ribavirin is also associated with side-effects, particularly anaemia. Professor Hayes said that the patients would best understand the side-effects themselves: individual tolerance varied widely but each addition to the cocktail of drugs expanded the range of side-effects. Managing side-effects by reducing doses impacted on success rates. With Ribavirin, it has proved more effective to maintain the standard (weight-based) dose and support haemoglobin by the use of drugs such as erythropoietin. New drugs, while likely to improve the chance of a cure, are likely to have the same side-effects 'plus extra'.<sup>166</sup>

**13.107** The common side-effects from pegylated Interferon and Ribavirin are summarised in paragraph 2.44 of the Preliminary Report. A more comprehensive list is set out in the SIGN (Scottish Intercollegiate Guidelines Network) guidelines.<sup>167</sup> In summary these are:

- Flu-like symptoms, such as fever, myalgia (muscle pain), rigors ('chills'), arthralgia (joint pain) and headache. These symptoms are similar to those experienced in acute hepatitis when the body produces interferon. In therapeutic use, interferon is administered in larger amounts than a body would otherwise produce, with the result that the same symptoms are caused and magnified.<sup>168</sup> These symptoms are usually treated with paracetamol, increased fluid intake and rest. Patients are advised to coordinate their injections of interferon with periods of reduced activity, such as weekends and holidays.
- Anaemia (decrease in number of red blood cells or less than the normal quantity of haemoglobin in the blood) and neutropenia (an abnormally low number of neutrophils, a type of white blood cell). Anaemia is primarily related to ribavirin. Initially this was treated by reducing the patient's dose of ribavirin which affected the success rate of the treatment.<sup>169</sup> More recently Erythropoietin is prescribed which enables a patient to continue taking the prescribed dose of ribavirin.<sup>170</sup> Likewise, Granulocyte colony stimulating factor may now be prescribed for patients who develop significant neutropenia instead of reducing ribavirin.
- Depression is a commonly reported and serious side-effect of pegylated interferon and ribavirin treatment in patients, whether they have experienced depression before or not. Occasionally patients experience suicidal ideation. All patients receiving this treatment should be monitored for symptoms of depression before, during and immediately after treatment. Those who experience depression should be considered for treatment with antidepressants and referred to a specialist.
- Severe skin reactions are uncommon during treatment but dry skin, pruritus (itch) and diffuse eczematous lesions occur in approximately 20% of patients. Psoriasis may be exacerbated by the treatment. Injection site reactions occur in over 50% of treated patients. Such conditions may be treated by emollients and topical corticosteroids.

<sup>165</sup> It is the body's natural production of interferon that makes a person with flu feel 'fluey'.

<sup>166</sup> Professor Hayes – Day 78, pages 100–104

<sup>167</sup> SIGN 92: Management of Hepatitis C (2006) [PEN.018.0298]; SIGN 133: Management of Hepatitis C (2013) [LIT.001.5550]

<sup>168</sup> Professor Thomas – Day 53, page 35

<sup>169</sup> Professor Hayes – Day 78, page 102

<sup>170</sup> Professor Hayes' report on Hepatitis C [PEN.018.0240] at 0247; Professor Hayes – Day 78, page 97

- Up to 6% of those treated may develop thyroid dysfunction, both over- and under-active thyroid, as a result of interferon therapy. Females are more at risk of this complication. This side-effect is not always reversible and a patient may require long-term treatment as a result.
- Weight loss is commonly reported in patients on antiviral treatment. Nutritional support may be required.
- Shortness of breath is a rarely reported side-effect of treatment. It may be linked to development of anaemia or may be caused by more serious cardiovascular or respiratory conditions.
- Retinopathy (damage to the retina) during interferon treatment is common but it is usually mild and transient. It resolves spontaneously when the treatment stops and treatment is seldom required.
- Alopecia is a relatively common reported side-effect of treatment. Hair usually grows again when the treatment stops.
- Fatigue is one of the most commonly reported side-effects of treatment, with anaemia, under-active thyroid, sleep disturbance and depression all contributing.
- Other reported side-effects include insomnia, poor concentration, oral disease, nausea and post-treatment withdrawal symptoms.

### *Timing of treatment and further procedures*

**13.108** Clinicians' views about when to treat a patient have evolved over the years within the reference period.<sup>171</sup> Prior to 2004, NICE<sup>172</sup> recommended that only those patients with severe disease should be treated and that the assessment of the severity of the disease should be based on a liver biopsy.<sup>173</sup> Due to the additional risks of a liver biopsy for those patients with haemophilia, they were excluded from this requirement.<sup>174</sup> In April 2004 at a Consensus Conference on Hepatitis C in Edinburgh it was decided that a liver biopsy was no longer essential to determine selection of patients for therapy. Then in 2005 the Scottish Executive produced the 'Hepatitis C Action Plan for Scotland'.<sup>175</sup> This highlighted the importance of treating as many people as possible rather than tailoring treatment to those persons clinicians believed needed it most.<sup>176</sup>

**13.109** Issues are raised as to how soon after the known date of infection, treatment should be instituted. Treatment within three months of infection as opposed to treatment within months four to six makes no significant difference and most people clear infection within three months anyway, if they are going to do so spontaneously. In the case of surgeons who may contract or transmit infection from or to patients, tests are carried out every two weeks. If viraemia occurs, treatment is instituted within the period three to six months.<sup>177</sup> This is highly successful.

<sup>171</sup> Professor Hayes' report on Hepatitis C [PEN.018.0240] at 0245

<sup>172</sup> NICE, the National Institute for Clinical Excellence (National Institute for Health and Clinical Excellence since 2005) publishes guidelines for use in the NHS in England and Wales on the use of health technologies and clinical practice.

<sup>173</sup> Professor Hayes – Day 78, page 81; Professor Hayes' Report on Hepatitis C [PEN.018.0240] at 0244. The severity of the disease is assessed by the pathologist who, having had regard to the amount of inflammation and scar tissue, grades the liver biopsy samples as mild, moderate and severe.

<sup>174</sup> Professor Hayes – Day 78, page 82

<sup>175</sup> *Hepatitis C Action Plan for Scotland* [LIT.001.4948]

<sup>176</sup> Professor Hayes – Day 78, pages 84–85

<sup>177</sup> Professor Thomas – Day 53, pages 82–84

**13.110** A person with cirrhosis may be less able to tolerate the treatment complications as well as the problems caused by cirrhosis.<sup>178</sup> It is far better to prevent a person developing cirrhosis than to deal with the consequences of it, although for a clinician it is difficult to identify when adverse developments may occur.

### Hepatocellular cancer

**13.111** The management of hepatocellular cancer (HCC) is complex. Recent literature on the subject has set out a number of options.<sup>179</sup> If possible, transplantation is the preferred treatment in generally 'well-compensated' patients (patients with good clinical and biochemical profiles) who have either one tumour less than five centimetres in size or up to three tumours each less than three centimetres in size. In these cases, there must be no extra-hepatic spread, and the tumour or tumours must not involve any blood vessels. However, the proportion of patients with hepatocellular cancer who are suitable for a liver transplant is very small.<sup>180</sup> Professor Hayes said:

[L]iver transplant is ... certainly indicated in some patients. It has the advantage that it gets rid of the cirrhotic liver. Once you have started to form one tumour in the liver, we believe that you are likely to form more. There is what we call a field change, and it is not uncommon that if you find a tumour you actually find two or three.<sup>181</sup>

**13.112** Liver transplantation is a complex, expensive and risky treatment. Transplant of the liver of a donor without haemophilia cures the haemophilia patient recipient of that condition: the implant synthesises Factor VIII normally.<sup>182</sup> Liver transplantation does not totally remove HCV from the recipient, however, as the virus infects parts of the body other than the liver. Immunosuppressant medication, given to prevent rejection of the transplanted liver, weakens the body's overall ability to deal with the virus. Hepatitis C will therefore always infect the new liver and the natural history from infection to cirrhosis is often considerably accelerated in the transplanted liver – a newly transplanted liver may become cirrhotic within two years of transplantation.<sup>183</sup> One of the reasons for this is that a patient is immunocompromised post-transplant and his ability to clear the virus is therefore impaired.<sup>184</sup> Recent SIGN advice is, therefore, that patients should be considered for antiviral therapy after liver transplant to achieve HCV clearance in cases of recurrent HCV-related liver disease.<sup>185</sup>

**13.113** In a very small proportion of clinically well patients with optimal liver function test scores who have small single nodules, surgical resection (to remove the segment of the liver containing the tumour) may be carried out. Professor Hayes noted that targeted treatment risks leaving a liver that is prone to developing new tumours.<sup>186</sup>

**13.114** In other patients who are not suitable for surgery, percutaneous radio frequency ablation may be used. This is a procedure whereby, under imaging control, heat generated from a high frequency alternating current is inserted directly into the tumour in order to

<sup>178</sup> Professor Hayes – Day 78, pages 87–88

<sup>179</sup> Bruix and Sherman, 'AASLD Practice Guidelines: Management of Hepatocellular Carcinoma: an Update', *Hepatology*, 2011; 53: 1020–22 [LIT.001.4326]; Compare Professor Hayes – Day 78, page 91

<sup>180</sup> Professor Hayes – Day 78, pages 90–92

<sup>181</sup> *Ibid* page 90

<sup>182</sup> *Ibid* page 90

<sup>183</sup> *Ibid* pages 90–91

<sup>184</sup> *Ibid* page 99

<sup>185</sup> SIGN 133: *Management of Hepatitis C* (2013) [LIT.001.5550]

<sup>186</sup> Professor Hayes – Day 78, page 90



kill it. Injection with ethanol is indicated for multiple tumours up to three centimetres in size. For tumours up to about five centimetres, trans-arterial chemoembolisation is used if patients do not have widespread disease, vascular involvement, or marked hepatic decompensation. In this procedure the blood vessels supplying the tumour are selectively blocked off following the introduction of the anticancer drugs directly into a tumour via its blood supply. Beyond this, chemotherapy or palliative care is used for cases which are unsuitable for liver transplantation.<sup>187</sup> Chemotherapy treatments are seldom very effective.

### Drug therapy

**13.115** Several drugs in the class of protease inhibitors (Telaprovir and Boceprevir) have recently been licensed for use alongside pegylated Interferon and Ribavirin and, according to trial data, will increase response rates in Genotype 1 patients to 70–80%. Telaprovir was approved for prescription in December 2011.<sup>188</sup> In addition, variations in the IL28 (lambda) gene appear to influence the chance of response (see paragraph 13.67 above) and this genetic predictive test is now finding a place in the selection of patients for treatment.<sup>189</sup> Health economics will affect availability. The side-effects of using protease inhibitors are expected to be more severe. Professor Thomas discussed both aspects:

I think the side effects will be more severe with the protease inhibitors because when similar ... but not identical compounds, are used in HIV, then they have caused liver toxicity... [A]ccumulation of fat in the liver, for instance, has been seen with some of the HIV-active protease inhibitors. So how that will work through with Hepatitis C is not 100 per cent clear.

Telaprevir has been causing quite severe rashes. But the final costing is going to be dependent on ... [the] predictive polymorphism of IL28, which is a lambda interferon ... strongly associated with response to treatment. So it might allow you to pick out those people who are going to respond to pegylated interferon and ribavirin from those who won't, and that latter group might then, instead of going through a trial of the pegylated interferon and ribavirin, they might start initially into those two drugs with the protease inhibitor.

And that will influence the health economics. And then there will be the issue of early-stopping rules of the type... [applied to] interferon and ribavirin because if you can, at an early stage, identify those that are going to be successfully cured, then again that will increase the cost-effectiveness. So there are several groups now looking at, in preparation for NICE, what the management algorithm might look like, and I presume that ultimately that may influence what the costs would be.

....

And the unknown, of course, is the competitive issue as well... telaprovir is made by Vertex and boceprevir is made by Schering-Plough, but they have just been bought by Merck Sharp and Dohme.

....

<sup>187</sup> Ibid pages 89 – 92

<sup>188</sup> Ibid page 130

<sup>189</sup> Professor Thomas' report on Hepatitis C [PEN.017.1071] at 1083

One of the figures that was cited was that it might cost up to £18,000 for a combined course of pegylated interferon, ribavirin and one of these protease inhibitors. And ... I think ... a full year's course of interferon and ribavirin probably costs about £10,000, that sort of level. So they are looking at doubling it in anticipation of the doubling the response rate, so that the cost per cure is slightly improved on what it is now. So when you do the cost-effectiveness analysis, it will come out as a significant improvement.<sup>190</sup>

**13.116** Professor Hayes said that trial data relating to these two new recently-licensed drug treatments suggests that they could herald a 'quantum improvement' in responses, at least for Genotype 1 patients. He also suggested that new treatments, with the added benefit of being taken in oral form over a short course (rather than by frequent injection), might be on the horizon which could be 'remarkably effective'.<sup>191</sup> Professor Thomas said that there was no condition with more drugs in the pipeline than Hepatitis C: by 2015 there will be about 30 waiting in the wings.<sup>192</sup>

**13.117** It is not known at present what the implications are for patients requiring treatment for different genotypes from each of the two relevant treatment groups (haemophilia or post-transfusion patients). Professor Thomas said there was only a relatively small number of relevant patients for whom this is an issue. In the case of haemophilia patients he said:

I think the other thing that has been a problem in treating the haemophilia population is that the interferons have been given subcutaneously and of course, we are worried about forming haematomas by having to inject three times a week. The pegylated interferons ... we only inject now weekly. So that problem is starting to diminish. And initially, when we had to give the injections more frequently, we gave them intravenously to make sure we didn't cause haematomas.

When we were only looking at 12 to 15 per cent response rates, when you are explaining the risk/benefit to the patient, the need for repeated intravenous injections was something that would be considered -- in genotype 1 it would have to continue for a year. That would be discouraging to the patient, I would think.<sup>193</sup>

### Co-infection with HIV

**13.118** Co-infection with HIV complicates the picture.<sup>194</sup> Professor Thomas explained that the issue has always been whether to give highly active retroviral therapy first and then Hepatitis C treatment, or to do it the other way round. In the main, patients are treated for HIV first and then interferon and ribavirin treatment would be added in. The progression of Hepatitis C in the main is much slower than untreated HIV. If the problems can be decoupled by treating HIV first, the situation is improved: a sustained viral response with standard pegylated interferon and ribavirin after treatment of HIV is more likely. Professor Thomas thought that the overall data suggested that the sustained viral response rates in co-infected patients are probably about half what one would otherwise see, so that,

<sup>190</sup> Professor Thomas – Day 53, pages 52–54

<sup>191</sup> Professor Hayes – Day 78, pages 105–106

<sup>192</sup> Professor Thomas – Day 53, page 55

<sup>193</sup> Ibid page 64

<sup>194</sup> Ibid pages 79–82

in the case of a Genotype 1 patient, there might be a response rate of around 20–25%, instead of 40%. How much of that would be corrected by prior treatment of the HIV he did not think was known at the moment but logically one would expect it to be improved. In terms of delay, prior treatment of HIV infection would be insignificant in relation to the progression of Hepatitis C.

### **Morbidity and mortality associated with HCV**

**13.119** The discussion so far has sought to describe the clinical features, natural history and treatment of chronic Hepatitis C, together with co-morbidities and factors which may accelerate the course of the disease. The two 'populations' affected by Hepatitis C who form the subjects for the Inquiry comprise (i) haemophilia patients, almost all male, the majority of whom were infected in the first 30 years of their lives and many of whom were co-infected with HIV; and (ii) those infected as a result of blood transfusion, the majority of whom were over age 40 at the time of infection. Many of the latter group died in the first two to five years after infection as a result of causes quite unconnected with HCV (very often connected, instead, to the primary condition that required medical intervention including blood transfusion). There have been numerous studies of cohorts of patients in each population that have contributed to understanding of the morbidity and mortality associated with HCV and HCV/HIV infection.

#### *HCV associated with haemophilia treatment*

**13.120** The clinical and treatment records of 310 haemophilia patients registered at the Royal Free Hospital Haemophilia Centre were analysed by Dr Thynn Thynn Yee and others.<sup>195</sup> The study provided concrete evidence for the generally held view that almost all haemophilia patients treated with Factor VIII concentrates prior to 1985 (when virucidal treatment of concentrates was introduced) were infected with HCV, at least after the introduction of large-pool clotting factors.<sup>196</sup>

**13.121** The study concluded that the 25-year follow-up of the whole group showed the potentially lethal combination of HIV and HCV co-infection. Individuals infected with HCV alone showed slow progression of liver disease. In terms of prognosis, the article stated:

HCV infection is now recognised as a major risk factor for HCC and there seems to be an incubation period of two or three decades on average ... HCC... is likely to become more common in this group of patients who were infected from 1977 (median year).<sup>197</sup>

**13.122** A major follow-up study among haemophilia patients from Sheffield, Utrecht and including the Royal Free cohort related to 847 patients with HCV antibodies extending for up to 42 years (median 27 years). Of these, 687 (81%) developed chronic Hepatitis C and 210 were co-infected with HIV. There were 199 deaths, 73 of which were attributable to AIDS, and 55 were 'liver related' of whom 31 had HIV/HCV co-infection. Twenty-four HIV-negative patients (4%) had died of liver disease. Seventy-one of the total cohort developed End-stage Liver Disease (ESLD). Thirteen had had a liver transplant. The

<sup>195</sup> Yee et al, 'The Natural History of HCV in a cohort of haemophilic patients infected between 1961 and 1985', *Gut*, 2000; 47: 845–851 [LIT.001.4318]

<sup>196</sup> Factor IX in 1961 and Factor VIII in 1976 in this population.

<sup>197</sup> Yee et al, 'The Natural History of HCV in a cohort of haemophilic patients infected between 1961 and 1985', *Gut*, 2000; 47: 845–851 [LIT.001.4318] at 4323

cumulative incidence of ESLD after 35 years was 11.5% in HIV-negative individuals. The risk of developing ESLD was also associated with age at HCV infection (older patients at date of infection being more at risk) and with history of alcohol abuse.<sup>198</sup>

**13.123** In Canada, the federal, provincial and territorial governments agreed to pay compensation to individuals who became infected with HCV through blood and blood product transfusions between 1 January 1986 and 1 January 1990 on the ground that surrogate marker testing for infection, which had been in place in the USA, had not been implemented in most Canadian jurisdictions. Between 10,000 and 16,000 Canadians were thought to have been infected in that period. Patients with post-transfusion chronic HCV infection, haemophilia patients, patients co-infected with HIV and patients with secondary infections (for example, the sexual partners of those with haemophilia and HCV) were covered by the compensation scheme. Compensation, for viraemic patients, was related to a scale of mutually exclusive stages:

Liver fibrosis stage:

- F0, no fibrosis, to F4, cirrhosis

Clinical status stages:

- Decompensated cirrhosis
- Hepatocellular Carcinoma (HCC)
- Death

**13.124** Accurate prognostic data were required to ensure the sufficiency of the compensation fund and that entailed assessment of the clinical characteristics of the claimant cohort to determine annual fibrosis stage-specific transition probabilities. HCV treatment efficacy was factored into the exercise. Dr Hla-Hla Thein and others reported their findings using base-line clinical data on 5004 patients from 2007.<sup>199</sup> By then, 1231 patients had died (including 401 haemophilia patients) and 3773 were alive (including 904 haemophilia patients). Biopsy evidence was available in 1082 cases (including 225 haemophilia patients).

**13.125** It was assumed that 20% of individuals who acquired HCV infection would clear the infection within six months, with an annual clearance rate thereafter of 2%.<sup>200</sup> The model did not assume a constant rate of progression of liver fibrosis; rather, it assumed use of up-to-date treatment with pegylated Interferon and Ribavirin for all in need. The researchers found that, 20 years after the index transfusion, 10% of all living claimants had cirrhosis and 0.5% had developed HCC. Predicting forward a further 20 years, the risks were computed, giving the following results for haemophilia patients (HCV and HCV/HIV co-infected patients combined):

- Risk of HCV-related cirrhosis      37%
- Risk of HCC                              12%
- Risk of liver-related death          19%

<sup>198</sup> Posthouwer et al, 'Progression to end stage liver disease in patients with inherited bleeding disorders and hepatitis C: an international, multicentre cohort study', *Blood*, 2007; 109: 3667-3671 [LIT.001.4090]

<sup>199</sup> Thein et al, 'Prognosis of hepatitis C virus-infected Canadian post-transfusion compensation claimant cohort', *Journal of Viral Hepatitis*, 2009; 16: 802-813 [LIT.001.4184]

<sup>200</sup> Professor Thomas – Day 52, pages 56-57. The lower end of the range proposed by Professor Thomas was 30%: see Professor Thomas' report on Hepatitis C [PEN.017.1071] at 1074

**13.126** It was noted that haemophilia patients were usually younger than patients infected post-transfusion and were often co-infected with HIV. For the haemophilia group, the cumulative lifetime risk of cirrhosis was estimated at 45%, and of liver-related death 30%. These figures did not include HCV/HIV co-infected patients.

### *Post-transfusion chronic Hepatitis C*

**13.127** Examination of long-term morbidity and mortality from post-transfusion HCV is bedevilled by a number of difficulties. Invariably, a very significant proportion of those infected following transfusion die before the study is completed, often of the morbidity which led to the original need for transfusion. A Scandinavian follow-up over 20 years of over a million transfusion recipients showed standardised mortality rates after one, five and 20 years of 17.6, 2.1 and 1.3 times the general public, respectively.<sup>201</sup> Of these, 65% were dead after 10 years and 77% were dead after 20 years. Furthermore, in look-back studies low proportions of potential subjects come to light and are available for study: there is an unavoidable risk of selection bias and this is reflected in the results brought out.

**13.128** In the UK, Dr Helen Harris and colleagues reported on a study of the natural history of HCV after 16 years of infection carried out on behalf of the HCV National Register Steering Group. The patients all had acquired infection from blood transfusion in the UK on an identified date. All had been traced through the national HCV look-back study. They estimated that at median seven years post-transfusion 61% of the patients identified in the look-back had died.<sup>202</sup> Almost none of these patients would have died of HCV-related causes after this short post-transfusion period.

**13.129** In Denmark, HCV antibody screening was introduced in 1991. Thereafter, 150 HCV-positive donors were identified.<sup>203</sup> A look-back study of post-transfusion chronic HCV in 1996 identified 1018 recipients of blood from those donors. By then 230 were alive, 22.6%, and 77.4% had already died. The Danish health information systems allowed much fuller and more complete ascertainment of subjects than in the UK. Results of a median follow-up of 18 years (21.8 years in survivors) were published in 2011. The authors found that by 2009 only 121 of 1018 known recipients (11.8%) were still alive.

**13.130** In the circumstances, individual studies of morbidity and mortality among surviving patients have to be treated with a degree of caution: the surviving cohort are not necessarily representative of the total population, including those who have died before the date of study. Additionally, data expressed in percentage terms may be misleading. General impressions can nevertheless be gained from a survey of a range of sources. There may be few subjects alive in any sub-group. In the Danish study by Dr Søren Just and colleagues, it was found that there was no difference in all-cause mortality among the 230 HCV-exposed recipients alive in 1996 and followed to 2009 when compared with unexposed controls (a matched group of transfusion recipients not exposed to HCV-infected blood). The authors also found that rates of liver-related disease were not significantly different between the infected and uninfected recipients of HCV-infected blood when adjusted for age, co-morbidity and other factors. Liver-related mortality overall was increased significantly. Relative risk of liver-related death in the HCV-infected group was increased tenfold, although this represented only nine deaths.

<sup>201</sup> Kamper-Jorgensen et al, 'Survival after blood transfusion', *Transfusion*, 2008; 48 [LIT.001.4069]

<sup>202</sup> Harris et al, 'Survival of a national cohort of hepatitis C virus infected patients, 16 years after exposure', *Epidemiology and Infection*, 2006; 134: 472–477 [LIT.001.3898]

<sup>203</sup> Just et al, 'Long-term follow up among Danish transfusion recipients identified in the national hepatitis C lookback', *Transfusion*, 2001 [PEN.018.0507]

**13.131** The study by Harris and colleagues found that, after 16 years of infection, transfusion recipients who tested positive or indeterminate for antibodies to HCV were at increased risk of dying from liver disease compared to anti-HCV negative transfusion recipients. They found that, at median 16 years post-transfusion, the relative risk of all-cause mortality compared with transfused but HCV-negative controls was 1.17 (NS);<sup>204</sup> and that relative risk of death directly from liver disease was 2.71 ( $p = 0.03$ ).<sup>205</sup> There was also a significant – indeed larger – difference in survival to death certified as *liver-related* at 5.04 ( $p=0.003$ ).

**13.132** A very long-term US follow-up (25 years) by Dr Leonard Seeff and colleagues of the original NANB Hepatitis cohort studies in the USA showed overall mortality of 67% in the HCV-positive cohort versus 65% in HCV-negative controls.<sup>206</sup> As with the UK and Danish studies, liver-related deaths, at 4.1% in HCV-positive patients versus 1.3% in controls, were significantly increased ( $p=0.05$ ), but represented only a small fraction of overall deaths. The authors stated that:

For the entire cohort of patients initially infected with HCV, the estimate for progression to cirrhosis is 17%. Thus, over an approximate 25-year interval, HCV infection did not lead to increased [overall] mortality and resulted in severe histological lesions in fewer than 20%.

Whether those with histologically defined chronic hepatitis alone will progress to cirrhosis, and whether mortality and morbidity will continue to derive mainly from those with established cirrhosis, remains to be determined.<sup>207</sup>

**13.133** In the Canadian study by Thein and colleagues, for post-transfusion HCV patients, among 3699 individuals of whom 857 had liver biopsy evidence, modelling showed:

- Risk of HCV-related cirrhosis                      23%
- Risk of HCC    7%
- Risk of liver-related death                              11%

**13.134** Dr Gary Davis and colleagues have recently reported the results of a multi-cohort natural history modelling study of disease progression in what has become an ageing population of US patients.<sup>208</sup> This study, which is most sophisticated and well-informed, used multiple disease cohorts to study cirrhosis, hepatic decompensation, HCC and death. Projections were developed, differentiated for sex, age at infection and duration of infection up to 30 years. Rates of liver-related morbidity and mortality at 30 years were derived as follows:

<sup>204</sup> 'NS' denotes that there is no significant difference, particularly when the difference between two categories is smaller than the amount of error that is expected to be in the data as 'noise'.

<sup>205</sup> A p-value expresses the probability that a given hypothesis is false. The lower the p-value, the more likely it is that the hypothesis is valid. In this case, the p-value indicates that the authors had estimated that, notwithstanding the calculated risk of 2.71 on available data, there was a 3% chance that the calculation was wrong.

<sup>206</sup> Seefe et al, 'Long-term mortality and morbidity of transfusion-associated non-A, non-B, and type C hepatitis: a National Heart, Lung, and Blood Institute collaborative study' *Hepatology*, 2001; 33: 455–463 [LIT.001.3951]

<sup>207</sup> Ibid [LIT.001.3951] at 3958

<sup>208</sup> Davis et al, 'Aging of hepatitis C virus (HCV)-infected persons in the United States: a multiple cohort model of HCV prevalence and disease progression', *Gastroenterology*, 2010; 138: 513–521 [LIT.001.4046]

**Table 13.1: Projections by cohort of all infected patients**

	Percentage after 30 years			
	Cirrhosis	Decompensated cirrhosis	HCC	Liver death
Females: Age 0–30 at infection	4.24	0.44	0.02	0.92
Females: Age 31–50 at infection	7.75	0.79	0.04	1.28
Females: Age over 50 at infection	7.36	0.80	0.12	2.29
Males: Age 0–30 at infection	13.92	1.55	0.19	2.91
Males: Age 31–50 at infection	38.11	5.13	0.50	11.14
Males: Age over 50 at infection	15.24	2.21	0.56	15.06

**13.135** The authors cite a number of other studies showing that, after long-term follow-up, all-cause mortality and non-liver mortality may also be increased in older individuals with chronic HCV infection.

**13.136** One such study, by Dr Anne Guiltinan and colleagues, dealt with a large number of blood donors for whom records were available at 17 blood centres in western and southern USA.<sup>209</sup> They identified 10,259 confirmed HCV-positive donors who had donated blood between 1991 and 2002, and 10,259 HCV antibody-negative donors matched for year of donation, age, gender and ZIP (postal) code. After a mean follow-up of 7.7 years, they found excess mortality in the HCV infected group as follows:

**Table 13.2: Excess mortality in HCV positive donors compared to HCV-negative donor controls<sup>210</sup>**

	HCV positive	HCV negative	Total	Hazard ratio <sup>211</sup>
Liver-related deaths	90	2	92	45.99
Drug/alcohol-related deaths	64	6	70	10.81
Cancer excluding liver	56	53	109	1.09
Trauma/suicide	106	36	142	2.99
Cardiovascular	60	28	88	2.21
Pulmonary	8	7	15	1.18
Stroke	13	6	19	2.20
Infection	23	2	25	11.73
Other/unknown	33	8	41	4.23
Total deaths	453	148	601	3.13

<sup>209</sup> Guiltinan et al, 'Increased all cause, liver, and cardiac mortality among hepatitis C virus-seropositive blood donors', *American Journal of Epidemiology*, 2008; 167: 743–750 [LIT.001.4061]

<sup>210</sup> 'Excess' meaning high relative to the general population.

<sup>211</sup> Hazard ratio: the risk of death expressed as a ratio of [deaths in HCV+ve donors]/[deaths in HCV-ve donors].

**13.137** The authors commented that the estimated annual risk of death due to liver disease was 1:1000 or, cumulatively, about 2% over 20 years of life following infection. Liver cancer accounted for about one fifth of these deaths, about 0.4% cumulative risk over the same period. Multivariate analysis did not change significantly the association between HCV infection and all-cause mortality.

**13.138** The donors were presumed to be unaware of their infection and to have been in apparently good health at the time of donation, having passed blood donor medical selection criteria. Under-reporting of HCV risk factors was likely, however.

**13.139** These studies, in unselected post-transfusion patients with acquired chronic HCV infection and in other populations of those infected with HCV, indicate consistently that after 18–25 years or more post-infection:

- (i) A relatively small proportion of post-transfusion infected patients remain alive, many having died within a few years of transfusion of causes not related to HCV.
- (ii) While mortality directly attributable to liver disease is increased in these patients compared to HCV-negative transfused controls, this has so far amounted to less than five per cent of total deaths among those surviving 10 or more years after transfusion.
- (iii) Of the survivors alive more than 25 years post-infection, a significant proportion (up to 25%) may ultimately go on to develop cirrhosis and become exposed to risk of its complications, namely liver failure and HCC.

**13.140** There is a possibility that, for reasons as yet unknown, those relatively few survivors of post-transfusion HCV, or the haemophilia patients with HCV in the UK who survive for more than 30 years after acquiring HCV infection, may have a slightly increased all-cause mortality and non-liver-related mortality. It seems more likely, however, that such findings in HCV-positive patients as a whole are due to factors associated with their previous lifestyles rather than to some as yet unidentified non-hepatic factor associated with long-term HCV.

**13.141** Many studies have demonstrated that older age at acquisition of HCV infection is associated with more rapid progression of liver disease. However the Inquiry has found no evidence that, in individuals who acquired HCV at younger ages, there is an age-dependent acceleration in the rate of progression of liver disease, independent of other variables (such as alcohol, obesity or smoking, discussed above).

**13.142** Finally, can these studies be improved upon? One of the doyens of the study of Hepatitis C, Dr Leonard Seeff (principal author of the study at paragraph 13.132 above), has recently written:

Some [of those infected with HCV] will even progress through life without ever knowing that they are HCV infected, while others may suffer from varying degrees of fatigue and a decreased quality of life. In order to accurately establish the frequency of these variable outcomes, it would be necessary to mount a life long study of a large cohort from the time of infection and follow them until their demise.... [I]t would be almost impossible to pursue a study of this duration...<sup>212</sup>

<sup>212</sup> Seeff, 'The History of the 'natural history' of hepatitis C (1968 – 2009)', *Liver International*, 2009; 29:, 89–99:[LIT.001.4100] at 4106



**13.143** It now seems unlikely that any further studies will provide much more definitive information in future. Because of the advent of effective treatment, the era of natural history studies of chronic Hepatitis C has probably passed.

#### *Impact of co-infection with HIV*

**13.144** As already noted, in patients co-infected with HIV the rate of HCV replication is higher, and the level of viraemia is also relatively high. In the UK many haemophilia patients became co-infected with HIV and HCV. Very few post-transfusion HCV patients, if any, had this problem. Overall, parenteral drug use has caused the majority of cases of HIV/HCV co-infection and studies of this cohort best inform current understanding of the problem.

**13.145** The Royal Free Hospital, Sheffield and Utrecht study of 847 haemophilia patients exposed to HCV infection, of whom 210 were co-infected with HIV, showed that the cumulative incidence of ESLD among co-infected individuals was 35.1% at 35 years as against 11.5% in HIV-negative subjects. Deaths from liver disease were 21 of 210, plus 73 deaths from AIDS in the co-infected patients.<sup>213</sup>

**13.146** Meta-analysis of 17 studies, reported in 2008, indicated more rapid progression to cirrhosis in patients co-infected with HIV than in patients infected with HCV alone.<sup>214</sup> Drawing on previous reports, 3567 patients were studied. The study also analysed data distinguishing results for patients treated with highly active anti-retroviral therapy (HAART). Over the period studied, HAART did not appear to correct fully the adverse effect on HCV prognosis of co-infection with HIV.

**13.147** The estimated mean transition probabilities between fibrosis stages were calculated. There was a significant association between the duration of HCV infection and the rate of progression of fibrosis: with longer duration the rate of progression slowed. By contrast, among co-infected individuals, it was concluded that the rate of fibrosis progression appeared to be constant.

**13.148** Prevalence of cirrhosis in co-infected individuals was 21% after 20 years and 49% after 30 years. The overall ratio of cirrhosis in co-infected individuals relative to cirrhosis in patients infected with HCV alone was 2:1. It was concluded that chronic Hepatitis C outcomes were worse for co-infected individuals.

#### **Conclusion**

**13.149** As indicated in paragraph 13.2, the narrative of patients' experiences of infection with NANB Hepatitis virus/HCV is best understood in light of the most up-to-date knowledge of the disease. In that way, patients' reports of signs and symptoms associated with infection can now be explained even when they would not have been understood at the time of report to be related to NANB Hepatitis virus/HCV infection. Current knowledge provides the appropriate background for an informed appreciation of the accounts patients and their relatives have given of their experiences of HCV infection, whatever the date or dates of those experiences. However, it has to be repeated that very little of the information relating to the natural history of HCV infection which is

<sup>213</sup> Posthouwer et al, 'Progression to end stage liver disease in patients with inherited bleeding disorders and hepatitis C: an international, multicenter cohort study', *Blood*, 2007; 109: 3667–3671 [LIT.001.4090]

<sup>214</sup> Thein et al, 'Natural history of hepatitis C virus infection in HIV-infected individuals and the impact of HIV in the era of highly active retroviral therapy: a meta-analysis', *AIDS*, 2008; 22: 1979–1991 [LIT.001.4077]

available now, in 2014, would or could have been known until well into the 1990s, after the patients with whom this Report is concerned were already infected by transfusion of blood, blood components or blood products. Hindsight cannot support a view of what should have been understood at earlier periods.

**13.150** The element of hindsight is less material in relation to the pain and discomfort associated with investigative procedures and the side-effects of drug therapy. These factors were available for observation at the time. The general information nevertheless also informs a proper appreciation of the accounts provided.

**13.151** Patients' reports of their individual histories are described in Chapters 4 and 6.

## CHAPTER 14

### KNOWLEDGE OF VIRAL HEPATITIS 1

#### Introduction

**14.1** Early developments in knowledge of viral hepatitis were noted in the introduction to Chapter 6 of the Preliminary Report. Key stages were:

- The discovery, in 1965, of the 'Australia' antigen, HBsAg, the surface antigen to the Hepatitis B virus (HBV), followed by the development of tests for the presence of the antigen, and subsequently other components of HBV, which became generally available from about 1970.<sup>1</sup>
- The identification of the Hepatitis A virus (HAV) by Dr Stephen Feinstone and others, published in 1973.<sup>2</sup>
- The realisation in around 1974–75 that Hepatitis A and Hepatitis B, as then understood, could not account for a substantial proportion of cases of post-transfusion hepatitis, and that there had to be another form or forms of viral hepatitis to explain the clinical manifestations of hepatic (liver) dysfunction that were known or becoming known.<sup>3</sup>

**14.2** In this Report, it is appropriate to discuss more fully the response of the UK Government and other agencies to the emerging knowledge of viral hepatitis during the period when it presented a threat to NHS patients receiving blood, blood components or blood products in the course of medical treatment.

#### Understanding the risk: background

**14.3** The aim of this part of the Report is to describe what was known at critical stages to scientists, practitioners and relevant authorities, not what 'ought' to have been known or accepted. In this early period, scientific developments were reported that, in time, became generally accepted medical knowledge. Developments can often be best identified and described chronologically, by date of publication, as was done in the Preliminary Report. However, inherent in this approach is a risk of representing as contemporaneous knowledge material that would not, and in some cases could not have, at that time, been known or understood by practitioners generally. Further, published data and discussion will reflect work carried out over a period prior to publication. In general, first publication of a finding or theory is more likely to mark the beginning of critical examination of ideas rather than the date of their general acceptance. Scientists exploring the boundaries of current knowledge inevitably develop theories that may be backed up by limited empirical data. Such theories are perhaps unlikely to meet with immediate acceptance by a critical peer group and even less likely to survive challenge by related, or unrelated, specialists. Scientific orthodoxy may resist novel ideas and inhibit their acceptance. Those with control of the funds necessary for the validation of a theory and the implementation of changes required to give practical expression to emerging ideas are even less likely to be easily satisfied.

---

<sup>1</sup> Preliminary Report paragraphs 6.12–6.14

<sup>2</sup> Ibid paragraphs 6.22–6.23

<sup>3</sup> Ibid paragraphs 6.28–6.32

**14.4** On the other hand, the convention that dictates that scientific ideas are presented tentatively where logical absolutes cannot be sustained should not be taken to undermine the impact of publication. Reputation is a significant factor of the author or authors of published work and of the journals in which they publish. It all makes for difficulty in saying when a given scientific proposition was 'established'. All of these comments are as relevant to the early 1970s as they are today.

### The early years

**14.5** The revolution in knowledge brought about by the discovery of the 'Australia' (or 'hepatitis-associated') antigen, later renamed the Hepatitis B surface antigen (HBsAg), the isolation of the Hepatitis A virus and the inference of the existence of one or more non-A, non-B Hepatitis (NANB Hepatitis) viruses can best be understood by looking in greater detail than was done in the Preliminary Report at some of the key early publications.

**14.6** Until the late 1960s, it was generally understood that 'hepatitis' could be transmitted in water-borne (enteral)<sup>4</sup> form or in blood-borne (parenteral)<sup>5</sup> form. It was thought likely that one or more agents causing enteral (also known as 'infectious') hepatitis were viruses and were different from the one or more agents – also thought probably to be viruses – which caused parenteral (also known as 'homologous' or 'serum') hepatitis. It was known that the development of serum hepatitis was associated with blood transfusion but it was thought that the hazard affected a very small proportion of recipients of whole blood, plasma or plasma products. In the mid-1960s, there was no single test or battery of liver function tests which would reliably distinguish carriers of any putative hepatitis virus from those not affected. The consequences of transmission, as understood at the time, varied:

Some patients suffer no upset from the transmitted virus, some may have only a transient liver dysfunction with or without jaundice and yet others may develop a rapidly fatal hepatic necrosis. The incubation period of infective hepatitis is about 20 to 40 days, whereas that of homologous serum hepatitis is 40 to 160 days.<sup>6</sup>

**14.7** The emphasis was on short-term signs and symptoms of infection and the two putative forms of hepatitis were distinguished by their periods of incubation before the appearance of clinical symptoms.

**14.8** A similar focus on the short term was reflected in early publications of the findings of haemophilia clinicians. Researchers in 1963 reported 'reactions' to the infusion of human AHG concentrate (a stable concentrate of human antihæmophilic globulin – a precursor to the industrial scale production of Factor VIII concentrates used for the treatment of haemophilia).<sup>7</sup> The reactions ranged from mild headaches to nausea, vomiting and pain. In all cases, the signs and symptoms of the reactions observed were reported to have disappeared quickly after the end of the infusion. These were almost certainly not related to the transmission of infection but rather were transient mild immune reactions to the 'foreign' proteins introduced by the AHG. The 1963 report also discussed three possible

<sup>4</sup> Strictly speaking, an enteral infection is one spread through the introduction of a pathogen to the gastrointestinal tract.

<sup>5</sup> Again, strictly speaking, a parenteral infection is one spread by a means other than by the introduction of a pathogen to the gastrointestinal tract and, in this general way, does not refer only to blood-borne infections. Medical literature of the time, however, used the term parenteral, at least as regards hepatitis, to mean 'blood-borne' and this usage is retained here.

<sup>6</sup> Grant, 'Complications of Blood Transfusion', *The Practitioner*, 1965; 1166:184-5 [LIT.001.5542] at 5547

<sup>7</sup> Maycock et al, 'Further Experience with a Concentrate Containing Human Antihæmophilic Factor', *British Journal of Haematology*, 1963; 9:215 [LIT.001.0063]. Dr Maycock and three of his colleagues were, at the time, associated with the Lister Institute of Preventative Medicine. One colleague was associated with the laboratory at Lewisham Hospital, London.

cases of homologous serum jaundice. It was said that no permanent harm was caused by the patients' reactions. The authors found that jaundice occurred but there was no firm view as to its cause. As with other adverse patient responses, it was not associated with apprehension of any long-term consequences of infection.

**14.9** Blood products were associated with a case of jaundice in a haemophilia patient reported in 1966,<sup>8</sup> and with a second, fatal case following the use of cryoprecipitate reported in September 1969.<sup>9</sup> The 1966 case was described as one of transient jaundice from which the patient recovered after a day of nausea and vomiting. The second case, of fulminant hepatitis (a rapidly progressing form of the disease), in retrospect almost certainly a case of fulminant Hepatitis B, presented after some four months of treatment using a total of 162 units of cryoprecipitate. The patient had developed nausea and continuous vomiting with cold, moist, jaundiced skin. He deteriorated rapidly and died. Post-mortem examination of the liver showed extensive hepatocellular damage. Tests for known viruses were carried out. Apart from a rather high titre (concentration) for cytomegalovirus (CMV), the samples tested were described as normal. Blood tested for serum hepatitis antigen, shortly to be called Hepatitis B antigen, gave a weak positive reaction. The conclusion was that the clinical and post mortem findings were 'fully compatible with a diagnosis of serum hepatitis'.<sup>10</sup>

**14.10** The report in 1969 stimulated correspondence. A letter published in the *British Medical Journal (BMJ)* in November of that year reported a further case with symptoms of nausea, itching and jaundice.<sup>11</sup> Biochemical laboratory tests disclosed high levels of alkaline phosphatase (ALP), and aspartate and alanine transaminase (AST and ALT).<sup>12</sup> A purported causal link between the use of concentrates and viral hepatitis was explicit in the letter but the focus remained on jaundice within a relatively short period after use of concentrates. More generally, the letter identified a need for screening for hepatitis infection to reduce transmission risk. It was recognised that, while careful questioning of donors would exclude those who had experienced clinical jaundice, effective reduction of risk depended crucially on a reliable test. The letter stated:

[U]ntil a reliable serological test for viral hepatitis is available the donor with anicteric hepatitis [hepatitis, that is, without jaundice] will go undetected. Cryoprecipitate will remain a potential source for the transmission of hepatitis virus until previous attacks of this form of hepatitis can be reliably diagnosed or an effective means of sterilization ... is produced.<sup>13</sup>

**14.11** The laboratory tests were not treated as diagnostic. The letter envisaged serum or viral hepatitis as a single entity requiring a single reliable serological test.

**14.12** There was a great deal of uncertainty at the time. The distinction between Hepatitis A and Hepatitis B was not fixed. Dr Rosemary Biggs, a prominent expert at the Oxford Haemophilia Centre, used the terms 'infective hepatitis' and 'viral hepatitis' interchangeably. An editorial in *The Lancet* in August 1970 cast doubt on the use of the terms 'serum' and 'infectious' to distinguish the two types envisaged at the time.<sup>14</sup> The

<sup>8</sup> Del Duca & Eppes, 'Hepatitis Transmitted by Antihemophilic Globulin, *New England Journal of Medicine*, 1966; 965 [PEN.018.1455]

<sup>9</sup> Whittaker & Brown, 'Serum Hepatitis in a Haemophiliac', *British Medical Journal*, 6 September 1969 [LIT.001.0248]

<sup>10</sup> Ibid [LIT.001.0248]

<sup>11</sup> Fitzpatrick & Kennedy, 'Serum Hepatitis in a Haemophiliac', *British Medical Journal*, 1 November 1969 [LIT.001.0249]

<sup>12</sup> These proteins, synthesised in liver cells and normally present in low levels in the blood, become elevated when the liver is disordered by virus infection or other hepatic disorders.

<sup>13</sup> Fitzpatrick & Kennedy, 'Serum Hepatitis in a Haemophiliac', *British Medical Journal*, 1 November 1969 [LIT.001.0249]

<sup>14</sup> 'More about Australia Antigen and Hepatitis', *The Lancet*, 15 August 1970 [DHF.002.7334]

general state of uncertainty was reflected in a paper presented to the Sub-Committee of Specialists on Blood Problems of the Public Health Committee of the Council of Europe in April 1970, where it was commented that the generally observed distinction between Hepatitis A and Hepatitis B might be artificial.<sup>15</sup>

**14.13** For some official purposes, any distinction between infectious hepatitis and serum hepatitis was treated as irrelevant. In the UK, growing awareness of the prevalence of hepatitis led to provision for the notification of cases of the disease.<sup>16</sup> As regards Scotland, the Public Health (Infectious Diseases) Regulations (Scotland) 1932<sup>17</sup> required notification of infective jaundice, then defined to mean spirochaetosis ictero-haemorrhagica (Weil's disease). Those Regulations were amended by the Public Health (Infectious Diseases) (Scotland) Amendment Regulations 1968<sup>18</sup> after which the relevant notifiable disease was simply 'infective jaundice' without further definition.<sup>19</sup> It was intended that all forms of 'infective jaundice' (including 'serum' hepatitis) would be covered. One aim of the regulations was to facilitate a study of the epidemiology of the disease.<sup>20</sup> The scope of the 1968 Regulations is reflected in the incubation periods mentioned in the relevant Scottish Home and Health Department (SHHD) circular.<sup>21</sup> Infective hepatitis was said to have an incubation period of usually 15–40 days, while serum hepatitis was described as occurring less frequently but as a potentially more serious condition with a longer incubation period of usually 60–160 days. The focus was again on 'jaundice' and, apart from differing incubation periods, the symptoms of jaundice did not appear to give rise to any need to differentiate between infective hepatitis and serum hepatitis.

**14.14** The official view of the scope of the Regulations was not immediately accepted by all. Dr John Wallace of the Glasgow and West of Scotland Blood Transfusion Service (then and thereafter frequently a member of UK expert advisory groups) wrote to Dr Ian Macdonald of the SHHD, on 27 February 1969 asking for the official position on notification of serum hepatitis.<sup>22</sup> The response was that 'infective jaundice' was notifiable and that that included serum hepatitis.<sup>23</sup> For reporting purposes, then, a distinction between infective and serum hepatitis was not recognised by SHHD in these exchanges but it was agreed that the subject of notification was worthy of further consideration by the Transfusion Directors.<sup>24</sup> The Regional Blood Transfusion Directors subsequently proposed that the notification system should disclose the following:

Patients developing infective jaundice at a relevant period after having had blood or blood products.

[And]

Cases where patients are donors and who might have given blood whilst infected.<sup>25</sup>

<sup>15</sup> Paper Submitted to the Sub-Committee of Specialists on Blood Problems of the Public Health Committee of the Council of Europe on the Subject of Hepatitis Associated Antigen and the Antibody to It [DHF.001.1745]

<sup>16</sup> Professor Zuckerman had pressed for notification in 1966 as essential for the measurement of the scale of post-transfusion hepatitis in the UK. See Zuckerman, 'Blood Transfusion and Infectious Hepatitis', *British Medical Journal*, 1966; 1136 [LIT.001.0247]

<sup>17</sup> S.I. 1932/1047

<sup>18</sup> S.I. 1968/1493

<sup>19</sup> SHHD *Health and Welfare Services Circular No. 26/1968* dated 27/09/1968 [SGH.002.3268]

<sup>20</sup> Memorandum [SGH.002.3266]. In the event, the regulations were ineffective for that purpose. See Chapter 3, *Statistics*, paragraphs 3.9–3.13

<sup>21</sup> Memorandum [SGH.002.3266]

<sup>22</sup> Dr Wallace's Letter [SGH.002.3256]

<sup>23</sup> SHHD Reply to Dr Wallace's Letter [SGH.002.3255]

<sup>24</sup> *Ibid* [SGH.002.3253]

<sup>25</sup> Undated letter to Dr Gordon [SGH.002.3248]; Extract from Minutes of Meeting of Regional Directors on 06/05/69 [SGH.002.3249]

**14.15** The emphasis on a 'relevant period' appears clearly to have implied that the reporting obligation would still extend only to cases of overt, clinical jaundice.

### UK research projects and reports

#### *Haemophilia Centre Directors' Report*

**14.16** The Directors of the (then) 36 Haemophilia Centres of Great Britain decided in 1967 to make a study of the incidence of transfusion hepatitis and inhibitors,<sup>26</sup> described as 'the two most alarming complications of treatment of patients with coagulation defects'.<sup>27</sup> During the years 1969 and 1970, before the ready availability of HBsAg screening tests, data were sought on the varieties and amounts of therapeutic materials used and on the incidence of 'inhibitors and jaundice'. On 5 April 1971 the results were presented to a meeting of the Haemophilia Centre Directors as a 'Report on the progress of the MRC Cryoprecipitate Working Party Survey of the Incidence of Transfusion Jaundice and the Incidence of Inhibitors in Haemophilic and Christmas Disease Patients'. The Inquiry has not found a follow-up from the Medical Research Council (MRC) to this particular report, although, as noted below (paragraphs 14.20–14.23), a Working Party of the MRC conducted its own research on recipients of blood transfusions at a single hospital in or around the same period. The relationship, if any, between this study and the later MRC study is not clear.

**14.17** The Haemophilia Centre Directors' report noted that transfusion-transmitted hepatitis was thought to be a viral infection and that there was every reason to suppose that the virus was contained in the various protein fractions used to treat haemophilia and Christmas disease (Haemophilia B), listed as cryoprecipitate, human antihemophilic globulin and Factor IX concentrate. It stated:

No attempt was made to record sub clinical hepatitis since the important feature from the point of view of these patients is clinical illness.<sup>28</sup>

**14.18** Of the 1066 patients reviewed in 1969, 34 had not been treated in the year, reducing the relevant cohort to 1032, in which 29 cases of clinical jaundice were recorded, an incidence of 2.8%. All of those patients were severely affected<sup>29</sup> by haemophilia or Christmas disease. The report contained detailed analyses of the materials used and the relationship between donor exposure and infection. The blood of 60 patients was tested for hepatitis associated antigen and antibody; and 11 tested positive, only one of which developed clinical hepatitis. The view expressed was that the overall low incidence of clinical illness was presumed to be due to the fact that the patients developed immunity in childhood. This led to the incorrect conclusion that patients with coagulation defects were very resistant to clinical infection with HBV. Lack of understanding of the natural history of the disease was a major contributory factor leading to incorrect inferences at this time (1971).

<sup>26</sup> Inhibitors are antibodies to Factor VIII. Haemophilia patients, particularly at this time, who developed inhibitors faced additional challenges in terms of therapeutic practice, as infusion of Factor VIII was not possible without serious risk.

<sup>27</sup> Appendix to Agenda for a Meeting of Haemophilia Centre Directors on 5 April 1971 entitled 'Report on the progress of the MRC Cryoprecipitate Working Party survey of the incidence of transfusion jaundice and Factor-VIII Antibodies in Treated Patients with Haemophilia and Christmas Disease' [DHF.001.1811] at 1812.

<sup>28</sup> Appendix to Agenda for a Meeting of Haemophilia Centre Directors 05/04/71 entitled 'Report on the progress of the MRC Cryoprecipitate Working Party survey of the incidence of transfusion jaundice and Factor-VIII Antibodies in Treated Patients with Haemophilia and Christmas Disease' [DHF.001.1811] at 1812

<sup>29</sup> See Chapter 2, *Patients at Risk*, paragraphs 2.24–2.27 for a discussion of the classification of haemophilia in to 'mild', 'moderate' and 'severe' categories.

**14.19** The results of the study were published by Dr Biggs in 1974.<sup>30</sup> By then, the text had been amended to cover the period 1969–71 and screening for HBV had been instituted. The study included 1837 patients, 62 of whom had 64 instances of clinical jaundice, an incidence of 3.48%. Again, most were severely affected haemophilia or Christmas disease patients. A total of 302 patients were tested by various methods for hepatitis associated antigen and antibody. About 30% were antigen or antibody positive. A smaller proportion was noticeably ill. The emphasis in the paper remained on clinically apparent hepatitis, typically manifested by jaundice.

#### ***Blood Transfusion Research Committee Cryoprecipitate Working Party***

**14.20** As noted above, the MRC Blood Transfusion Research Committee Cryoprecipitate Working Party conducted further research in the early 1970s to look into the relationship between transfusion and hepatitis in the UK. Members of the group included Professor Sheila Sherlock, Professor Ari Zuckerman, Dr William Maycock and Dr John Wallace. Its final report was published in 1974.<sup>31</sup> After excluding several groups of patients who fell out of the study for various reasons, 768 patients who had received blood transfusions at the Central Middlesex Hospital were studied intensively for six months after transfusion, both clinically and by laboratory tests for liver function.

**14.21** The overall incidence of icteric and anicteric hepatitis (that is, hepatitis with or without jaundice) was 1%. Of the 768 patients, eight were judged to have developed post-transfusion viral hepatitis on the criteria applied by the group. The study identified 35 other patients who showed ‘conspicuous or sustained’ elevated liver function (specifically, ALT) test results but were judged not to have symptoms or physical signs suggestive of viral hepatitis. A further 115 patients had ALT rises after transfusion but ‘were thought not to have viral hepatitis’.

**14.22** In discussing the criteria used for the diagnosis of hepatitis, the report stated:

Liver biopsy may provide incontrovertible confirmatory evidence of hepatitis but this procedure is seldom undertaken. Where liver biopsy was not performed, that is to say in the majority of the survey patients, reliance was placed on clinical evidence and measurement of serum ALT. The duration and degree of elevation of the enzyme that qualify a patient for inclusion in the hepatitis group must be critically examined. Neither a rise in ALT, nor its magnitude, is a specific indication of hepatitis. In some previous studies a transaminase level was arbitrarily defined below which a diagnosis of hepatitis was not made ... In the present survey no such arbitrary lower limit was set. However, if other factors were present which might have caused the enzyme rise these patients were not considered to be suffering from viral hepatitis; it was accepted that these other factors were a more likely cause of the liver damage ... This rigid exclusion of all patients having other possible causes for their liver damage may have contributed to the low incidence of hepatitis in the present study.<sup>32</sup>

**14.23** Other possible causes of an underestimate were also explored.

<sup>30</sup> Biggs, ‘Jaundice and antibodies directed against factor VIII and IX in patients treated for haemophilia or Christmas disease in the United Kingdom’, *British Journal of Haematology*, 1974; 26: 313–329 [LIT.001.0099]

<sup>31</sup> Medical Research Council Working party on Post-Transfusion Hepatitis, ‘Post-transfusion hepatitis in a London hospital: results of a two-year prospective study’, *Journal of Hygiene Cambridge*, 1974; 73:173–188 [LIT.001.0116]

<sup>32</sup> *Ibid* [LIT.001.0116] at 0127



**14.24** By 1974, the tests available for HBsAg and antibody to Hepatitis B (anti-HBs) remained relatively insensitive. The work of the MRC group was carried out in an era when overt clinical jaundice was still regarded as a good marker of 'post-transfusion hepatitis'. The existence of non-A, non-B Hepatitis (NANB Hepatitis) had yet to be reported and, therefore, the incidence of post-transfusion NANB Hepatitis virus infection could not have been, and was not, discussed. Though understandable in context, the firm exclusion of raised ALT without other clinical manifestations of infection as a diagnostic feature of viral hepatitis, even where there was no other indicator of liver inflammation, was to have a significant and continuing impact on the understanding in the UK of viral hepatitis generally.

**14.25** These studies represented significant initiatives in hepatitis research in the late 1960s and early 1970s. The approach adopted towards the identification of viral hepatitis in those studies would characterise UK research for a considerable period. As a result, in retrospect, the true incidence of post-transfusion hepatitis was underestimated. Dr Harvey Alter and Dr Leonard Seeff later analysed the data relating to the patients reported in the MRC Working Party study and concluded, in retrospect, that 80% of those with sustained elevated liver function test results had NANB Hepatitis, although in the original report the patients were not judged to have had 'post-transfusion hepatitis', as there defined, at all.<sup>33</sup> Arithmetically, if the report's assessment of HBV infection had been sound, the proportion of patients with NANB Hepatitis would have been even higher than indicated by Alter and Seeff.

**14.26** The MRC report represented the views of Professor Zuckerman and Professor Sherlock, both recognised at the time as authoritative commentators. In December 1975, the SNBTS Directors agreed with the main recommendations of the report when it was presented by Dr Wallace, a member of the group from the Glasgow and the West of Scotland Blood Transfusion Service.<sup>34</sup> In light of later knowledge, the MRC study was not a sound basis upon which one could draw conclusions about the prevalence of post-transfusion hepatitis in the UK, though it clearly represented informed opinion at the time. In his evidence to the Inquiry, Dr Brian McClelland, South East Scotland Blood Transfusion Service, stated that when he read the 1974 report in the early 1980s he realised that it did not tell transfusionists and others what they needed to know.<sup>35</sup> His efforts aimed at promoting research into the prevalence of post-transfusion NANB Hepatitis, against the resistance generated by established views, are discussed in Chapter 27, *Surrogate Testing of Donated Blood for non-A, non-B Hepatitis*. The erroneous conclusion drawn from the study, that post-transfusion hepatitis was rare in the UK, persisted until 1980 and was promoted even later by some experts.

**14.27** At the same time as these studies were taking place, there were also developments at the UK Government level and internationally.

<sup>33</sup> Zuckerman and Thomas (eds), *Viral Hepatitis: Scientific Basis and Clinical Management* 1993; page 472, table 29.2. Ironically, it is possible that the MRC approach was influenced by the views of Professor Zuckerman.

<sup>34</sup> Minutes of the SNBTS Directors' Meeting of 17 December 1975 [SNF.001.0011] at 0013

<sup>35</sup> Day 63, page 71

## The Advisory Group on Testing for the Presence of Hepatitis B Surface Antigen: First Report

**14.28** The Department of Health and Social Security (DHSS) responded promptly to advice received in July 1970<sup>36</sup> that it should give any assistance it could in instituting testing for the 'Australia' antigen. In September 1970 the three territorial Health Departments appointed the Advisory Group on Testing for the Presence of Hepatitis B Surface Antigen, to advise them on 'the organisation of and responsibility for testing blood donations and other specimens of blood for Australia (hepatitis-associated) antigen and its antibody in the hospital service' and related matters.<sup>37</sup> The initial members of the advisory group included some who would play a central role in the development of policy advice in the UK: Dr Maycock, the chairman, Dr David Dane,<sup>38</sup> Professor Albert Marmion (Edinburgh University Medical School), Dr Wallace (Glasgow and West of Scotland Blood Transfusion Service) and Dr, later Professor, Zuckerman.

**14.29** The Group published a first (revised) report in May 1972.<sup>39</sup> It set out the understanding of viral hepatitis of this group of experts at that date:

The association between the [hepatitis associated/Australia] antigen and serum hepatitis, commonly accepted as the most frequent form of hepatitis observed following the injection of blood and blood products, is well-established and the antigen can now be detected by a variety of laboratory tests .... Australia antigen appears not to be associated with infectious hepatitis which may also be transmitted by blood and blood products.<sup>40</sup>

**14.30** It was suggested that the 'hepatitis agent' might be less widely dispersed in the UK than in some other countries but it was nonetheless recommended that testing, for both the antigen and its antibody, should be introduced generally. The principal recommendations included:

[T]he Regional Transfusion Centres should begin, at the earliest possible date, to test all blood donations for the presence of Australia (hepatitis-associated) antigen and its antibody....

[And]

[A] donor found to be antigen or antibody positive should not be allowed to continue as a donor of blood intended for clinical use.<sup>41</sup>

## World Health Organization Scientific Group on Viral Hepatitis 25–30 September 1972

**14.31** Professor Zuckerman was a member of the Secretariat of the World Health Organization (WHO) Scientific Group on Viral Hepatitis, a body composed of eminent international experts, including Professor Marmion of Edinburgh. The report 'Viral

<sup>36</sup> Note of a Meeting held on 20 July 1970 to Discuss the Problems of the Hepatitis Associated Antigen in Relation to Blood Transfusion and Associated Matters [DHF.001.1751]

<sup>37</sup> Revised (first) Report of the Advisory Group on Testing for the Presence of Australia (Hepatitis Associated) Antigen and its Antibody [DHF.001.1980] at 1983

<sup>38</sup> Dr Dane led the team of scientists who, in 1970, discovered the complete Hepatitis B virus.

<sup>39</sup> Revised (first) Report of the Advisory Group on Testing for the Presence of Australia (Hepatitis Associated) Antigen and its Antibody [DHF.001.1980] at 1983

<sup>40</sup> Ibid [DHF.001.1980] at 1984

<sup>41</sup> Ibid [DHF.001.1980] at 2000

Hepatitis', Number 512 of the Technical Report Series, set the scene more widely and reflected an international understanding of the position.<sup>42</sup> The Introduction to the report indicated that the focus for the group was on viral Hepatitis A, epidemic or infectious hepatitis, and viral Hepatitis B, serum hepatitis. In comparison with the group's earlier reports, in 1953 and 1964, it was stated:

[B]ecause of the discovery of the Australia antigen in 1961<sup>43</sup> and its subsequent recognition as a specific marker of infection with the agent of viral hepatitis B, there has been great progress in the understanding of the clinical, epidemiological and immunological behaviour of this form of the disease. Relatively speaking there has been much less progress in the understanding of viral hepatitis A but there have been some advances ....<sup>44</sup>

**14.32** The report noted the change in terminology, from reference to 'Australia' as a descriptive term in describing the antigen and antibody, to the abbreviations 'HB Ag', and 'HB Ab', explaining that:

The terminology of the actual disease is more difficult. The general term viral hepatitis refers, by common usage, to hepatitis caused by two presumptive viruses, although it is recognised that other viruses may also be implicated.

It is proposed that the common forms of viral hepatitis be subdivided principally on epidemiological grounds, taking into consideration the presence of hepatitis B antigen, into:

Viral hepatitis type A,

and

Viral hepatitis type B.

There is substantial historical, epidemiological, and experimental evidence to suggest that these two types of hepatitis are caused by antigenically distinct agents. It is appreciated that it is not possible to allocate every patient with hepatitis to one of these two groups and that viral hepatitis infections exist that are due to other agents, only some of which have been recognised. This is a problem frequently confronting epidemiologists, clinicians, and pathologists that will only be resolved when the different etiological agents of hepatitis have been identified.<sup>45</sup>

**14.33** The clear inference from this discussion is that, while there were other aetiological agents, it was understood that the common forms of hepatitis were caused by what was called 'viral hepatitis type A' and HBV, although the Hepatitis A virus was not isolated until 1973. The characterisation of the most common forms of hepatitis as comprising (only) two aetiological groups was soon to be undermined.

<sup>42</sup> 'Viral Hepatitis: Report of a WHO Scientific Group', *World Health Organization Technical Report Series*, No. 512, 1973 [SGH.002.9746]

<sup>43</sup> 1961 is the date noted, but accurate dates for 'discovery' range from 1965 to 1967. See the quotation from Dr Cash at paragraph 14.56, below.

<sup>44</sup> 'Viral Hepatitis: Report of a WHO Scientific Group', *World Health Organization Technical Report Series*, No. 512, 1973 [SGH.002.9746] at 9750

<sup>45</sup> *Ibid* [SGH.002.9746] at 9751–9752

**14.34** The discovery of the Hepatitis B surface antigen, HBsAg, and demonstration of its persistence, resulted in the re-examination of theories and to the conclusion that HBV had a worldwide distribution similar to that previously attributed only to Type A. The report noted that there was developing understanding that not all cases of post-transfusion hepatitis were caused by HBV infection. It continued:

The proportion due to hepatitis B or other undesigned agents probably varies with the circumstances. However, as more hepatitis B carriers are eliminated from serving as blood donors, the proportion of cases due to other types of hepatitis will increase.<sup>46</sup>

**14.35** The report also commented:

The present widely employed techniques for detecting hepatitis B antigen in blood are thought to be capable of preventing approximately 30% of cases of post-transfusion hepatitis .... Cases not due to virus B are thought to be due to a variety of causes, including Hepatitis A virus, cytomegalovirus, and other, as yet unidentified agents.<sup>47</sup>

**14.36** These comments were an early and explicit recognition that there might indeed be other viruses, in addition to HBV, responsible for post-transfusion hepatitis.

**14.37** At the same time as the understanding of the serology and epidemiology of HBV infection was developing, the use of needle biopsy of the liver was becoming much more routine. Hence, for the first time, attempts could be made to correlate serological, biochemical and clinical features of a disease, Hepatitis B, with pathological features seen in the liver.

**14.38** The report defined a 'carrier state' of Hepatitis B, which might be associated with liver damage, as a persistent state in individuals in whom the antigen had been detected repeatedly for more than three months. A proportion of carriers had been found to have liver abnormalities ranging in severity from minor changes in the nucleus of the cell to severe hepatitis and cirrhosis:

Two forms of the chronic disease can be distinguished, persistent and aggressive. Clinically, chronic persistent hepatitis is a mild, benign disease, while chronic aggressive hepatitis tends to conform to the clinical syndrome of chronic active hepatitis, in which liver cell dysfunction is often severe and the prognosis is poor. However, considerable overlap exists between the clinical categories and their pathological counterparts. Aggressive changes may be seen in the course of uncomplicated acute viral hepatitis, but the prognosis in these cases is usually excellent.

Chronic persistent hepatitis is characterized ... by preserved lobular architecture, portal inflammatory infiltration, and slight or no fibrosis. It is not always preceded by a recognizable acute illness, and malaise, hepatomegaly and minor abnormalities of liver function are the clinical features. There is no progression to cirrhosis and the prognosis is good.<sup>48</sup>

---

<sup>46</sup> Ibid [SGH.002.9746] at 9754

<sup>47</sup> Ibid [SGH.002.9746] at 9762

<sup>48</sup> Ibid [SGH.002.9746] at 9757

**14.39** Discussing prevalence among blood donors, the report stated:

Great variations in the prevalence of hepatitis B antigen in apparently healthy blood donors have been found in different parts of the world. Prevalence also varies with such factors as the socioeconomic status and sex of the donor, whether he is a volunteer or paid, and whether he lives privately or in an institution. Antigen has been detected most frequently in males in the younger age-groups.<sup>49</sup>

**14.40** Further, the picture was changing at that stage:

During the past decade marked shifts in the age- and sex-specific rates for hepatitis have been observed in the USA and some European countries. These changes were subsequently found to be due to an increase in the number of Hepatitis B infections, particularly among males within the 15-29-year age group. The infections were not related to blood transfusion or other medical procedures. These features, together with the loss of seasonal peaks and the increasingly large proportion of urban cases suggested a likely association with the illicit use of drugs. It is quite possible that in addition to the increased risk of parenteral transmission, the mode of life of drug abusers may increase the level of non-parenteral transmission.<sup>50</sup>

**14.41** In addition to discussion of the epidemiology of hepatitis, the paper commented on changing perceptions of the relevance of a history of jaundice. Limited surveys had shown that the prevalence of Hepatitis B antigen was no higher amongst blood donors with a past history of jaundice than in those without such a history:

Studies of Hepatitis B infection among volunteers and those naturally infected with the virus suggest that a greater proportion of individuals who have had a mild or inapparent infection become chronic carriers of the antigen than those who have had a more severe illness. For this reason exclusion from blood donation of individuals with a clinical history of hepatitis B infection, but who do not have detectable antigen, may not materially reduce the frequency of hepatitis among the recipients of blood.<sup>51</sup>

**14.42** Dr McClelland commented that the 'more sensitive techniques' referred to in the report were actually 'very insensitive' and failed to detect many cases of Hepatitis B. In addition, while noting that there might be 'as yet other unidentified agents', the paper did not develop the risk that one or more might be responsible for significant transmission of infection. Dr McClelland said that the paragraph 'slightly confounded' the extent to which the techniques missed cases of Hepatitis B and their inability to detect non-B cases.<sup>52</sup> This was, nevertheless, an important juncture. The report was authoritative. It drew attention to the existence of a 'carrier state' and associated chronic liver disease, at least for HBV, which was not necessarily associated with a history of clinical jaundice. It provided a remarkable and, in many ways, prescient summary. It was the beginning of a move away from the exclusion of donors with a relatively distant history of hepatitis.<sup>53</sup> By 1973, therefore, to some extent at least, the idea that most post-transfusion hepatitis was attributable to HBV was already beginning to be superseded.

<sup>49</sup> Ibid [SGH.002.9746] at 9761

<sup>50</sup> Ibid [SGH.002.9746] at 9755

<sup>51</sup> Ibid [SGH.002.9746] at 9761

<sup>52</sup> Day 9, page 108

<sup>53</sup> Day 9, page 106

## The Advisory Group on Testing for the Presence of Hepatitis B Surface Antigen: Second Report

**14.43** The WHO 1973 report was cited in an article on Hepatitis B in hospitals, published in 1974 by Dr Wallace and others.<sup>54</sup> The article quoted the suggestion that individuals with a history of overt hepatitis may not have a high incidence of HBsAg and commented that Dr Wallace had recently published evidence<sup>55</sup> supporting that contention. It was to have a more direct impact on the second report of the Advisory Group on Testing for the Presence of Hepatitis B Surface Antigen. The Group was reconvened on 6 December 1973 and reported in September 1975.<sup>56</sup> By then there had been a considerable advance in knowledge, including a second WHO technical paper, number 570, published in 1975.<sup>57</sup>

**14.44** Membership of the Advisory Group in 1975 comprised, among others, the individuals already mentioned in paragraph 14.28 as members of the original 1970 group. By that stage, the Australia (hepatitis-associated) antigen had become universally known as the Hepatitis B surface antigen. The second Advisory Group report discussed current knowledge of the antigen, HBsAg, its homologous antibody, anti-HBs, and the Hepatitis B core antigen-antibody system which was by then becoming recognised. The report stated:

The association between the presence of HBsAg in donor blood and the occurrence of HBsAg positive hepatitis in the recipients after an incubation period of 40-180 days is established. Blood and blood products can also transmit other forms of hepatitis which do not appear to be associated with the presence of HBsAg.<sup>58</sup>

**14.45** This second topic was not developed. It was thought likely that exclusion of HBsAg-positive donors would diminish the number of cases of Hepatitis B transmitted in blood and blood products, as it had in the USA.<sup>59</sup> It was also thought, on the basis of published reports, that the incidence of Hepatitis B in recipients of antibody-positive blood was no greater than that of recipients of blood in which neither HBsAg nor anti-HBs was demonstrable. The recommendations were amended to confirm the exclusion from clinical use of blood found to be HBsAg-positive but to recommend that donors whose blood contained anti-HBs might be retained on the panel and their blood used clinically.

**14.46** By the date of the second report, it was understood that Hepatitis B antibodies did not necessarily signal recovery from infection. The available evidence suggested that core antibodies might not be protective and that they were present in persistent carriers of HBsAg.<sup>60</sup> The association between HBsAg in donor blood and the occurrence of HBsAg-positive hepatitis in recipients was established.<sup>61</sup>

<sup>54</sup> Payne, Barr and Wallace, 'Hepatitis B antigen (HBsAg) and its antibody (HBsAb) in hospital patients', *Journal of Clinical Pathology*, 1974; 27:15-129 [PEN.002.0830]

<sup>55</sup> Wallace et al, 'Total Screening of Blood Donations for Australia (Hepatitis Associated) Antigen and its Antibody', *British Medical Journal*, 11 March 1972 [SGH.002.9831]

<sup>56</sup> Second Report of the Advisory Group on Testing for the Presence of Hepatitis B Surface Antigen and its Antibody [SGH.003.0079]

<sup>57</sup> 'Viral Hepatitis: Report of a WHO Meeting' *World Health Organization Technical Report Series*, No.570, 1973 [LIT.001.3272]

<sup>58</sup> Second Report of the Advisory Group on Testing for the Presence of Hepatitis B Surface Antigen and its Antibody [SGH.003.0079] at 0083

<sup>59</sup> *Ibid* [SGH.003.0079] at 0084

<sup>60</sup> *Ibid* [SGH.003.0079] at 0083

<sup>61</sup> *Ibid* [SGH.003.0079] at 0083

**14.47** The paragraphs from the WHO 1973 report are substantially paraphrased in the observations that:

Published reports show that the incidence of hepatitis B in recipients of antibody positive [blood] is no greater than that of recipients of blood in which neither HBsAg nor anti-HBs is demonstrable. Therefore... we now recommend that donors whose blood contains anti-HBs may be retained on the panel and their donations used clinically.

....

We have given much thought to the problem of donors with a history of jaundice but in whom neither HBsAg nor anti-HBs is detected. We are not aware of any evidence that a relationship exists between a history of jaundice in donors and the occurrence of icteric or anicteric hepatitis in recipients of their blood. We therefore recommend that the practice of permanently excluding from the panel donors with a history of jaundice should be discontinued provided that HBsAg is not detected by reversed passive haemagglutination or a test of at least equal sensitivity... and that the donor has not suffered from hepatitis or jaundice during the previous twelve months.<sup>62</sup>

**14.48** Individuals positive for HBsAg were to continue to be excluded from blood donation.

### Scotland

#### *The Joint Symposium of the Royal College of Physicians of Edinburgh and the Royal Society of Edinburgh*

**14.49** Scottish experts were represented on the panels reporting nationally and internationally, discussed above. In addition, there was more local study. A joint symposium was held in 1972 by the Royal College of Physicians of Edinburgh and the Royal Society of Edinburgh. The report of the joint symposium provides a base line for assessing Scottish views on many aspects of the topics under review at the start of the reference period.<sup>63</sup> The symposium was largely concerned with blood transfusion and therefore reflected a particular interest within the medical community related to the use of blood and blood products. The discussion also had wider relevance, however.

**14.50** Dr Robert Cumming, Regional Director of the Edinburgh and South East Scotland Blood Transfusion Service at the time, gave an introductory talk.<sup>64</sup> He discussed the prevention of adverse effects of transfusion, highlighting improvements in the equipment for handling blood, processing procedures and changes in practice aimed at minimising the traditional risks of incompatibility and bacterial contamination. However, diminishing risks of incompatibility had been offset by an increase in immune-system based risks arising from repetitive transfusion.<sup>65</sup> He referred to, but did not discuss, the detection of diseases transmissible by blood. He emphasised the need for greater knowledge of the dangers inherent in the intensive use of 'potent therapeutic agents of biological origin'.<sup>66</sup>

<sup>62</sup> Ibid [SGH.003.0079] at 0084–0085

<sup>63</sup> *Proceedings of the Royal Society of Edinburgh Section B (Biology) 1972*; vol 71 Supplement [PEN.002.0407]

<sup>64</sup> Ibid [PEN.002.0407] at 0408

<sup>65</sup> This phenomenon was to re-emerge in the 'antigen overload' theory, developed in the early 1980s as an alternative to the 'infective agent' theory of AIDS. See Chapter 9, *Knowledge of the Geographical Spread and Prevalence of HIV/AIDS 1*.

<sup>66</sup> *Proceedings of the Royal Society of Edinburgh Section B (Biology) 1972*; vol 71 Supplement [PEN.002.0407] at 0410.

**14.51** Professor Alexander Douglas, Regius Professor of Medicine at Aberdeen University, discussed the use of plasma coagulation factors. His comments on possible adverse effects of therapy were brief:

Side-effects to factor VIII include febrile reactions, the transmission of serum hepatitis and the induction of antibodies to factor VIII .... Using human factor VIII preparations the risk of hepatitis is proportional to the number of donations involved in the material given. In the production, for example, of cryoprecipitate the blood should be screened for Australia antigen.<sup>67</sup>

**14.52** On the other hand, while plasma therapy for Haemophilia B patients was associated with non-specific reactions, in Scotland prothrombin therapy (for Haemophilia B) using concentrated materials was thought to be problem-free.<sup>68</sup>

**14.53** These contributions by Dr Cumming and Professor Douglas reflected similar interests to those investigated by Dr Biggs. Dr Wallace promoted the advantages of pasteurised albumin product (Plasma Protein Solution) as the product of choice thanks to the heating process involved in its manufacture.<sup>69</sup> It could be presented in stable liquid form as Stable Plasma Protein Solution (SPPS), pasteurised at 60°C for 10 hours, and in that form it was said to be free from the risk of transmitting viral diseases, thus eliminating the hazard of hepatitis. He noted that in general surgery there was progress towards the use of blood components in preference to whole blood. A policy of total fractionation (the division of blood in to its component parts) was advocated as the ideal towards which transfusion services should aim.

**14.54** However, it was in the presentation of Dr John Cash,<sup>70</sup> then Deputy Director of the Edinburgh and South East Scotland Blood Transfusion Service, that the risk of hepatitis transmission was most clearly identified.

**14.55** By way of introduction, he wrote:

Although the medical profession has long recognised the concept that there are no therapeutic roses without thorns, there is no doubt that the dangers of blood transfusion, in all its forms, have yet to be fully defined. However, in the ardour of therapeutic endeavour, we are frequently guilty of forgetting those hazards which have already been well documented ....

Recent data published by the Registrar General (1971) would suggest that the numbers of deaths attributable to blood transfusion are comparable to those complicating general anaesthesia. Almost 50 per cent of the post-transfusion deaths were due to hepatitis. While not intending to underemphasise the importance of incompatible red cell, white cell and platelet transfusions, allergic reactions to plasma proteins, systemic effects of bacterial pyrogens and heavily contaminated blood and blood products, air embolism, citrate intoxication and haemosiderosis, the magnitude of the hepatitis problem and the recent explosion of highly productive research in this area is so great that it

<sup>67</sup> Douglas, 'Plasma Coagulation Factors', *Proceedings of the Royal Society of Edinburgh 1972*; Section B (Biology), vol 71 Supplement [PEN.002.0575] at 0578

<sup>68</sup> *Ibid* [PEN.002.0575] at 0579

<sup>69</sup> Wallace, 'New Approaches to the Supply of Blood and Plasma', *Proceedings of the Royal Society of Edinburgh 1972*; Section B (Biology) vol 71 Supplement [PEN.018.1026] at 1029

<sup>70</sup> Cash, 'Principles of Effective and Safe Transfusion', *Proceedings of the Royal Society of Edinburgh 1972*; Section B (Biology), vol 71 Supplement [PEN.002.0559]



seems appropriate on this occasion to consider this particular feature of safety in some detail.<sup>71</sup>

**14.56** Apart from demonstrating considerable literary panache, Dr Cash's assessment of the problem of hepatitis, as then understood, placed it squarely before the medical profession in Scotland. His discussion is, therefore, of particular importance in defining the scope of general knowledge of the risk at this time. He continued:

In 1965, Blumberg *et al* (1965) reported that sera from two multi-transfused haemophiliac patients formed precipitin lines in the micro-Ouchterlony gel diffusion test when tested against serum from an Australian aborigine. The substance in this serum did not appear to be the usual lipoprotein and was tentatively labelled 'Australia antigen'. Subsequent studies revealed that the presence of Australia antigen was closely associated with viral hepatitis (Blumberg *et al*, 1967; Blumberg *et al*, 1968; Prince 1968), and that virus-like particles could be isolated from antigen-positive sera (Bayer *et al*. 1968). Confirmation of these findings came from all over the world along with the observation by Okochi and Murakami (1968) which clearly indicated that hepatitis frequently followed the transfusion of antigen-positive blood.

These primary observations heralded an explosive research effort in which clinicians, biochemists, geneticists, microbiologists and immunohaematologists have all made important contributions.<sup>72</sup>

**14.57** After citing a range of publications on specific issues, which emphasised the familiarity of the NHS in Scotland at this early stage with world-wide research, Dr Cash proceeded:

From the early beginnings of this work, debate has gone on as to whether Australia antigen is responsible for serum hepatitis alone or both infectious hepatitis and the serum form of this disease. Recent work has shown that the classical long incubation (serum) form, while more commonly acquired by the parenteral route, can also be transmitted orally. This suggests that Australia antigen is responsible for the classical serum hepatitis and sporadic cases of infectious hepatitis and that other agents are casually [*sic* – causally] related to epidemic infectious hepatitis (Simon 1971). However, there seems little doubt that the agents responsible for the epidemic variety can be transmitted parenterally and, therefore, by means of blood transfusion (Koff and Isselbacher 1968).

In 1968, Okochi and Murakami first suggested a possible relationship between hepatitis and the administration of Australia antigen-positive blood. This observation was confirmed by Gocke and Kavey (1969) and both groups have confirmed and extended their original findings (Gocke *et al*. 1970; Okochi *et al*. 1970).<sup>73</sup>

---

<sup>71</sup> Ibid [PEN.002.0559] at 0563

<sup>72</sup> Ibid [PEN.002.0559] at 0563

<sup>73</sup> Ibid [PEN.002.0559] at 0564

**14.58** This review was written before Feinstone and Prince's work enabled the provision of markers for HAV and before the publication of evidence for one or more NANB Hepatitis viruses that followed.<sup>74</sup> It appears that, while the presentation contained a number of assertions not ultimately established, the medical profession in Scotland was made aware that (i) there was a causal relationship between transfusion and hepatitis infection; (ii) the Australia antigen/HBsAg was not solely responsible for the transmission of hepatitis infection; and (iii) post-transfusion hepatitis was fatal in some cases. In common with other parts of the UK, some trends in research that were to mark step changes in understanding of viral hepatitis in the USA were not taken into account.<sup>75</sup> It nevertheless appears to be clear that, at the beginning of the reference period, the NHS in Scotland was aware of international research on Hepatitis B and, indeed, was participating in it.

### *Local research*

**14.59** Scottish scientists had certainly played a part in developing knowledge of viral hepatitis, however. By 1970, the Blood Transfusion Centres in Edinburgh and Glasgow had started research on hepatitis.<sup>76</sup> In the case of the Glasgow study, this was a direct response to the 1970 WHO Bulletin recommending the detection and exclusion of blood donors carrying Australia antigen.<sup>77</sup> The study distinguished donors tested for the first time and those returning who had previously tested negative. The reported incidence of 0.115% for the general donor population on first testing was in agreement with the general level of about 0.1% for unpaid donors in the USA and in Western Europe. The Glasgow researchers recognised that their test was relatively insensitive and commented that it was 'too early to assess the full significance of total screening ...'. A contemporaneous study on behalf of the National Blood Transfusion Service (N BTS) for England and Wales found that the incidence of Hepatitis B antigen in donations from new general public and factory donors in 1973 was 1:1107 (0.09%).<sup>78</sup> Routine blood screening for what became known as HBsAg and its antibody, Anti-HBs, was instituted in 1974.

**14.60** In Edinburgh, systematic study of bleeding patterns in haemophilia patients began in the 1960s and 1970s and progressed to the study of risks of virus transmission, initially focused on HBV.<sup>79</sup> These studies continued into the 1980s.<sup>80</sup> They were initiated by Dr Howard Davies of the Edinburgh Haemophilia Centre and Dr John Peutherer, a virologist; Professor Christopher Ludlam became involved when he succeeded Dr Davies.<sup>81</sup> During the early 1970s it was found that, despite screening, about 10% of susceptible patients became infected each year with HBV but that only a tiny proportion of these became infective HBV carriers.<sup>82</sup> Until the end of the 1970s, screening tests for HBsAg were not sensitive enough to detect all blood donations infected with HBV.

<sup>74</sup> Feinstone et al, 'Hepatitis A: Detection by Immune Electron Microscopy of a Viruslike Antigen Associated with Acute Illness', *Science*, 1973; 182:1026 [PEN.010.0110]

<sup>75</sup> See paragraph 14.63 *et seq* below

<sup>76</sup> Dr McClelland – Day 9, pages 20–22

<sup>77</sup> Wallace et al, 'Total Screening of Blood Donations for Australia (Hepatitis Associated) Antigen and its Antibody', *British Medical Journal*, 11 March 1972 [SGH.002.9831]

<sup>78</sup> 'Frequency of HBAg and Anti-HBAg Exported by RTCs New General Public and Frequency Donors and in Donors in Armed Forces and in Prison Borstals and Similar Institutions' [SGH.001.7095]

<sup>79</sup> Edinburgh Haemophilia and Thrombosis Centre – Appendix to Professor Ludlam's Witness Statement [PEN.012.0351]; Burrell et al, 'Antibody to hepatitis B surface antigen in haemophiliacs and their household contacts', *Journal of Clinical Pathology*, 1974; 27:323–325; Burrell, 'Antibody to hepatitis B surface antigen in haemophiliacs on long term therapy with Scottish Factor VIII', *Journal of Clinical Pathology*, 1978; 31:309–12. Abstract at [SNB.008.2073]

<sup>80</sup> Edinburgh Haemophilia and Thrombosis Centre – Appendix to Professor Ludlam's Witness Statement [PEN.012.0351]; Stirling et al, 'Liver function in Edinburgh haemophiliacs: a five year follow-up', *Journal of Clinical Pathology*, 1981; 34:17–20 [LIT.001.0748]

<sup>81</sup> Professor Ludlam Day 44, page 7; Edinburgh Haemophilia and Thrombosis Centre – Appendix to Professor Ludlam's Witness Statement [PEN.012.0351]

<sup>82</sup> Day 44, page 6; Stirling et al, 'Incidence of Infection with Hepatitis B virus in 56 patients with haemophilia A 1971 – 79', *Journal of Clinical Pathology*, 1983; 36:577–80. Abstract at [SNB.008.2056]

**14.61** The incidence of anti-HBs in haemophilia patients suggested that a significant proportion had become infected by HBV. Dr Biggs' 1974 paper, discussed above (paragraph 14.19), recognised that factor concentrates generally were associated with a risk of transmitting hepatitis.<sup>83</sup> Others were more definite in their conclusions. Writing in 1974, Dr Donald Buchholz said that, 'hepatitis reigns supreme as the major cause of transfusion-associated disease'.<sup>84</sup>

**14.62** Dr Biggs' 1974 review also noted that post-transfusion hepatitis was caused by several viruses which might occur in donor plasma and hence in the various protein fractions used to treat haemophilia and Christmas disease. The ability to identify both the Hepatitis B antigen and antibody enabled scientists to estimate the proportion of cases of post-transfusion hepatitis associated with Hepatitis B, within the limits of sensitivity and specificity of the tests available from time to time.

### Research in the United States of America

**14.63** It is appropriate at this point to take note of research that had not entered into the UK reports already discussed. Research projects in the USA in the early to mid-1970s, led by Alter, Aach, Knodell and Seeff, led to a conclusion by 1974–75 that Hepatitis B, the main focus of attention in the UK, was responsible for only a low proportion of transfusion-associated hepatitis. This research is discussed in more detail in the next chapter (Chapter 15, *Knowledge of Viral Hepatitis 2*).

**14.64** The Hepatitis A virus, responsible for most enteric hepatitis was identified in 1973 by Feinstone and others.<sup>85</sup> At that time, however, there were still no blood tests to detect either its presence in the blood or the fact that an individual had been exposed to the virus but subsequently cleared it. That development would come in 1974–75. At the beginning of the reference period, in 1974, scientists were approaching a critical change in understanding that would lead to the identification of forms of hepatitis that were neither form A nor form B, but that stage had not yet been reached.

### Towards non-A, non-B Hepatitis/Hepatitis C

**14.65** Following the opinion that Hepatitis B accounted for a relatively small proportion of cases of post-transfusion hepatitis, doubts grew on epidemiological grounds over whether Hepatitis A could account for the majority of cases of post-transfusion hepatitis as was implied in earlier discussion.<sup>86</sup> In 1974, Alfred Prince and others suggested that a substantial proportion of post-transfusion hepatitis cases were caused neither by the Hepatitis A virus nor by the Hepatitis B virus and they suggested the existence of an additional hepatitis virus or viruses which would require 'identification of a hepatitis virus(es) type C'.<sup>87</sup> It was to be long before the term 'Hepatitis C' entered the vocabulary but Dr Prince and colleagues had clearly noted the need for differentially identified types of hepatitis virus in their original work.

<sup>83</sup> Biggs, 'Jaundice and antibodies directed against factor VIII and IX in patients treated for haemophilia or Christmas disease in the United Kingdom', *British Journal of Haematology*, 1974; 26: 313–329 [LIT.001.0099]

<sup>84</sup> Buchholz, 'Blood Transfusion: Merits of Component Therapy', *The Journal of Pediatrics*, 1974; 84: 165 [LIT.001.0141] at 0145

<sup>85</sup> Feinstone et al, 'Hepatitis A: Detection by Immune Electron Microscopy of a Viruslike Antigen Associated with Acute Illness', *Science*, 1973; 182:1026 [PEN.010.0110]

<sup>86</sup> Preliminary Report, paragraph 6.28

<sup>87</sup> Prince et al, 'Long-Incubation Post-Transfusion Hepatitis Without Serological Evidence of Exposure to Hepatitis-B Virus', *The Lancet*, 3 August 1974 [LIT.001.0363]

**14.66** The identification of the specific Hepatitis A virus by Stephen Feinstone's team provided a basis for proof of Prince's hypothesis.<sup>88</sup> Serological analysis in 1975 of stored sera from the earlier studies revealed that none of the cases of transfusion-associated hepatitis could be attributed to HAV.

**14.67** Following this work, the expression 'non A, non B hepatitis' (frequently abbreviated to 'NANBH' or 'NANB Hepatitis') was coined as a collective term for hepatitis from which, at that time, Hepatitis A and Hepatitis B, as well as CMV and Epstein-Barr virus (both of which can cause liver inflammation), had been excluded.<sup>89</sup> In due course, and much later, further research led to the identification of the Hepatitis C virus as the principal cause of the condition described.<sup>90</sup> As at 1974, knowledge of HAV, HBV and NANB Hepatitis infection was not developed and was not widely disseminated. Awareness of the risk of viral infection from blood and blood products was relatively unrefined and unsophisticated.

**14.68** There is a serious risk, in citing the work of researchers such as Feinstone and Prince, of giving the impression that their ground-breaking research immediately entered the common currency of general medical knowledge and informed clinical practice. That would be as unfair as it would be unrealistic. The view that there were only two relevant hepatitis viruses had support in the UK in the 5th edition of Professor Sherlock's book, *Diseases of the Liver and Biliary System*, published in 1975. The book can be taken to provide an authoritative description of the state of knowledge available to the medical profession in the UK generally in 1974–75.<sup>91</sup> Hepatitis A was not identified as a separate cause of concern; despite Professor Sherlock's observation that the disease might be transmitted parenterally, it was not thought to be associated with transfusion.<sup>92</sup> Hepatitis B was described as a 'long incubation disease'. It was said to be spread classically by therapeutic administration of blood and blood products but could also be spread orally and sexual spread was considered likely.<sup>93</sup> The 5th edition contained no reference to the NANB Hepatitis virus.

### ***Diseases of the Liver and Biliary System (1975)***

**14.69** Professor Sherlock's description of the clinical course of hepatitis included the following comments:

Hepatic involvement, particularly to the extent of jaundice, is an *infrequent* complication of rather a common virus infection. The picture varies widely, ranging from slight malaise to a severe and fatal disease culminating in hepatic coma ....

In general, type A and type B hepatitis run the same clinical course. Type B tends to be more severe and may be associated with a serum sickness-like syndrome. The relationship of type B to chronic liver disease has been established ....

<sup>88</sup> Though published first, Feinstone's work is said to have been later in date (see, for example, *Viral Hepatitis: Scientific Basis and Clinical Management* ed Zuckerman and Thomas: 1993 page 470) but this must be questioned in view of the citation in the Prince paper of one paper read at the 6th symposium of the American Red Cross in May 1974. See the Preliminary Report, paragraph 6.29.

<sup>89</sup> See, for example, Alter et al, 'Clinical and serological analysis of transfusion-associated hepatitis', *The Lancet*, 1975; 2: 838–841 [LIT.001.3926] where Cytomegalovirus (CMV) and Epstein-Barr Virus (EBV) were excluded as causal agents of NANB Hepatitis.

<sup>90</sup> Identified by the Chiron Corporation in spring 1988 and announced on 10 May 1988. See Chapter 16, *Knowledge of Viral Hepatitis 3 – 1986 Onwards*. In the mid 1970s, the position was not clear. A letter to *The Lancet* of 16 November 1974 by Fiala and others of California and two Abbott workers, Overby and Ling, in response to Prince, suggested that more work was required on the possible role of cytomegalovirus in hepatitis. Fiala et al, 'Cytomegalovirus in non-B post-transfusion hepatitis', *The Lancet*, 16 November 1974 [LIT.001.3930]

<sup>91</sup> Later editions remained authoritative while Professor Sherlock was general editor.

<sup>92</sup> Sherlock, S. *Diseases of the Liver and Biliary System*, 5th ed. 1975, Blackwell, Oxford, page 305

<sup>93</sup> *Ibid* page 306

The severity is very variable. The mildest attack is without symptoms and marked only by a rise in serum transaminase levels. If it is of type B there is transient HBAg positivity. Alternatively, the patient may still be anicteric but suffer gastro-intestinal and influenzal-like symptoms ....

The usual icteric attack in the adult is marked by a prodromal period usually about 3 or 4 days but even up to 2 or 3 weeks.

....

The prodromal period is followed by darkening of the urine and lightening of the faeces. This heralds the development of jaundice and symptoms decrease .... Appetite returns and abdominal discomfort and vomiting cease. Pruritus [itching] may appear transiently for a few days.

....

The adult loses about 10 lb weight. A few vascular spiders may appear transiently.

After an icteric period of about 1–4 weeks the adult patient makes an uninterrupted recovery .... After apparent recovery lassitude and fatigue persist for some weeks. Clinical and bio-chemical recovery is usual within 6 months of onset.<sup>94</sup>

**14.70** Professor Sherlock noted the possibility of prolonged jaundice, also followed by complete recovery, and commented on 'post-hepatitis syndrome' as a condition leaving the patient feeling 'below par' for weeks or months.<sup>95</sup> She commented that chronic persistent hepatitis, chronic active hepatitis, post-hepatitic scarring and cirrhosis could all develop.<sup>96</sup> Of these, the author described chronic persistent hepatitis as benign. She continued:

*Chronic active hepatitis* often proceeds to or is associated with cirrhosis. Chronic active hepatitis also has many causes. The mechanism by which hepato-cellular necrosis proceeds in any individual to chronic active hepatitis and finally to the irreversible stage of cirrhosis is in most instances unknown. Knowledge of the factors determining this course would give the key to the development of cirrhosis.<sup>97</sup>

**14.71** For comparison, the observations of Prince and others in their 1974 paper are noteworthy. The authors suggested, albeit tentatively, that there were long-term risks associated with Hepatitis B and non-B viruses:

Long-term complications of acute hepatitis-B infection, such as chronic hepatitis, cirrhosis, and hepatoma, have been reported to follow mild anicteric infections more frequently than severe icteric cases; consideration must thus also be given to the possibility that non-B hepatitis may play a role in the aetiology of some forms of chronic liver disease.<sup>98</sup>

<sup>94</sup> Ibid page 321-322 (emphasis in original)

<sup>95</sup> Ibid page 324

<sup>96</sup> Ibid page 333

<sup>97</sup> Ibid page 390

<sup>98</sup> Prince et al, 'Long-Incubation Post-Transfusion Hepatitis Without Serological Evidence of Exposure to Hepatitis-B Virus', *The Lancet*, 3 August 1974 [LIT.001.0363] at 0368

**14.72** Notwithstanding these differences, Professor Sherlock's analysis would have been understood by most, if not all, clinicians in the UK to be an authoritative exposition of knowledge of viral hepatitis at the beginning of the reference period.

### **Knowledge of blood-borne hepatitis at the outset of the reference period:**

#### **Summary**

**14.73** Knowledge of blood-borne hepatitis was rudimentary in the early 1970s. The results of reported studies were just beginning to make an impact on thinking among scientists at the leading edge of research. Among clinicians generally, Professor Sherlock's views would have been definitive of the state of knowledge. In other respects, there was uncertainty:

- The work of Blumberg and others initiated a new era of research but knowledge of hepatitis and the forms recognised at the time remained incomplete.
- Routine (fairly sensitive) testing for HBsAg in all donor blood meant that from this time new cases of post-blood transfusion hepatitis caused by HBV would become rare in the UK, although that would become clear only later.
- Early surveys with relatively insensitive tests suggested that the prevalence of HBsAg positivity was about 1:1000 of the donor population in Scotland and England.
- The fact that at least 20% of haemophilia patients treated with clotting factor had markers of past infection with HBV was recognised.
- Serum markers of HBV in routine use were still confined to HBsAg – correctly thought to be an indicator of potential infectivity – and anti-HBs – correctly thought to indicate past infection with HBV and to indicate immunity from further infection as well as lack of infectivity.
- Understanding of the natural history of HBV infection, and particularly of the groups at risk of developing chronic HBV infection, was still poorly developed.
- Factor therapy had become more and more popular with haemophilia patients and their doctors<sup>99</sup> and there was a consequent significant increase in demand on the supply of blood from which these factors were extracted.<sup>100</sup>

---

<sup>99</sup> In 1974 Peter Jones, a Haemophilia specialist, published *Living with Haemophilia* (Lancaster: Medical and Technical Publishing Co. Ltd). This was written as an introductory guide to haemophilia for haemophilia patients and their families, and reflected the contemporaneous views of haemophilia groups.

<sup>100</sup> See Spencely & Cash, 'Factor VIII replacement in the treatment of haemophilia A – a simple illustration of a need-supply-demand spiral', *British Journal of Preventative Medicine*, 1974; 28: 71 [LIT.001.0149]

**14.74** Matters that were just beginning to be reported yet had a significant impact on knowledge in the UK were:

- Recognition that HBV accounted for only a relatively small proportion of cases of post-transfusion hepatitis was beginning to be reported.
- HAV had been discounted as a cause of most post-transfusion hepatitis infections following Feinstone's characterisation of the virus and the development of serological tests for it.
- The term NANB Hepatitis was coined for hepatitis from which, at that time, HAV and HBV, CMV and Epstein-Barr virus had been excluded as causative agents.
- Prince and colleagues had already reported that long term complications of acute Hepatitis B infection, such as chronic hepatitis, cirrhosis and hepatoma, appeared to have followed mild anicteric infections more frequently than severe icteric cases.
- However, the prevalence of what would become NANB Hepatitis was not known, and there was no understanding of its natural history or of its epidemiology.





## CHAPTER 15

### KNOWLEDGE OF VIRAL HEPATITIS 2 – 1975 TO 1985

#### Introduction

**15.1** This chapter will trace developments in the understanding of viral hepatitis from 1975 to around 1985. As noted at the end of the last chapter, at the end of 1974 expert views published widely in the UK on the aetiology and natural history of viral hepatitis did not reflect developing understanding of the disease in the USA. In this period there were continuing differences in the timing of general acceptance of emerging theories. There were also differences between UK and US sources in the definition of the markers of non-A, non-B Hepatitis (NANB Hepatitis) infection. These differences had a material bearing on the perception of the prevalence of infection in the UK and, correspondingly, of the risks potentially associated with transfusion of blood, blood components and blood products.

**15.2** While much of the information from this period is taken from published sources which were available, at least to relevant experts in their particular fields of study, it is apparent that there were also informal exchanges of information among researchers. For example, on 6 January 1975, Dr J Garrott Allen of the Stanford University Medical Centre wrote to Dr William Maycock, Director of the National Blood Transfusion Service (NBTS).<sup>1</sup> The substance of the letter and Dr Allen's wider involvement in the assessment of risk in the UK are discussed later.<sup>2</sup> It is an example of written communication. More frequently, telephone exchanges and discussion at international conferences maintained the dialogue. It would not be correct to assume that UK experts were entirely unaware of what was happening elsewhere, particularly in the USA.

**15.3** However, between the USA and European countries, including the UK, there were differences in response to emerging knowledge at certain stages. In the background, there was probably a lower prevalence of NANB Hepatitis infection in the UK as a whole than in the USA and the perception that this was the case appears clearly to have influenced opinion. It is therefore appropriate to deal with the bodies of research material from the USA separately from other sources, at least to the end of this period.

**15.4** In this chapter, US research dating from the mid-1970s to about 1981 will be described first. By that stage, some firm views had emerged on the prevalence of NANB Hepatitis as understood in the USA. Progress in UK research over approximately the same period, where there was a different view of the diagnostic features of NANB Hepatitis, will be described next. Thereafter, discussion will focus on the second half of the period, 1980–81 to about 1985, but including publications from 1986 which related to the first half of the decade.

---

<sup>1</sup> Dr Allen's letter [SGH.004.6061]

<sup>2</sup> See Chapter 26, *Donor Selection – Higher Risk Donors*, paragraphs 26.73–26.76

## Viral hepatitis mid-1970s to 1981

### *Aetiology and natural history of NANB Hepatitis: research in the United States of America*

**15.5** For present purposes, it is not necessary to trace in any detail the general history of developments in the knowledge and understanding of hepatitis before about 1973–74. One series of studies on post-transfusion hepatitis in open-heart surgery patients at the National Institutes of Health (NIH), initiated in 1965 and led by Dr Harvey Alter, was to play a major part in developing knowledge, however.<sup>3</sup> Together, these studies reflect the views of a group of respected researchers working after Blumberg's seminal work on the Australia antigen,<sup>4</sup> and before the published work of Prince, Feinstone and others on the prevalence of Hepatitis A in post-transfusion hepatitis, discussed below, that led to the conclusion that one or more non-A, non-B hepatitis viruses were implicated in post-transfusion hepatitis. The initial 1965 study demonstrated that there was a high risk of transmission of icteric and anicteric hepatitis (that is, hepatitis with or without clinical jaundice) associated with commercial blood. The second study, begun in 1968, demonstrated that there was a high risk of developing hepatitis from receiving blood contaminated with Hepatitis B surface antigen (HBsAg): half of the patients infected developed icteric hepatitis. By 1970, when the third study began, it had become feasible to fulfil blood requirements solely from volunteer sources and to screen donor blood prospectively for HBsAg. The study examined the effect of the combined exclusion of all commercial and voluntary HBsAg-positive donations. It was concluded that the exclusion of all commercial and volunteer blood donors testing positive for the HBsAg, significantly reduced the rate of transmission of hepatitis.

**15.6** As noted in paragraphs 14.32–14.36 of the last chapter, research projects in the USA up to the mid-1970s led to a conclusion that the Hepatitis B virus (HBV) was responsible for only a small proportion of the residual cases of transfusion-associated hepatitis. Research based on cardiac patient groups continued and by 1975 the conclusion on HBsAg was more broadly and starkly expressed in an article by Stephen Feinstone and others:

The preponderance of hepatitis after blood transfusion is unrelated to the hepatitis B virus.<sup>5</sup>

**15.7** By 1974–75 it was also understood that Hepatitis A was not implicated to any material extent in post-transfusion hepatitis.

### New York University Hospital

**15.8** Opinion had quickly developed to reach that point, however, and it is appropriate to begin the account at a slightly earlier date, with the article by Alfred Prince and others referred to in the last chapter at paragraph 14.65.<sup>6</sup> The reported research project involved 299 patients. They had undergone major surgery (mostly cardiovascular surgery) at New York University Hospital between May 1969 and August 1972 and presented as an intensively-managed group of patients available for research across a broad front.

<sup>3</sup> Alter et al, 'Posttransfusion Hepatitis After Exclusion of Commercial and Hepatitis-B Antigen Positive Donors', *Annals of Internal Medicine*, 1972; 77: 691-699 [PEN.002.0811]

<sup>4</sup> See Chapter 14, *Knowledge of Viral Hepatitis 1*.

<sup>5</sup> Feinstone et al, 'Transfusion-associated hepatitis not due to Viral hepatitis Type A or B', *New England Journal of Medicine* 1975; 767-770 [LIT.001.0137]

<sup>6</sup> Prince et al, 'Long-Incubation Post-Transfusion Hepatitis Without Serological Evidence of Exposure to Hepatitis-B Virus', *The Lancet*, August 3 1974 [LIT.001.0363]

**15.9** Blood sera from the patients were tested for HBsAg or Hepatitis B antibody (anti-HBs) and serum-transaminases<sup>7</sup> were measured. All cases with transaminase abnormalities were reviewed by a panel of clinicians, to exclude cases likely to have causes of liver-function abnormality other than post-transfusion hepatitis. 'Hepatitis' was defined as two or more consecutive elevations of serum-transaminase above the upper limit of normal when tested internally or, if tested by an outside laboratory, 2.5 times the upper limit of normal applied by that laboratory, all within specified time limits. This was an approach typical of US researchers at the time. Follow-up was completed for 204 patients. Hepatitis, as defined, was developed in 51 and jaundice in 21. Of the hepatitis cases, 15 showed exposure to Hepatitis B virus by HBsAg or anti-HBs response. A Hepatitis B response without developing hepatitis, as defined, was shown in 25 more. The conclusion of the article, as summarised, was:

An agent other than hepatitis-B (HB) virus seemed to be the cause of 36 (71%) of 51 cases of post-transfusion hepatitis identified during prospective biweekly serological follow-up of 204 cardiovascular-surgery patients. The sera of the 36 cases showed no evidence of the antigen or antibody response expected to accompany infection by HB virus and to be detectable by the sensitive assays used. Incubation periods and clinical and epidemiological features were inconsistent with Hepatitis A. Cytomegalovirus-associated seroconversion was no more common among the HB-negative cases than among HB-positive cases or among patients who did not develop hepatitis. The data suggest that a large proportion of long-incubation post-transfusion hepatitis is unrelated to Hepatitis B ....<sup>8</sup>

**15.10** The paper sought to demonstrate that the condition described was probably not Hepatitis A or Hepatitis B and inferred that the cause was some other, as-yet unidentified virus. This agent proved to be elusive and defied many wide-ranging efforts to identify it. As noted in paragraph 14.71 of the last chapter, the article also commented on the risk that the condition might be associated with progressive liver disease and long-term complications such as chronic hepatitis, cirrhosis, and hepatoma.

### National Institutes of Health

**15.11** The article by Feinstone and others, published in April 1975 and cited in paragraph 15.6 above, took matters further, and examined 22 patients. The team had continued their work on patients who had received corrective cardiac surgery, covering patients treated at the National Institutes of Health. They postulated that a viral agent, other than the Hepatitis A virus (HAV) or HBV but yet to be identified, was commonly transmitted by blood transfusion and caused hepatitis. The patients in this cohort were selected for study because a diagnosis of hepatitis was well established, serial serum samples were available and HBsAg had not been detected in acute-phase serum samples obtained from them. Hepatitis was defined by transaminases 2.5 times the upper limit of normal within specified time limits and the exclusion of other possible causes for elevated levels of transaminases. The method of identifying Hepatitis A antibody described by Feinstone and others in 1973 was applied.<sup>9</sup>

<sup>7</sup> Proteins synthesised in liver cells, normally present in low levels in the blood, which become elevated when the liver is disordered by virus infection or other disorders of the liver.

<sup>8</sup> Prince et al, 'Long-Incubation Post-Transfusion Hepatitis Without Serological Evidence of Exposure to Hepatitis-B Virus', *The Lancet*, August 3 1974 [LIT.001.0363]

<sup>9</sup> Feinstone et al, 'Hepatitis A: Detection by Immune Electron Microscopy of a Viruslike Antigen Associated with Acute Illness', *Science*, 1973; 182:1026 [PEN.010.0110]

**15.12** Some of the patients had been exposed to the HAV before transfusion. However, nine patients did not have HAV antibody before transfusion and none of them acquired the antibody after their illness. This was said to be strong evidence that their hepatitis was not caused by HAV. The authors also relied on incubation periods (the common ground of distinction between 'infectious' and 'serum' hepatitis, as discussed in the last chapter) and the lack of intra-familial transmission, in support of their conclusions. As noted in the previous chapter at paragraph 14.66, this work provided a basis for proof of Prince's hypothesis.<sup>10</sup>

**15.13** Further research was reported in an article in *The Lancet* of 1 November 1975.<sup>11</sup> Eight of the cases reported by Feinstone and his colleagues in April of that year were subsequently included in a prospective study of post-transfusion hepatitis by Dr Alter and colleagues (including Feinstone). For the purposes of this study a patient was considered to have post-transfusion hepatitis if, other factors being excluded,<sup>12</sup> between 14 and 180 days after transfusion the patient's alanine-aminotransferase level rose to 2.5 times the upper level of normal and if a second sample not less than a week later exceeded two times the normal level. 108 patients were followed and 12 developed hepatitis, as defined. Four of the 12 developed markers for Hepatitis B in the course of acute hepatitis and the remaining eight were classed as cases of non-B Hepatitis. Testing excluded a serological association with the Hepatitis A virus. The article concluded:

The strongest evidence that non-A, non-B hepatitis is a transfusion-related (and, by inference, virus-related) event is the fact that it appears to occur with a defined incubation period and, more important, that, like type-B hepatitis, it is considerably more common after the receipt of commercial blood than of voluntary donor blood. Thus there is increasing suspicion that there exists one or more previously unrecognised human hepatitis virus(es).<sup>13</sup>

**15.14** These three studies from 1974 and 1975 have been quoted and discussed at some length since they form the cornerstone upon which the recognition of the existence of NANB Hepatitis (subsequently Hepatitis C) is based. The expression 'non-A, non-B Hepatitis' was coined as a collective term for hepatitis in which, at that time, Hepatitis A and Hepatitis B, as well as Cytomegalovirus and Epstein-Barr virus, had been excluded.<sup>14</sup>

**15.15** Studies of post-transfusion hepatitis in the USA over this period increasingly identified the existence of an NANB Hepatitis agent and demonstrated that post-transfusion NANB Hepatitis was by no means uncommon. Depending on the source of the blood, 10% or more of transfusion patients developed ALT levels that remained elevated for weeks or even months, indicating probable non-A, non-B post-transfusion Hepatitis.

**15.16** Further work by Dr Alter and colleagues was reported in 1976.<sup>15</sup> Episodic cyclic patterns of alterations in serum transaminase levels, namely the levels of alanine transaminase (ALT) and aspartate transaminase (AST), had been identified, with raised levels alternating with near normal levels in cases of NANB Hepatitis.

<sup>10</sup> Though published first, Feinstone's work is said to have been later in date (see, for example, Zuckerman and Thomas, ed, *Viral Hepatitis: Scientific Basis and Clinical Management*,: 1993, page 470) but this must be questioned in view of the citation in the Prince paper of one paper read at the 6<sup>th</sup> symposium of the American Red Cross in May 1974. See the Preliminary Report, paragraph 6.29.

<sup>11</sup> Alter et al, 'Clinical and serological analysis of transfusion-associated hepatitis', *The Lancet*, 1975; 2:838–841 [LIT.001.3926]

<sup>12</sup> For example, an aetiological relationship with HAV, Cytomegalovirus or Epstein-Barr virus.

<sup>13</sup> Alter et al, 'Clinical and serological analysis of transfusion-associated hepatitis', *The Lancet*, 1975; 2: 838–841 [LIT.001.3926] at 3929

<sup>14</sup> See paragraphs 14.66–14.67 of the last chapter for references.

<sup>15</sup> Purcell et al, 'Non-A, non-B hepatitis', *Yale Journal of Biology and Medicine*, 1976; 49: 243 [LIT.001.3932]

### Non-A, non-B post-transfusion hepatitis

**15.17** On 12 March 1977, Jules Dienstag and others (including Feinstone and Alter) produced a report, 'Non-A, Non-B post-transfusion hepatitis'.<sup>16</sup> This study, based on an enlarged group of 32 cardiovascular patients, provided powerful evidence that HAV was not the cause of transfusion-associated hepatitis unrelated to HBV and supported the existence of one or more NANB Hepatitis viruses.

**15.18** In July, 1977, Jay Hoofnagle and others reported the results of a rather singular study.<sup>17</sup> Stored sera from experimental studies in the 1950s, in which volunteers had been inoculated with sera from blood donors suspected of having transmitted hepatitis to transfusion recipients, were re-examined. Feinstone was again a member of the group of researchers. The discussion noted that:

Several clinical and epidemiologic features of non-A, non-B hepatitis have become clear from studies such as the present one. First, non-A, non-B hepatitis closely resembles type B hepatitis. The incubation period, the clinical symptoms and signs, and the potential for chronicity appear to be similar to type B hepatitis. Undoubtedly, what was once referred to as "serum hepatitis" included both type B and non-A, non-B hepatitis. Second, non-A, non-B hepatitis appears to be spread predominantly by the parenteral route. Most cases have been described in association with transfusion, intravenous drug use, or serum inoculation. However, as in type B hepatitis, the importance of "non-parenteral" routes of transmission (by saliva, sexual and intimate contact, biting insects) needs to be assessed. Third, non-A, non-B hepatitis appears to be associated with a chronic carrier state in chronic liver disease ... These "implicated" blood donors were, for the most part, asymptomatic, although liver function tests and liver biopsy examinations frequently showed evidence of underlying chronic hepatitis. Finally, non-A, non-B hepatitis appears to be common ... Previous studies on post-transfusion hepatitis have shown that 40% to 71% of such hepatitis is non-A, non-B. Currently all blood donations are screened for HBsAg by radioimmunoassay (or a method of similar sensitivity). Data generated from post-transfusion hepatitis studies done since the institution of such sensitive screening methods suggest that at the present time more than 90% of post-transfusion hepatitis is due to non-A non-B hepatitis.<sup>18</sup>

**15.19** They also stated that:

More and more evidence ... indicates that non-A, non-B hepatitis is due to a transmissible agent that is most likely a virus.

....

Data generated from post-transfusion hepatitis studies... suggest that... at the present time more than 90% of post-transfusion hepatitis is due to non-A, non-B hepatitis. All these features suggest the presence of one or more other human hepatitis viruses....<sup>19</sup>

<sup>16</sup> Dienstag et al, 'Non-A, Non-B Post-Transfusion Hepatitis' *The Lancet*, 1977, 1:560–62 [LIT.001.0492]

<sup>17</sup> Hoofnagle et al, 'Transmission of Non-A, Non-B Hepatitis', *Annals of Internal Medicine*, 1977; 87:14–20 [LIT.001.3657]

<sup>18</sup> Ibid [LIT.001.3657] at 3662

<sup>19</sup> Ibid [LIT.001.3657] at 3662

**15.20** This important paper strengthened the case for a viral aetiology for NANB Hepatitis, predominantly if not exclusively parenterally transmitted, with a significant association with chronic liver disease.<sup>20</sup> Hoofnagle's figures showed the combined effect of the protective measures introduced, in particular:

- The exclusion of commercial blood and prospective screening of donations for HBsAg from about 1970 in reducing Hepatitis B transmission as a component of total post-transfusion hepatitis.
- The elimination of Hepatitis A as a material component of post-transfusion hepatitis.
- Increasing confidence in the inference that non-A, non-B Hepatitis was the major component of all post transfusion hepatitis.

### Other studies

**15.21** These US studies of surgical patients and blood donors were quickly followed by a study of hepatitis in haemophilia patients, published in 1977 by Henry Lesesne and others.<sup>21</sup> Six haemophilia patients who had persistent raised serum transaminase values over a period of six months were studied. Liver biopsies were taken and half of them were found to have 'chronic active hepatitis', characterised by severe liver cell dysfunction and with a frequently poor prognosis. This was the first study in which liver biopsies were taken from haemophilia patients. Patients in the Lesesne study were given prophylactic clotting factor concentrates prior to the biopsy as liver biopsy studies on haemophilia patients were very difficult to organise due to the risk of bleeding from the biopsy site.<sup>22</sup> The authors argued that biopsy was appropriate in a range of cases because of the therapeutically important histological information obtained and their assessment of the risks associated with the procedure.

**15.22** On 22 June 1978, Joel Spero and others published 'Asymptomatic Structural Liver Disease in Hemophilia' in *The New England Journal of Medicine*.<sup>23</sup> The paper concluded:

Our results suggest that, throughout the world, a large number of asymptomatic hemophilic patients who have received numerous transfusions must have histologic liver disease. In some, it must be severe. Adequate information is not yet available to evaluate fully hemophilic patients treated only with blood products negative by radioimmunoassay for HBsAg in both donors and final product.<sup>24</sup>

**15.23** By 1978, commercial pharmaceutical companies were beginning to issue hepatitis warnings with their blood products. While a reference to 'hepatitis' was explicit, there was little specification. For example, an information leaflet provided in 1978 with Koate, a Factor VIII product produced by Cutter Biological, contained a warning that 'the presence of hepatitis virus should be assumed' and suggested that the risk of administering the

<sup>20</sup> In July 1977 Meyers et al, (including Dienstag) re-examined data previously reported in 1972 and concluded that most cases of post-transfusion hepatitis were not caused by the hepatitis A or hepatitis B virus, but by an as yet unidentified hepatitis agent: Meyers et al, 'Parenterally transmitted non-A, non-B hepatitis: an epidemic reassessed', *Annals of Internal Medicine*, 1977; 87; 57-9 [LIT.001.0183].

<sup>21</sup> Lesesne et al, 'Liver biopsy in Hemophilia A', *Annals of Internal Medicine*, 1977; 86: 703-707 [LIT.001.3712]

<sup>22</sup> It was later estimated in one study that clinically significant haemorrhage occurred in 12.5% of procedures: Aledort et al, 'A study of liver biopsies and liver disease among haemophiliacs', *Blood*, 1985; 66: 367-372 [LIT.001.0505].

<sup>23</sup> Spero et al, 'Asymptomatic Structural Liver Disease in Hemophilia', *New England Journal of Medicine*, 1978; 289: 1373-1378 [LIT.001.0177]

<sup>24</sup> Ibid [LIT.001.0177] at 0182

concentrate should be weighed against the medical consequences of withholding it, particularly for persons with few previous transfusions.<sup>25</sup> A patent for this product was granted, based on discoveries made in the Bayer (Cutter Laboratories) research laboratory during 1978–79.<sup>26</sup> The patent itself specified that therapeutically active proteins isolated from plasma might contain viruses, for example hepatitis viruses. Among commercial pharmaceutical companies, the view underpinning research by the end of the 1970s was that there was viral transmission of hepatitis by these products generally.

### Aggregated research and the emerging ALT screening debate

**15.24** In 1978, Alter and others summarised data from a number of countries concerning post-transfusion hepatitis.<sup>27</sup> Having noted the seminal work of Blumberg and others on Hepatitis B, and Prince and others on Hepatitis A, they stated:

To date, the existence of an infectious agent(s) as the cause of non-A/non-B hepatitis has not been proved since no associated particle has been observed, no growth in tissue culture has been documented, and no specific immunologic test has been developed. In the face of elevated hepatic enzymes, the diagnosis of non-A/non-B hepatitis can only be made by the serologic exclusion of other known hepatitis viruses and by the clinical exclusion of other causes of hepatocellular injury. Nonetheless, there is a rising ground-swell of evidence that substantiates the existence of at least one human hepatitis virus distinct from HAV and HBV....<sup>28</sup>

**15.25** Alter and others tabulated the findings of other researchers for the period 1975–1977, showing that in the cited reports NANB Hepatitis accounted for 63–93% of all cases of post-transfusion hepatitis.<sup>29</sup> In non-transfusion studies a wider range of NANB Hepatitis infection was noted. With no diagnostic viral blood markers, however, NANB Hepatitis remained a diagnosis of exclusion. The underlying hypothesis was that proof of elevated hepatic enzymes, particularly ALT, coupled with the exclusion of other hepatitis viruses and other causes of hepatic damage, was sufficient for a diagnosis of NANB Hepatitis. This was to divide US and UK researchers. In the USA, it was to have practical implications for clinicians.

**15.26** The scene was set for a debate on ALT screening of donors. Dr Alter and his colleagues resisted screening for a time. Their research from the early 1970s had suggested that transaminase tests had not proved to be a practical method of screening donors for hepatitis.<sup>30</sup> Richard Aach and his colleagues, who had been involved in an extensive study in the USA, the Transfusion-Transmitted Viruses (TTV) study, promoted ALT screening as a safety procedure.<sup>31</sup> The TTV study had suggested a significant association between the ALT

<sup>25</sup> See 'Examples of warnings issued with coagulation factor concentrates' [LIT.001.4488] at 4518 and 'Events concerning the safety of blood and blood products with special reference to haemophilia' [PEN.013.0220] at 0229

<sup>26</sup> Patent 4,440,679: 'Pasteurised Therapeutically Active Protein Compositions' [SNB.004.5922]

<sup>27</sup> Alter et al, (1978) 'Non-A/Non-B Hepatitis: a Review and Interim Report of an Ongoing Prospective Study' in Vyas et al (eds), *Viral Hepatitis*, 1978; The Franklin Institute Press, Philadelphia, 359–369 [PEN.019.0863]

<sup>28</sup> Ibid [PEN.019.0863] at 0864. This was a notable application of Koch's postulates to NANB Hepatitis, associated with a disposition to examine emerging evidence independently of whether the formal requirements stipulated by the postulate were met. See the discussion in Chapter 11, *AIDS Aetiology*, paragraphs 11.28–11.30.

<sup>29</sup> Alter et al, (1978) 'Non-A/Non-B Hepatitis: a Review and Interim Report of an Ongoing Prospective Study' in Vyas, GN et al, (eds), *Viral Hepatitis*, 1978; The Franklin Institute Press, Philadelphia, 359–369 [PEN.019.0863] at 0865

<sup>30</sup> Alter et al, 'Posttransfusion Hepatitis After Exclusion of Commercial and Hepatitis-B Antigen Positive Donors', *Annals of Internal Medicine*, 1972; 77: 691 – 699 [PEN.002.0811]

<sup>31</sup> The TTV study is described in Aach, RD et al, 'Serum Alanine Aminotransferase of Donors in Relation to the Risk of Non-A, Non-B Hepatitis in Recipients', *New England Journal of Medicine*, 304: 989–994. [LIT.001.0753]

levels of a donor and the likelihood of subsequent hepatitis in the recipient. Alter and his colleagues' reservations had not been overcome by the end of this period, however. The competing positions of the protagonists are discussed more fully in Chapter 27, *Surrogate Testing of Donated Blood for non-A, non-B Hepatitis*.

### Further research

**15.27** Meantime, fundamental research continued to be reported. *The Lancet* published an article by Alter and others, 'Transmissible agent in NANB Hepatitis', on 4 March 1978.<sup>32</sup> In the study reported, chimpanzees were inoculated with serum from patients with post-transfusion NANB Hepatitis. Histological changes (changes in the microscopic anatomy of cells) in the animals ranged from mild to 'conspicuous' hepatitis and generally correlated with the degree of ALT elevation. There was said to be no evidence of clinical disease and all of the animals went on to biochemical and histological recovery. There was no serological evidence of Hepatitis A or Hepatitis B infection. Hepatitis was transmitted by serum derived from patients with chronic as well as acute hepatitis, strongly suggesting a chronic carrier state for the agent responsible for NANB Hepatitis. It was concluded that NANB Hepatitis seemed to be due to a transmissible agent which could persist and remain infectious for long periods.

**15.28** In July 1979, Dr Mones Berman and others (including Dr Alter) published 'The chronic sequelae of NANBH' in the *Annals of Internal Medicine*.<sup>33</sup> The conclusions from this study included, importantly for present purposes, a finding that although it could be clinically severe, acute NANB Hepatitis after transfusion was usually an anicteric, mildly symptomatic disease and probably went undetected in most patients not prospectively followed. It was suggested that a very large number of NANB Hepatitis cases might occur each year but that an accurate assessment of its incidence would not be possible until tests were developed that could detect specific serological markers. Among other conclusions, Berman reported that many cases of NANB Hepatitis were associated with prolonged elevation of ALT and that the predominant pathological change associated with chronic NANBH appeared to be chronic active hepatitis.

**15.29** In September 1979, Dr Athol Ware and others published a paper entitled 'Etiology of Liver Disease in Renal-Transplant Patients', also in the *Annals of Internal Medicine*.<sup>34</sup> No aetiological agent was defined in 27 of 38 patients found to have chronic hepatitis. They concluded that some if not most of these patients had chronic hepatitis secondary to infection with NANB Hepatitis. Almost without exception, the patients had received blood transfusions at the time of transplantation. The analysis added to the growing body of evidence supporting a viral aetiology for NANB Hepatitis.

### From aetiology to natural history

**15.30** At about this time the debate in the USA was moving on from discussion about whether NANB Hepatitis had a viral aetiology, which was broadly accepted, to discussion of the natural history of NANB Hepatitis infection. In July 1980, Edward Tabor and others made an unqualified comment that:

---

<sup>32</sup> Alter et al, 'Transmissible Agents in Non-A, non-B Hepatitis', *The Lancet* 4 March 1978 [LIT.001.1645]

<sup>33</sup> Berman, 'The Chronic Sequelae of Non-A, Non-B Hepatitis', *Annals of Internal Medicine*, 1979; 91:1-6 [LIT.001.0189] See the description of the study in the Preliminary Report paragraph 6.82

<sup>34</sup> Ware et al, 'Etiology of Liver Disease in Renal-Transplant Patients', *Annals of Internal Medicine*, 91: 364 [LIT.001.1052]



Non-A, non-B hepatitis is a major health problem, present in up to 89 per cent of patients with post-transfusion hepatitis and 25 per cent of hospitalized patients with sporadic hepatitis. Experimental transmission to chimpanzees of human non-A, non-B hepatitis and passage of an agent of non-A, non-B hepatitis to additional chimpanzees have demonstrated the cause to be a transmissible agent or agents.<sup>35</sup>

**15.31** The natural history of the disease continued to attract comment thereafter. On 16 December 1980, Ronald Koretz and others from the University of California, Los Angeles, published the results of research on 'The Long Term Course of Non-A, Non-B Post-transfusion Hepatitis'.<sup>36</sup> Sixty-six patients who had contracted NANB Hepatitis had been followed from 1972 for up to five years, the longest defined follow-up available at the time. Liver biopsy had revealed chronic persistent and chronic active hepatitis in all 18 patients on whom biopsy was carried out. Two developed cirrhosis. A third, not biopsied, had signs and symptoms suggesting cirrhosis. Most had, however, remained asymptomatic. The conclusion drawn was that post-transfusion NANB Hepatitis often resulted in chronic biochemical liver disease. However, if the disease progressed to liver failure it was found to do so over a number of years. It appeared to be benign in most instances. This was an influential paper because it reflected at least two to five years' follow-up of the patients in question.

**15.32** By this stage, the live issues in the USA were the relevance of elevated enzyme levels, particularly in donors, and the long-term prognosis for patients thought to be infected with NANB Hepatitis. Those disputes had not been resolved but, by the end of this period, it can safely be concluded that in the USA it had been established to a high degree of probability that NANB Hepatitis was due to a transmissible agent that was most likely to be a virus or viruses, though the agent(s) had not been identified.

### *Aetiology of NANB Hepatitis: UK and other research*

#### **Diagnosis**

**15.33** The US studies referred to are a few only within a large volume of research reports in the later 1970s and into 1980. There were almost no equivalent studies carried out in the UK. There was a significant difference of opinion on what constituted hepatitis. In the US view, 'hepatitis' was defined by raised levels of the enzyme alanine-aminotransferase by specified percentages or factors within specified periods and the absence of other causes of enzyme elevation, such as congestive heart failure and drug, alcohol or anaesthesia-induced conditions. In their 1974 report, the UK's Medical Research Council (MRC) Working Party included in their definition of 'hepatitis' a finding of enzyme elevation in association with other clinical indications of hepatitis. The requirement for additional positive indicators in the UK automatically reduced the groups of patients likely to be identified and hence yielded much lower numbers of infections attributed to post-transfusion hepatitis in UK studies than in equivalent studies in the USA.

**15.34** In clinical practice, it appears that the same view of the diagnostic features of hepatitis had a bearing on the diagnosis of post-transfusion NANB Hepatitis in the UK until 1990–91 when a test for the Hepatitis C virus (HCV) became available. Professor Peter

<sup>35</sup> Tabor, 'Chronic non-A, non-B Hepatitis Carrier State', *New England Journal of Medicine*, 1980; 303:140–143 [LIT.001.5521]

<sup>36</sup> Koretz et al, 'The Long-Term Course of Non-A, Non-B Post-transfusion Hepatitis', *Gastroenterology*, 1980; 79:893–8 [LIT.001.0201]. The paper was submitted on 18 September 1979 and accepted for publication on 16 May 1980.

Hayes, Professor of Hepatology and Honorary Consultant Gastroenterologist at the Royal Infirmary of Edinburgh, said that until there was a test for Hepatitis C, NANB Hepatitis was a very uncommon diagnosis in the UK. There were many causes of abnormal liver test results and, in his opinion, unless there was a 'trigger event', such as a blood transfusion followed by abnormal results, it was relatively unlikely that a putative viral diagnosis would have been made.<sup>37</sup>

**15.35** The UK approach was, in retrospect, too demanding. The resulting difference in diagnostic criteria applied in the UK probably led to some complacency concerning the prevalence of a possible infective agent affecting UK recipients of blood and blood products (as compared to US recipients) which lasted for over a decade. By way of example only, a comparison of the numbers thought to be infected illustrates the difference. The study by Alter and others (reported in November 1974) identified 12 of 108 patients followed (11%), as having developed hepatitis, as defined in the USA. This compared to the finding of eight out of 768 cases (1%) in which post-transfusion hepatitis had been thought to occur in the UK MRC study reported in the same year. The perception that post-transfusion hepatitis was very rare in the UK appears to have been due largely to the selection of criteria for diagnosis.

**15.36** In the UK in particular, so far as there were studies in the period to about 1981, different views developed among transfusion specialists, haemophilia specialists, virologists and public health doctors and it is appropriate to distinguish the haemophilia specialists from other groups. The response of haemophilia clinicians to the use of blood products in the light of growing knowledge is discussed in Chapters 21 and 22.

### **NANB Hepatitis and haemophilia**

**15.37** Even among haemophilia clinicians, the position was not uniform throughout Europe. In February 1975, Pier Mannucci and others published a paper on the incidence of asymptomatic liver disease in haemophilia patients treated in Milan.<sup>38</sup> Seventy-five patients with Haemophilia A and 16 with Haemophilia B were studied and classified according to age group. All had been exposed to replacement therapy with cryoprecipitate, commercial factor concentrates and, in the case of the older patients, fresh-frozen plasma. In the absence of records of the numbers of transfusions, age was selected as a 'rough but reliable parameter' to investigate any relationship between the degree of transfusion exposure and abnormality of liver function tests. Clinically, all were asymptomatic of liver disease. On physical examination five showed mild to moderate liver enlargement and two had hepatosplenomegaly (enlargement of the liver and spleen, implying possible cirrhosis). On testing, there was a high incidence of abnormal liver function test results, increasing with age. Raised ALT levels were observed in 45% of haemophilia patients, possibly caused by one or more NANB viruses. The article noted that the rate of exposure to agent(s) implicated in post-transfusion hepatitis had probably increased after the introduction of highly purified freeze-dried concentrates of Factor VIII and Factor IX manufactured by pools of plasma from many donors.

**15.38** The paper, which was published at the very outset of this period and probably written before the papers of Prince, Alter, Feinstone and others had appeared, noted that the data collected suggested that, in haemophilia patients, repeated contact with

---

<sup>37</sup> Day 78, pages 46–47

<sup>38</sup> Mannucci et al, 'Asymptomatic Liver Disease in Haemophiliacs', *Journal of Clinical Pathology*, 1975; 28:620 [SNB.008.5621]

the NANB Hepatitis agent might cause chronic liver damage that was not associated with overt illness. The discussion is instructive of the state of knowledge among Dr Mannucci's highly respected team at this time. The paper noted:

The clinical and prognostic significance of the observed abnormalities is presently unknown, and the lack of liver biopsies renders the task of clarifying them rather difficult. The great majority of the patients were completely asymptomatic and free of physical signs of liver involvement. It is possible that constant exposure to the infective agent(s) induces a general immunological tolerance conditioning an attenuated pattern of chronic hepatitis. It also seems reasonable to suggest that antibody to hepatitis B surface antigen occurring in haemophiliacs may offer protection.

However, the evidence accumulated with the investigation of asymptomatic carriers of HBsAg suggests that these humoral abnormalities are not entirely benign, since they may be associated with structural changes of the liver similar to those occurring in patients with chronic hepatitis. In haemophiliacs, an answer to these problems can be given only by a long-term prospective evaluation of any possible relationship between the observed abnormalities and the development of overt hepatic dysfunction.<sup>39</sup>

**15.39** The authors recommended regular testing. While still qualified by reservations, this was probably the first suggestion outside the USA that what became known as NANB Hepatitis occurring in haemophilia patients might be more than just a benign condition.

#### Factor concentrates

**15.40** In the UK, the MRC definition of hepatitis persisted. In August 1975, John Craske of the Public Health Laboratory, Dorset, published data on an outbreak of hepatitis following the infusion of commercial Factor VIII in the Bournemouth Haemophilia Centre.<sup>40</sup> The criteria used for diagnosis of hepatitis were jaundice or raised transaminase levels associated with compatible history and clinical signs of infection. With this publication, NANB Hepatitis had been recognised and reported by a UK haemophilia centre. The references cited did not include the earlier US publications already mentioned. As in the 1974 MRC study, the additional diagnostic criteria differentiated the approach adopted from that generally followed in the USA.

**15.41** Work by Prince and Feinstone, as well as Dr Craske's report from Bournemouth, were among the references cited in a draft protocol dated September 1975 for a prospective study of hepatitis in haemophilia associated with the use of factor concentrates in England and Wales.<sup>41</sup> The reasons for the preparation of the protocol are not clear but, at planning meetings held in 1975 for the World Health Organization (WHO) conference on Economic Aspects of Viral Hepatitis, member states who had sent representatives to the WHO conference in Copenhagen were invited to design 'study protocols' on a limited number of diseases, to carry out pilot studies which would be used to inform regional governments and to invite them to apply and adapt the methodology developed.<sup>42</sup> The UK protocol provides an insight into the views held in the UK at the time. It acknowledged

<sup>39</sup> Ibid [SNB.008.5621] at 5623

<sup>40</sup> Craske et al, 'An outbreak of hepatitis associated with intravenous injection of Factor VIII concentrate', *The Lancet*, 2 August 1975; 221–223 [LIT.001.0360]

<sup>41</sup> Study Protocol [SNB.001.6929]

<sup>42</sup> Report of a WHO Meeting on Economic Aspects of Viral Hepatitis – Copenhagen, 9–11 November 1976 [DHF.003.0283]

that the current assays had been of limited efficiency in excluding HBsAg positive donors and said:

This failure to prevent post transfusion hepatitis may be explained by the following hypotheses:

- (a) That current methods of detecting HBsAg are still not sensitive enough.
- (b) That other known viral agents are responsible, e.g., hepatitis 'A', [Epstein-Barr] virus, cytomegalo virus.
- (c) That other, as yet unknown viruses, cause a significant amount of post transfusion hepatitis which is supported by the recent work of Feinstone et al.<sup>43</sup>

**15.42** Against the background of emerging data, the study proposed to address the question:

“Does the administration of factor VIII concentrates to haemophiliacs on regular replacement therapy significantly increase the incidence of transfusion hepatitis?”<sup>44</sup>

**15.43** The proposed study also aimed to identify any difference in ‘attack rates’ as between commercial and NHS products; the value of the HBsAg positive test; further information on unknown viruses or agents; and the role of radioimmunoassay (RIA) testing for HBsAg of Factor VIII concentrates in the prevention of post-transfusion Hepatitis B. A pilot study was proposed, with the results to be provided at a meeting in Glasgow with a view to enlisting all of the UK Haemophilia Centres in the study. Had the study been carried fully into effect, it would have been a major exercise along the lines of the US investigations initiated in 1974. It was not, however, fully implemented in the UK.

### False trails

**15.44** UK experts were not alone in finding difficulties with the identification of NANB Hepatitis. At this stage, eminent researchers worldwide continued to develop hypotheses to explain NANB Hepatitis, which were later disproved. In October 1978, Ryoichi Shirachi and others published a paper entitled ‘Hepatitis “C” antigen in non-A, non-B post-transfusion hepatitis’.<sup>45</sup> They claimed to have found evidence for a new hepatitis-specific antigen in sera obtained from patients with post-transfusion NANB Hepatitis. They proposed the designation ‘hepatitis C (HC) antigen’. It was to prove to be among a number of false trails.<sup>46</sup>

**15.45** The work of the UK Haemophilia Centre Directors Hepatitis Working Party was an example of another. The Working Party met in Glasgow on 30 September 1980.<sup>47</sup> Dr Craske presented the Working Party’s report for 1979 which set out the results of surveillance for 1978 and 1979.<sup>48</sup> The report noted that the prevalence of hepatitis was about the same level as that observed in 1976–77. There had been an increase in the

<sup>43</sup> Study Protocol [SNB.001.6929]

<sup>44</sup> Ibid [SNB.001.6929]

<sup>45</sup> Shirachi et al, ‘Hepatitis “C” antigen in non-A, non-B post-transfusion hepatitis’, *The Lancet*, 21 October 1978 [LIT.001.0383]

<sup>46</sup> The overall consensus at the end of 1978 is summarised in the Preliminary Report at paragraph 6.74

<sup>47</sup> See Minutes of the Eleventh Meeting of UK Haemophilia Centre Directors Held in Glasgow, 30 September 1980 [SNB.001.7296] and the Preliminary Report para 6.99. Substantially the same material was repeated by Dr Craske at an International Symposium held on 1 and 2 October 1980 at the Royal College of Physicians, Glasgow, on ‘Unsolved Problems in Haemophilia’ [DHF.003.0649]. See also: Preliminary Report para 6.100

<sup>48</sup> Dr Craske’s report [LOT.003.5665]

proportion of cases of NANB Hepatitis reported in patients with mild disease receiving concentrates for the first time to cover operations. It was suggested that the observed increase in mildly affected haemophilia patients contracting hepatitis was probably due to the fact that most severely affected patients had already been exposed to viruses present in all brands of concentrates and were therefore immune to re-infection, while patients with mild disease had not been so exposed.

### Further haemophilia and factor concentrate research

**15.46** The natural history of NANB Hepatitis was not understood: as is now known, exposure to HCV does not confer immunity. It was concluded at the time, however, that transaminitis (elevated liver enzyme levels in the blood) was unrelated to current Factor VIII therapy and the level of anti-HBs antibody and was unrelated to a previous history of overt hepatitis. The report stated:

These results suggest that if transaminitis is related to viral hepatitis, the patients who become carriers and develop chronic liver disease will only contract mild or symptomless acute hepatitis, and the most overtly jaundiced patients will fully recover. This is supported by our observations of hepatitis B infections in haemophiliacs.<sup>49</sup>

**15.47** There were other views. As already noted in Chapter 13, *Knowledge of Viral Hepatitis Now*, paragraph 13.45, in 1978 Dr David Triger and colleagues, of Hallamshire Hospital, Sheffield, published the results of liver biopsies carried out on haemophilia patients with persistent abnormal liver function test results.<sup>50</sup> These provided a comparison with the work of Lesesne (paragraph 15.21, above). They considered it reasonable to conclude from their findings that a large proportion of haemophilia patients receiving treatment with Factor VIII had important chronic liver disease and that NANB Hepatitis may well have been an important factor, supported by observations in half of the cohort of patients studied. One patient had chronic lobular hepatitis and one micronodular cirrhosis. As indicated earlier, this work does not appear to have had wide immediate impact for the reasons set out in Chapter 13, *Knowledge of Viral Hepatitis Now*, paragraphs 13.43–13.44.

**15.48** In Europe and the USA, however, commercial companies' research had moved ahead and reflected the view that transmission of viral hepatitis by blood products, which was otherwise implicitly assumed, could be avoided by changes to manufacturing processes. A prominent example was illustrated in the work of Norbert Heimburger and a group of employees of the German pharmaceutical company Behringwerke, who in 1980 wrote a paper entitled 'Factor VIII concentrate – now free from hepatitis risk: progress in the treatment of haemophilia'.<sup>51</sup> Behringwerke had produced a heat-treated factor concentrate which they claimed did not transmit hepatitis. The product was called Factor VIII HS (ie 'hepatitis safe') and had been heated in solution to 60°C for 10 hours. It had been tested first on chimpanzees and then on 12 patients. Both groups had been monitored for a period of six–12 months and there had been no evidence of hepatitis infection. This was claimed to be the first heat-treated concentrate produced and reflected the commercial

<sup>49</sup> Ibid [LOT.003.5665] at 5667

<sup>50</sup> Preston et al, 'Percutaneous Liver Biopsy and Chronic Liver Disease in Haemophiliacs', *The Lancet*, 19 September 1978; 592–594 [LIT.001.0387]. Details are given in Preliminary Report paragraph 6.71. Professor Thomas identified this as Dr Triger's work: Day 52, page 129.

<sup>51</sup> Heimburger et al, 'Factor VIII concentrate – now free from hepatitis risk: progress in the treatment of haemophilia', *Die Gelben Hefte*, (trans. *The Golden Notebook*), 4:165–174 [SGF.001.1761]

appreciation of transmission risk and of the need to deal with it. This topic is discussed more fully in Chapter 23, *Viral Inactivation of Blood Products for Haemophilia Therapy up to 1985*.

**15.49** In November 1980, Dr Craske, in a report to the Department of Health, 'Studies on the epidemiology and chronic sequelae of FVIII and IX associated hepatitis in the UK, Appendix II: Chronic Liver disease in Haemophiliacs', stated that, despite multiple transfusions and large numbers of grossly abnormal liver function tests, very few patients showed any evidence of chronic liver disease.<sup>52</sup>

**15.50** Subsequently, on 19 March 1983, the *British Medical Journal (BMJ)* published a report on behalf of the UK Haemophilia Reference Centre Directors on the treatment of haemophilia and related disorders in the UK between 1976 and 1980.<sup>53</sup> The paper tabulated the numbers and percentages of patients treated who developed acute hepatitis. The diagnosis was based on clinical and laboratory findings and did not include patients with a known previous history of persistent abnormalities in liver function tests. Furthermore, the term 'acute hepatitis' was not defined in the report and it is likely to have missed many asymptomatic cases of NANB Hepatitis with low elevation of ALT. In the years 1976–80 the incidence in patients with Haemophilia A varied between 1.7% and 3.5% of those treated in any year and was very little different from that seen in the period 1969–74. However, with the first use of US commercial Factor VIII concentrates on a wide scale in haemophilia centres in the UK, the overall incidence of diagnosed hepatitis in patients with Haemophilia A rose from 2.3% to 5.2% in 1974 and then declined to 3.1% in 1976, remaining at about that level thereafter. Although the incidence of overt hepatitis had increased, the level of infection in the UK remained below levels in the USA. The report included the following statement:

In view of the widespread concern about the transmission of hepatitis viruses by giving blood products it is interesting to note that only two deaths were attributed to hepatitis during the five year period. There have been several reports recently of persistently abnormal liver function values and abnormal histological findings in liver tissue from haemophiliacs treated with blood products. Most of these patients are asymptomatic but it remains to be seen how many will develop severe chronic liver disease with the passage of time.<sup>54</sup>

**15.51** In 1981, a paper by Dr May Bamber and others, 'Short incubation NANB transmitted by Factor VIII concentrates in patients with congenital coagulation disorders', was published in the journal *Gut*.<sup>55</sup> The patients studied had received infusions of cryoprecipitate and commercial and NHS Factor VIII concentrate. This paper was produced by the leading UK liver unit at the Royal Free Hospital, London, in conjunction with the Royal Free Hospital Haemophilia Unit. Professor Sherlock and Professor Thomas were involved. It described 10 cases of NANB Hepatitis occurring after infusion of Factor VIII concentrates and was mainly concerned with the acute clinical course of the disease. In one group of five cases there was evidence of a direct link to a specific single infusion. In the others the patient's

<sup>52</sup> Second Annual Report on Project Number J/S240/78/7 [DHF.003.0351]

<sup>53</sup> Rizza et al, 'Treatment of haemophilia and related disorders in Britain and Northern Ireland during 1976-80: report on behalf of the directors of haemophilia centres in the United Kingdom', *British Medical Journal*; 286:929–933 [LIT.001.0234] Preliminary Report paragraph 7.38

<sup>54</sup> Rizza et al, 'Treatment of haemophilia and related disorders in Britain and Northern Ireland during 1976-80: report on behalf of the directors of haemophilia centres in the United Kingdom', *British Medical Journal*, 286:929–933 [LIT.001.0234] at 0238

<sup>55</sup> Bamber et al, 'Short incubation NANB transmitted by Factor VIII concentrates in patients with congenital coagulation disorders', *Gut*, 1981; 22: 854–859 [LIT.001.0483].

history of therapy confused the position. In another group of five cases the disease was asymptomatic and anicteric but in five it was more severe. None of the patients recovered within six months. The paper concluded that the failure of these patients to recover within the period of study (six–45 months) suggested that NANB Hepatitis was an important cause of liver disease in patients with coagulation disorders. The paper dealt with the histology (appearance under the microscope) of the liver in these patients. The clinical course was not dissimilar to the other clinical descriptions around that time and became much quoted. The paper stated:

Follow-up, both clinical and histological, will be needed to establish the natural history of this disease.<sup>56</sup>

**15.52** The paper also stated that there was evidence for more than one type of short incubation NANB Hepatitis virus, 'only one of which has a high rate of induction of chronic liver disease'. This view was wrong but was entertained by others at the time. The findings were affirmation of the work done at Sheffield, which had previously been controversial.<sup>57</sup> The Bamber paper, published in 1981, marked the beginning of a significant change in expert opinion. US research published in 1982 pointed in the same direction.<sup>58</sup>

**15.53** On 4 July 1981, an editorial in the *BMJ* discussed the risk to haemophilia patients. It described post-transfusion hepatitis as the major complication of the modern treatment of haemophilia and stated:

The diagnosis is usually inferred from abnormalities in the results of hepatic biochemical tests rather than from clinical evidence.<sup>59</sup>

**15.54** It referred to the biopsy-based research by Eric Preston and others at Sheffield, reported in 1978, (paragraph 15.47, above) as indicating that changes in liver architecture had occurred in haemophilia patients which were consistent with previous viral assault, including chronic persistent and chronic active hepatitis and cirrhosis. The editorial narrated rather starkly that, in some cases, early death from liver disease might prove to be the price paid by haemophilia patients for the improved quality of life afforded by the easy availability of clotting-factor concentrates. Steps taken to counter the risks were focused on three practices: the risks of collecting plasma from paid as opposed to volunteer donors; the optimum size of the donor plasma pool; and attempts at removing the several viruses of hepatitis from blood products.

**15.55** The editorial went on to identify NANB Hepatitis viruses (at least two) as the main cause of chronic liver disease in patients with haemophilia. In relation to the volunteer/paid donor issue, it referred to US evidence of a material reduction in risk when a hospital changed from commercial to volunteer blood. In relation to the attempts at removing viruses of hepatitis from blood products, there was again relevant evidence. The final paragraph stated:

[I]n the absence of specific markers for non-A, non-B hepatitis, overall protection against hepatitis appears remote. A more likely possibility is that hepatitis-free blood products will become available ....<sup>60</sup>

<sup>56</sup> Ibid [LIT.001.0483] at 0489

<sup>57</sup> Professor Thomas – Day 52, page 129; Bamber et al, 'Clinical and histological features of a group of patients with sporadic non-A, non-B hepatitis', *Journal of Clinical Pathology*, 1981; 34: 1175–1180 [LIT.001.0759] at 0762

<sup>58</sup> Koretz et al, 'Non-A, non-B post-transfusion hepatitis: disaster after decades', *Hepatology*, 1982; 2:687 [LIT.001.3738]; Professor Thomas' Report [PEN.017.1079] at 1080

<sup>59</sup> 'Post-transfusion hepatitis', *British Medical Journal*, 4 July 1981 [LIT.001.0227]

<sup>60</sup> Ibid [LIT.001.0227]

**15.56** The editorial referred to three recent reports dealing with heat-inactivation, chemical treatment with  $\beta$ -propiolactone and wet-heat treatment processes as more likely to achieve the removal of viral contamination.<sup>61</sup> By this stage it was being recognised that where NANB Hepatitis was established in blood coagulation patients it carried a risk of chronic liver disease and the biopsy findings reported by Preston and colleagues were being noted.

### Post-transfusion NANB Hepatitis

**15.57** In contrast to the work published in relation to hepatitis in haemophilia patients, work on post-transfusion hepatitis between 1975 and 1981 was less homogeneous and tended to arise from specific issues. At government level, a plethora of committees and working parties was established by the Department for Health and Social Security (DHSS), the MRC and the Haemophilia Centre Directors. NANB Hepatitis and its relevance to transfusion and haemophilia therapy were discussed, but no studies of post-transfusion hepatitis were established in the UK comparable to the several carried out in the USA.

**15.58** There were some peripheral developments in regulation. In the context of public health, 'infective hepatitis' had been listed as a notifiable disease from 1968.<sup>62</sup> In February 1976, 'viral hepatitis' was prescribed as an industrial disease for the purposes of the Social Security Act 1975. Employees infected in the course of work became entitled to certain forms of benefit, including injury benefit. The circular announcing the development stated:

The prescription includes the two commoner forms of viral hepatitis known as hepatitis A (infectious hepatitis) and hepatitis B (serum hepatitis; Australia antigen positive hepatitis).<sup>63</sup>

**15.59** NANB Hepatitis, in absolute terms or relative to Hepatitis A and B, was not acknowledged.

**15.60** Precisely because the signs and symptoms were so mild and the blood tests lacking the results of a comprehensive study, the general opinion in Scotland (outwith haemophilia care) at this stage was that NANB Hepatitis was a rare and relatively unimportant disease. In a letter written on 26 March 1975 to John Wallace, Regional Director of the Glasgow and West of Scotland Blood Transfusion Service, Major General Jeffrey, National Medical Director, SNBTS, commented that in the light of current knowledge a few cases of post-transfusion hepatitis were 'bound to arise'. The letter was copied to Dr McIntyre at SHHD. The General referred to US literature which was clearly known but which, at that stage, had not impressed him as giving rise to significant concern.<sup>64</sup>

**15.61** In 1979, Dr Ajay Chaudhuri and others published in the *Communicable Diseases Scotland Weekly Report* a paper based on haemophilia and non-haemophilia patients, 'Viral Hepatitis in Glasgow, 1976 – 1977'. It found that:

During the two-year period from January, 1976, to December, 1977, 164 patients with viral hepatitis were admitted to the Infectious Diseases Units at Ruchill and Belvidere Hospitals, Glasgow. Of these, 52 (32 per cent) patients had hepatitis B as they were found to be HBsAg positive. In 112 patients who

---

<sup>61</sup> The article refers to them as 'specific processing by chemicals, ultraviolet light, or heating'.

<sup>62</sup> See Chapter 14, *Knowledge of Viral Hepatitis 1*, paragraph 14.13.

<sup>63</sup> Scottish Home and Health Department circular [SGF.001.2818]

<sup>64</sup> General Jeffrey's letter [SGF.001.2780]



were HBsAg negative, a diagnosis of non-B hepatitis was made; however, in a majority of these patients, epidemiological findings and clinical course suggested a diagnosis of hepatitis A.<sup>65</sup>

**15.62** Retrospective testing for antibody to HAV showed that two thirds of the non-B cases were attributable to Hepatitis A. Under the heading 'Non-A – non-B Hepatitis' the authors stated:

In four patients with non-B hepatitis, hepatitis developed within 2-6 months of transfusion of blood products. Three male haemophiliacs and a female patient with Christmas disease had received numerous transfusions of factor VIII and cryoprecipitate. These four patients and also two drug addicts with hepatitis had no evidence of hepatitis B infection, nor of hepatitis A infection nor of infection with cytomegalovirus, nor EB virus. At present they are classified as cases of non-A -- non-B hepatitis. Evidence from other countries suggests that a virus (or viruses) may be associated with this type of hepatitis and that a carrier state is possible. With laboratory tests now permitting definitive diagnosis of hepatitis A virus infection, as well as hepatitis B, in 1979 it should be possible to determine the prevalence of non-A – non-B hepatitis in the general population in West Scotland.<sup>66</sup>

**15.63** The paper reflected experience in an infectious diseases unit: only a small proportion of NANB Hepatitis patients had overt clinical symptoms of disease sufficiently severe to lead to referral to the infectious diseases hospital.

**15.64** In the international context, there was some recognition of the risk of hepatitis other than A or B at a WHO meeting on the Economic Aspects of Viral Hepatitis in Copenhagen, held between 9 and 11 November 1976. Viral hepatitis was defined as acute inflammation of the liver caused by HAV, HBV, 'or by other hepatitis viruses'. It was reported:

Progress in the specific diagnosis of viral hepatitis has revealed a new type of hepatitis that is unrelated to hepatitis A or B virus. It appears to be now the most common form of hepatitis occurring after blood transfusion in some areas. There are no laboratory tests available as yet for identifying this agent or agents.<sup>67</sup>

**15.65** This report indicated an increasing international awareness of a problem but little direction towards a solution.

**15.66** On 8 January 1979, a doctor (name redacted) of the School of Pathology, the Middlesex Hospital, wrote to the DHSS advising that the stimulus for re-convening the Advisory Group on Testing for the Presence of Hepatitis B Surface Antigen was to 'upgrade' the 'viral safety' of UK Factor VIII concentrates. The letter also stated:

I have a note to write to you about non-A, non-B hepatitis.

If one or more of these viruses is responsible for the abnormal livers which are evidently common among haemophiliacs then chronic liver disease due to

<sup>65</sup> Chaudhuri et al, 'Viral Hepatitis in Glasgow', 1976-1977', *Communicable Diseases Scotland Weekly Report*, 1978; 78(8) [PEN.002.0511]

<sup>66</sup> Ibid [PEN.002.0511] at 0513

<sup>67</sup> Report of a WHO Meeting on Economic Aspects of Viral Hepatitis – Copenhagen, 9–11 November 1976 [DHF.003.0283] at 0285

these viruses might also be found among other transfused individuals. What I was asking Y [name redacted]<sup>68</sup> was whether she could question her patients with chronic liver disease about past transfusions. There could be merits in starting with an actual clinical problem and working backwards.

If we are going to consider non-A, non-B seriously in the Advisory Group it would be logical to co-opt Z [name redacted]<sup>69</sup> of the PHLS, Manchester. He is making a continuing study of the problem of hepatitis in haemophiliacs.<sup>70</sup>

**15.67** The identity of the author of this letter is not disclosed but may have been Dr David Dane. If it was Dr Dane (a member of the original and reconvened Advisory Group on Testing for the Presence of Hepatitis B Surface Antigen, an eminent pathologist and commentator),<sup>71</sup> it is unlikely that he was at this stage unaware of the US literature on NANB Hepatitis among transfused patients: the work of Prince and others in and after 1974 had reported on cardiac surgery patients. That they were at risk was known from the earliest days of NANB Hepatitis. However, it appears at least to have been an opening for study of the wider problem and progress followed.

#### Medical Research Council ad hoc meeting

**15.68** On 7 February 1979, a letter was sent out by a Senior Medical Officer of the MRC thanking individuals for agreeing to attend an ad hoc meeting to be held on 12 February 1979.<sup>72</sup> The meeting was to discuss growing anxiety about the threat of NANB Hepatitis to patients and laboratory staff and the need for research to characterise the agent causing the disease and to develop a test for the organism or its marker. The letter noted that a commercial concentrate had been found to transmit NANB Hepatitis to chimpanzees and, as a result, it had not been given a licence. It quoted advice received from the Institute of Allergy and Infectious Diseases, Bethesda, Maryland:

1) The non-A, non-B agent has not yet been purified from the livers of infected individuals or animals, or from the stool. Most recently it has been reported that the agent has been transmitted to chimpanzees. There is a preliminary report that the non-A, non-B agent has been visualized by electron microscopy in the livers of infected chimpanzees. This, however, needs further documentation. While the chimpanzee is a clumsy experimental animal, this will provide new opportunities for characterising the agent. As with all the hepatitis viruses, non-A, non-B has yet to be cultivated.

2) Your second question concerns antigenic markers and diagnostic tests. These are not yet available, because of the negative results listed in the paragraph above.<sup>73</sup>

**15.69** On 12 February 1979, the MRC hosted the proposed ad hoc meeting.<sup>74</sup> The meeting was attended by eminent experts including Professors Sherlock and Zuckerman, Sir William Maycock, Dr Craske and Dr Philip Mortimer. Professor Zuckerman had led

<sup>68</sup> Y was probably Dame Sheila Sherlock.

<sup>69</sup> Z was probably Dr Craske, who by this time had moved to Manchester.

<sup>70</sup> Letter of 8 January 1979 [DHF.003.0324]

<sup>71</sup> See Chapter 14, *Knowledge of Viral Hepatitis 1*, paragraph 14.28

<sup>72</sup> Letter of 2nd February 1979 [DHF.003.0323]

<sup>73</sup> Ibid [DHF.003.0323]

<sup>74</sup> Meeting minutes [PEN.017.1737]. This unredacted version of this document became available after publication of the Preliminary Report.

the previous MRC study published in 1974. The discussion of parenterally transmitted NANB Hepatitis provides an insight into the state of knowledge at the time. There was a view, advanced by Dr Thomas Cleghorn and supported by Professor Sherlock, that post-transfusion hepatitis (PTH) 'must now be rare and that it would be difficult to find many cases.' The ground for the observation appears to have been that, despite the transfusion of 1.5 million units of blood in the previous year, 'very little had been heard of non-A, non-B PTH'. Professor Zuckerman countered by observing that much NANB Hepatitis might be anicteric and that the risk of progression to chronic liver disease remained, however mild the initial infection. Professor Sherlock was concerned about the risks of transmission associated with imported commercial products but Dr Craske reported that his group had also found NANB Hepatitis associated with blood products of NHS origin. The conclusion of this discussion was reported as follows:

The Chairman [Professor Mollison] then asked what exactly constituted a case of non-A non-B hepatitis. It was agreed that HBV infection must be excluded by sensitive tests for HBsAg and anti-HBc, and that recent infection with HAV, EB virus and cytomegalovirus must also be excluded. Blood enzyme tests, particularly SGPT, could be a useful pointer to non-A non-B infection, but there was an urgent need for specific markers of non-A non-B viruses. The Chairman suggested, and Professors Sherlock and Zuckerman agreed, that until there were such markers, a survey of PTH – as suggested by Sir William Maycock – was not warranted.<sup>75</sup>

**15.70** More limited research and arrangements to store sera for later examination were then discussed. The decision not to initiate a survey of post-transfusion hepatitis was to lead to the serious long-term consequences of postponing investigation of the prevalence of post-transfusion NANB Hepatitis in the UK. At that time there was no reasonable prospect of developing a specific marker for NANB Hepatitis in early course. Rather, diagnosis depended on exclusion of other causes of hepatitis in the patient and the participants clearly understood that, as the minute shows. The committee's remit was related to the allocation of research funds and that may explain the decision taken that, until specific markers for non-A, non-B viruses had been developed, a survey of post-transfusion hepatitis was not warranted. The discussion demonstrated, however, that among this eminent group the risk of transfusion-transmitted NANB Hepatitis as understood in the USA was not accepted, though a paper by Dr Alter and colleagues on the 'Transmissible Agent in Non-A, Non-B Hepatitis' was included in the literature before the committee.<sup>76</sup> As events were soon to show, it was the view of Dr Brian McClelland<sup>77</sup> that a well-structured study could be devised but the decision at the 1979 meeting hardened views against that course.<sup>78</sup>

**15.71** The Regional Transfusion Directors held their 176th meeting on 3 October 1979.<sup>79</sup> It was reported that the Advisory Group on the Testing for the Presence of Hepatitis B Surface Antigen and its Antibody was concerned about the incidence of post-transfusion

<sup>75</sup> Meeting minutes [PEN.017.1737] at 1738

<sup>76</sup> Alter et al, 'Transmissible agent in non-A, non-B hepatitis', *The Lancet*, 4 March 1978; 459–463 [LIT.001.1645]; Agenda: [DHF.003.0323]. Other papers circulated were: Tabor et al, 'Transmission of Non-A, Non-B Hepatitis from Man to Chimpanzee', *The Lancet*, 4 March 1978; 463–466 [LIT.001.1642], and the Shirachi paper referred to at paragraph 15.44, above.

<sup>77</sup> Director, Edinburgh and South East Scotland RTC.

<sup>78</sup> See Chapter 27, *Surrogate Testing of Donated Blood for non-A, non-B Hepatitis*, for more detailed discussion on the fate of Dr McClelland's proposals.

<sup>79</sup> Meeting minutes [DHF.002.8109]

jaundice. The group was particularly anxious to receive from the regions details of patients suffering from NANB Hepatitis and stated that it would appreciate receiving samples of serum from these patients. Directors were reminded of the need to report all cases of post-transfusion hepatitis. It is noteworthy that, as far as the Transfusion Directors were concerned, post-transfusion hepatitis was still being discussed in terms of jaundice at this date.

**15.72** At about this time, other evidence of severe liver disease associated with NANB Hepatitis was being reported. In 1979 Sten Iwarson and others reported two cases in which there was a well-documented progression to serious liver disease, in a paper entitled 'Progression of hepatitis non-A, non-B to chronic active hepatitis'.<sup>80</sup>

### Working Party on Post-Transfusion Hepatitis

**15.73** The ad hoc meeting in February 1979 led to the MRC setting up a Working Party on Post-Transfusion Hepatitis which met for the first time on 14 February 1980.<sup>81</sup> The Working Party was chaired by Dr Harold Gunson<sup>82</sup> and its members included Professors Sherlock and Zuckerman, Dr WJ Jenkins,<sup>83</sup> Dr McClelland, Drs Craske, Polakoff and Tobin of the Public Health Laboratory Service (PHLS) and Dr Diana Walford of the DHSS.<sup>84</sup> The function of the Working Party was agreed to be:

[T]o promote research to assess the nature and size of the problem of PTH in the UK, with particular reference to changes in transfusion practice .... Studies should include (1) an assessment of any further need for research into Hepatitis B... (2) investigations to assess the incidence of non-A, non-B hepatitis in the UK, particularly with the risk of introducing the infection by blood transfusions, and (3) the position of research to characterise the agent(s) associated with this form of hepatitis, and to derive diagnostic tests.<sup>85</sup>

**15.74** In respect of the incidence of post-transfusion hepatitis in the UK, it was noted that '[n]o cases of NANB Hepatitis related to whole blood transfusions had yet been reported despite enquiry of hospitals in London where open heart surgery was carried out'. Dr McClelland proposed a multi-centre study, which might be sponsored by the MRC, into the association of NANB Hepatitis with blood transfusion. It was minuted that this proposal was deferred.

**15.75** Deferral of Dr McClelland's proposal in effect repeated the decision taken at the ad hoc meeting of the MRC. However, Dr McClelland proceeded to propose a multi-centre prospective study at the next meeting of the Working Party, held on 25 June 1981.<sup>86</sup> In his evidence to the Inquiry Dr McClelland stated that, in doing so, he clearly behaved as though there had been no agreement to defer the study.<sup>87</sup> Whatever the accuracy of the minute, Dr McClelland made no progress.

<sup>80</sup> Iwarson et al, 'Progression of Hepatitis Non-A Non-B to Chronic Active Hepatitis', *Journal of Clinical Pathology*, 1979; 32:351 [LIT.001.0196]

<sup>81</sup> Minutes of MRC Working Party on Post-Transfusion Hepatitis – 14 February 1980 [PEN.017.1710]

<sup>82</sup> Then Director of the Oxford Regional Transfusion Centre (RTC) who would later become Director of the Manchester RTC and Chairman of the Regional Directors of the National Blood Transfusion Service for England and Wales.

<sup>83</sup> Director, North East Thames RTC and successor to Sir William Maycock as Chairman of the Advisory Group on Testing for the Presence of Hepatitis B Surface Antigen and its Antibody

<sup>84</sup> List of members – MRC Working Party on Post-Transfusion Hepatitis – 14 February 1980 [PEN.017.1715]

<sup>85</sup> Minutes of MRC Working Party on Post-Transfusion Hepatitis – 14 February 1980 [PEN.017.1710] at 1711

<sup>86</sup> Minutes of MRC Working Party on Post-Transfusion Hepatitis – 25 June 1981 [PEN.017.1478] at 1480

<sup>87</sup> Day 63, page 63. See Chapter 27, *Surrogate Testing of Donated Blood for non-A, non-B Hepatitis*.

**15.76** The second meeting of the MRC Working Party, on 25 June 1981, proved to be the last.<sup>88</sup> Professor Zuckerman gave a summary of the research work that had been carried out over the past two years on post-transfusion hepatitis among other forms of the disease. He and Dr Howard Thomas spoke of difficulties that had been encountered in devising serological and radioimmunoassay techniques for identifying NANB viruses. Other aspects of the meeting, related to the question of a prospective study of post-transfusion hepatitis and particularly in relation to potential surrogate screening, are dealt with in paragraphs 27.78–27.83 of Chapter 27, *Surrogate Testing of Donated Blood for non-A, non-B Hepatitis*. However, in brief, the demise of the Working Party, implying the exhaustion of its wide remit, put an end to Dr McClelland's proposal for the time being.

**15.77** Dr McClelland was not alone in his concern that there should be an investigation. The Advisory Group on the Testing for the Presence of Hepatitis B Surface Antigen and its Antibody presented its third report in 1981.<sup>89</sup> The group included Professor Sherlock, Professor Zuckerman, Dr Craske, Professor John Cash and Dr Edward Follett among others. In relation to NANB Hepatitis, it stated:

Non-A, non-B hepatitis viruses are a common cause of PTH in the United States and are thought to have been responsible for cases of PTH in the UK. Hepatitis due to these viruses is common among haemophiliacs and follows the administration of imported, and occasionally of British Factor VIII and Factor IX. There is evidence for the occurrence of sporadic cases of non-A, non-B hepatitis in the general adult population and in association with cryoprecipitate therapy in the UK.

There are at the present time no screening tests for detecting non-A, non-B hepatitis viruses in blood donation.

We recommend that research is undertaken in the UK to determine the extent and severity of PTH due to non-A, non-B hepatitis viruses. Unless this is done we will not have the knowledge on which to base any possible future recommendations about screening blood donations for these viruses.<sup>90</sup>

**15.78** Reporting of relevant evidence was encouraged. Separately, in relation to liver function tests, the report stated:

Several categories of people are found to have raised blood transaminase levels which are not associated with viral hepatitis. Some 3% of new donors may be excluded if the criteria of one raised transaminase level is applied. In addition to the need for confirmatory transaminase testing the worry and inconvenience caused to donors would be unlikely to be compensated for by any clinical benefit. Therefore we advise against these tests in screening blood donors at the present time but the subject should be kept under review.<sup>91</sup>

### ***Knowledge of NANB Hepatitis: Summary as at 1981***

**15.79** The relevance of elevated enzyme levels was still a live issue in the USA at this stage. The final paragraph of advice quoted above was not altogether out of line with

---

<sup>88</sup> Meeting Minutes [PEN.017.1478]

<sup>89</sup> Third Report of the Advisory Group on Testing for the Presence of Hepatitis B Surface Antigen and its Antibody [DHF.003.0037]

<sup>90</sup> Ibid [DHF.003.0037] at 0045–46

<sup>91</sup> Ibid [DHF.003.0037] at 0046

that position. However, along with the reports from other meetings in and after 1979 discussed above, it reflects some of the confusion prevalent at the time. It was correctly acknowledged that several categories of people can have raised transaminases not associated with viral hepatitis. Alcohol and obesity may play a part, for example, but unless all cases of elevated liver enzymes were associated with those categories there had to be a cohort whose elevated enzyme levels might be associated with NANB Hepatitis. The recommendation that there should be research was not followed up, however.

**15.80** There were clearly differences in attitude to the possible occurrence of NANB Hepatitis infection. By 1980–81, haemophilia doctors saw NANB Hepatitis as a very frequent infection in haemophilia patients but one usually mild in both course and outcome. Haemophilia clinicians had close and continuing contact with their patients and haemophilia care involved frequent testing of patients' blood. Other health professionals saw NANB Hepatitis following blood transfusion as rare and relatively unimportant. That there were these differences was due at least in part to the fact that there had been no appropriate studies of post-transfusion hepatitis in the UK for a decade.

**15.81** Things were, however, beginning to change. By the start of 1981, the UK Advisory Committee on Dangerous Pathogens had been established.<sup>92</sup> In Scotland also, there was some practical progress. In March 1981, Professor Cash, Medical Director, SNBTS, prepared a brief report for discussion by the SNBTS Directors entitled 'Hepatitis and the Transfusion Service'.<sup>93</sup> He proposed that the West of Scotland Centre should be nominated as a Hepatitis Reference Centre and that it should establish and issue the necessary protocols and reagents for effective quality assurance. Provision was made for supervision, procedures and reporting. The report set out specific proposals for optimal collection of plasma, screening for anti-HBs and standards for testing. Professor Cash proposed to ask Professor Zuckerman for advice on the safety of current vaccination preparations. There were specific proposals for infants born of mothers who were chronic HBsAg carriers.

**15.82** The series of US studies referred to above show that, while there was no proof to the standard of the mathematical certainty of a viral aetiology, the clear balance of opinion in the USA was that a viral aetiology for NANB Hepatitis had been established, probably by the end of 1978 and clearly by 1980.<sup>94</sup>

**15.83** The position in the UK is less easy to define. Virologists and public health experts appear to have implicitly accepted in their publications that there was a viral aetiology. Dr Craske's reports adopted that position in August 1978 and it was implicit in his November 1978 paper. The same position can be inferred from the Middlesex Hospital and MRC letters of January and February 1979. The view was explicit in the reason for setting up the Hepatitis Advisory Group in September 1980. The *BMJ* editorial of 4 July 1981 explicitly noted two or more NANB Hepatitis viruses as the main cause of chronic liver disease in haemophilia patients.

**15.84** So far as haemophilia clinicians were concerned, while some may have been less committed to a viral aetiology, most commentators were aligned with Dr Craske. The papers from Bamber, the Haemophilia Unit at the Royal Free Hospital and from Norkrans and colleagues and the *BMJ* editorial all subscribed to a viral aetiology. Dr Craske's third and final report of the Oxford project of the United Kingdom Haemophilia Centre

<sup>92</sup> Minutes of Advisory Group on Hepatitis Meeting, 5 December 1980 [DHF.001.0620]

<sup>93</sup> Hepatitis and The Transfusion Service – Status Report and Proposals for Discussion by SNBTS Directors [SNB.003.5831]

<sup>94</sup> Paragraph 15.30: Tabor and colleagues.

Doctors Organisation (UKHCDO), for 1980–81, as presented to the UKHCDO Hepatitis Working Party in September 1980, referred explicitly to NANB viruses. It was not strongly questioned. The minutes of the Glasgow meeting of the Working Party appear less positive. 'Transaminitis' was not unequivocally accepted to be associated with viral hepatitis. The report as published in 1981 still treated the question of the significance of chronic hepatitis in patients with chronically elevated transaminases as unanswered.

**15.85** Most UK blood transfusion directors still maintained that NANB Hepatitis was a rare condition, seldom seen because they were looking for the wrong thing: acute jaundice. They did, however, acknowledge that a viral aetiology was very probable.

**15.86** The 6th edition of *Diseases of the Liver and Biliary System* by Professor Sheila Sherlock was published in 1981. Excerpts from the book are quoted in the Preliminary Report at paragraphs 6.110–6.114. Significant points made were:

- NANB Hepatitis was largely spread by blood and accounted for about 75% of PTH and possibly 15–20% of sporadic hepatitis; and
- Haemophilia patients receiving factor concentrates obtained from commercial sources were particularly at risk.<sup>95</sup>
- The NANB Hepatitis agent had not been 'conclusively identified' and its identity remained uncertain; and
- The clinical course of the disease progressed to a 'mild, chronic hepatitis' in about a quarter of patients but this usually improved with time although cirrhosis could develop.<sup>96</sup>

**15.87** Professor Sherlock commented that:

Non-A, non-B hepatitis often progresses to a mild chronic hepatitis. The prognosis of this is, at the moment, uncertain but probably benign.<sup>97</sup>

**15.88** Commenting on this edition, Dr McClelland said in oral evidence:

Well, all I can really say to that is that Professor Sherlock was obviously the doyenne of hepatology in the UK at the time. I would assume that in preparing the various successive editions of her textbook, she would have firstly read the literature pretty well and secondly have consulted experts internationally. So I mean this has to be considered as an authoritative view, which may not be the same as being a correct view.<sup>98</sup>

**15.89** By the end of 1981 there had been further advances. However, particularly because there was still no known reliable marker for the putative virus or viruses causing NANB Hepatitis, there was continuing controversy around the natural history of the disease. Differences among professional groups reflected the fact that, by 1981, there was still very little evidence as to the natural history of NANB Hepatitis – whether arising post-transfusion in general medical or surgical contexts or among haemophilia patients.

---

<sup>95</sup> Sherlock S, *Diseases of the Liver and Biliary System*, 1981, Blackwell, Oxford, page 257

<sup>96</sup> Ibid page 258

<sup>97</sup> Ibid page 259

<sup>98</sup> Day 9, page 66

**15.90** The apparent incidence of post-transfusion NANB Hepatitis varied substantially according to the population of blood donors used and to the methods used to detect it, adding to the complexity of the issues. However, positive developments included the following:

- Discussion was beginning concerning ways of reducing post-transfusion hepatitis by using possible surrogate markers to identify blood carrying a high risk of transmitting NANB Hepatitis virus(es). (The subject of 'surrogate markers' – markers, short of a reliable serological test, that might be indicative of infection – is dealt with in Chapter 27, *Surrogate Testing of Donated Blood for non-A, non-B Hepatitis*).
- The first attempts were made at viral inactivation in blood products and the recognition (though not satisfactory resolution) of difficulties of maintaining yield of effective Factor VIII and Factor IX activity during processing, especially with heat treatment methods (dealt with in Chapter 23, *Viral Inactivation of Blood Products for Haemophilia Therapy up to 1985*).
- There was recognition that there was already a problem, namely that the vast majority of severely affected and moderately severely affected haemophilia patients receiving replacement therapy already had been exposed to NANB Hepatitis virus(es) and that many had chronic, although, it was perceived, probably usually mild and asymptomatic, liver disease.

**15.91** At this stage, there was no understanding, or probably even perception, of the less tangible symptoms of lethargy, depression and other neurological symptoms of chronic HCV infection which have come to be understood increasingly over the last 15 years. These symptoms are discussed in Chapter 13, *Knowledge of Viral Hepatitis Now*. At the beginning of the 1980s, and for long thereafter, descriptions of patients as 'asymptomatic' referred to recognised symptoms of significant chronic liver disease, regardless of cause, as they were perceived from time to time. It is now impossible to know what proportion of individuals described as having 'asymptomatic chronic liver disease' did in fact have less tangible, but real, symptoms of disease, since no systematic inquiry was carried out.

**15.92** In the UK, studies based on biopsy findings in haemophilia patients with putative NANB Hepatitis, first published by researchers in Sheffield in 1978, were just beginning to be taken up more widely. Work at Sheffield and the Royal Free Hospital was reported at the 11th meeting of the UKHCDO on 30 September 1980.<sup>99</sup> This would make an impact as the second half of the period progressed.

### **Viral hepatitis 1982–1985**

**15.93** The most pressing issues in the period 1982–85, for those dealing with blood and blood products, were AIDS and the steps taken to tackle that disease. These are more fully discussed elsewhere in this Report.<sup>100</sup> There was increasing apprehension of a disease of epidemic proportions with high mortality. There is at least an element of artificiality in discussing events that had a direct bearing on the developing knowledge of NANB Hepatitis dissociated from the far more pressing background preoccupation with AIDS. As it became accepted that AIDS was a viral disease, the implications of viral infection

<sup>99</sup> Minutes of the Eleventh Meeting of UK Haemophilia Centre Directors Held in Glasgow on 30 September 1980 [SNB.001.7296] at 7304

<sup>100</sup> Chapters 9 and 10, *Knowledge of the Geographical Spread and Prevalence of HIV/AIDS 1 and 2* and Chapter 12, *HIV/AIDS – Response and Clinical Practice*.



more generally, including NANB Hepatitis infection, were inevitably examined in a wider context. However, there were important developments in knowledge of NANB Hepatitis, even while the major preoccupation was with AIDS, and the following discussion seeks to identify and comment on these developments.

**15.94** In the period 1982–85, evidence from biopsy investigation became more significant in promoting an understanding of the natural history of NANB Hepatitis. A number of studies were reported between 1982 and 1985 in which liver biopsies were taken from patients with NANB Hepatitis – both haemophilia patients and those with presumed NANB Hepatitis following blood transfusion. The studies showed that some patients developed cirrhosis.<sup>101</sup> These histological findings of extracted liver samples under microscopic analysis suggested that the disease might be more serious than previously thought, despite the fact that few patients, even among those who developed cirrhosis, otherwise suffered clinical symptoms.

**15.95** Also in this period, studies in England showed that most haemophilia patients who routinely received Factor VIII and Factor IX blood products, whether manufactured by the National Health Service (NHS) or by commercial companies, were likely to develop NANB Hepatitis.<sup>102</sup>

**15.96** Early heat-treated Factor VIII concentrates were developed but were found to transmit NANB Hepatitis notwithstanding heat-treatment.<sup>103</sup> Effective heat-treatment would be developed and brought into the production processes after the end of this period.

**15.97** Throughout this period, the Hepatitis C virus had still to be identified with the result that there was no direct test for the virus or its antibody. Instead, consideration was given to testing blood donations for certain indirect, or surrogate, markers in the blood of donors (particularly elevated ALT and antibody to the Hepatitis B core antigen (anti-HBc) that studies in the USA had indicated might be so closely associated with the development of NANB Hepatitis in recipients as to be indicative of infection).

**15.98** Much of the source material for this period is set out in Chapter 7 of the Preliminary Report. Sources are not repeated here unless it is necessary for an understanding of developing knowledge on particular matters. As before, developments in the USA are noted first.

### ***NANB Hepatitis aetiology and natural history: research in the United States of America***

**15.99** In the USA, published research dealt increasingly with the natural history of NANB Hepatitis. In 1982, there were conflicting reports of biopsy results. A study by Koretz and others of presumed post-transfusion NANB Hepatitis found chronic hepatitis and/or cirrhosis in about a third of patients. There was a significant association of cirrhosis with

<sup>101</sup> The following studies, and the conclusions drawn from them at the time, are more fully discussed below: Realdi (1982), Koretz (1982), Mannucci (1982), White (1982), Stevens (1983), Hay (1985), Aledort (1985).

<sup>102</sup> Fletcher et al, 'Non-A non-B hepatitis after transfusion of factor VIII in infrequently treated patients', *British Medical Journal*, 1983; 287:1754–57 [LIT.001.0239]; Kernoff et al, 'High risk of non-A, non-B hepatitis after a first exposure to volunteer or commercial clotting factor concentrates: effects of prophylactic immune serum globulin', *British Journal of Haematology*, 1985; 60:469–479 [LIT.001.0800]

<sup>103</sup> Informally reported by Professor Mannucci at a meeting of the European Society of Haematology in Barcelona in September 1983. (See Mannucci, 'AIDS, hepatitis and hemophilia in the 1980s: memoirs from an insider', *Journal of Thrombosis and Haemostasis*, 2003; 1:2065–69 [LIT.001.1101] at 1104) and subsequently published by Colombo et al, 'Transmission of [NANB Hepatitis] by heat-treated factor VIII concentrate', *The Lancet*, 1985; 2:1–4 [LIT.001.0369]

those who had persistently abnormal ALT values.<sup>104</sup> They reported that cirrhosis developed in a clinically silent fashion and usually only after years of virus activity. In another 1982 paper, RJ Gerety and DL Aronson reported progression to chronic hepatitis characterised by widely fluctuating serum aminotransferase levels and histologically severe liver disease in a high proportion of infected individuals and referred to similar findings by Pier Mannucci.<sup>105</sup>

**15.100** In contrast to these reports, the study by Gilbert C White and others of 15 haemophilia patients with intermittently (not persistently) raised ALT, values found no suggestion of chronic liver disease.<sup>106</sup> They reported that liver biopsies showed chronic persistent hepatitis or other mild forms of liver disease including mild chronic portal inflammation. The authors concluded:

The high frequency of liver function abnormalities in patients with hemophilia coupled with biopsy evidence of chronic active hepatitis and the documentation of progression to cirrhosis have led some authors to question current policies of replacement with concentrates of factor VIII for some patients. While some patients, primarily those with moderately severe and severe enzyme elevations, will have histologic evidence of chronic active hepatitis and/or cirrhosis, the results of the present study indicate that a larger proportion of patients will have milder degrees of enzyme abnormalities and predominantly chronic persistent hepatitis or milder forms of liver disease. Thus, for many transfusion-requiring hemophiliacs, the frequent exposure to factor VIII concentrates is not accompanied by the development of the more severe forms of chronic liver disease.<sup>107</sup>

**15.101** A review by Dienstag in 1983 concluded that after transfusion with blood or blood products, as many as 40–60% of patients with acute NANB Hepatitis would have chronic elevations of serum aminotransferase activity, often in a fluctuating pattern, and histologic features of the liver consistent with chronic active hepatitis, with approximately 10–20% of chronic cases eventuating in cirrhosis.<sup>108</sup>

**15.102** Against this uncertain background, regulators were cautious. The issue of *Morbidity and Mortality Weekly Report (MMWR)*, the journal of the US Centers for Disease Control (CDC), of 7 June 1985 set out a fairly comprehensive statement of current knowledge in the USA of hepatitis viruses and diseases, with guidance on protection against viral hepatitis, including vaccination.<sup>109</sup> Reflecting only established scientific knowledge, the treatment of NANB Hepatitis was brief. The paper noted that the epidemiological characteristics of NANB Hepatitis were similar to those of Hepatitis B, occurring most commonly following blood transfusion and parenteral (injecting) drug use. Multiple episodes had been observed in the same individuals and were thought to have perhaps been due to different agents. Chronic hepatitis following acute NANB Hepatitis infection varied in frequency from 20%

<sup>104</sup> Koretz et al, 'Non-A, non-B transfusion hepatitis: Disaster after decades?', *Hepatology*, 1982; 2:687 [LIT.001.3738]; Preliminary Report para 7.11

<sup>105</sup> Gerety and Aronson, 'Plasma derivatives and viral hepatitis', *Transfusion*, 1982; 22:347–351 [LIT.001.5510]; Mannucci et al, 'A clinicopathological study of liver disease in haemophiliacs', *Journal of Clinical Pathology*, 1978; 31:779–783 [LIT.001.1624]. Preliminary Report paragraphs 7.23 – 7.25.

<sup>106</sup> White et al, 'Chronic hepatitis in patients with hemophilia A: Histologic studies in patients with intermittently abnormal liver function tests', *Blood*, 1982; 60:1259–1262 [LIT.001.0535] Preliminary Report paragraphs 7.29–7.30

<sup>107</sup> *Ibid* [LIT.001.0535] at 0538

<sup>108</sup> Dienstag, 'Non-A, Non-B Hepatitis: I. Recognition, Epidemiology, and Clinical Features', *Gastroenterology*, 1983; 85:439–462 [LIT.001.1239] and Dienstag, 'Non-A, non-B Hepatitis: II. Experimental Transmission, Putative Virus Agents and Markers, and Prevention', *Gastroenterology*, 1983; 85:743–768 [LIT.001.1213] Preliminary Report paragraph 7.36

<sup>109</sup> *MMWR* 7 June 1985 [LIT.001.0465]

to 70%. Experimental studies in chimpanzees had confirmed the existence of a carrier state which might be present in up to eight per cent of the population.<sup>110</sup> There were no recommendations for action, although other US comment was more forthright.

**15.103** The tentative views set out in the *MMWR* proved to be incorrect in certain respects. The conclusion that apparent multiple episodes of NANB Hepatitis in the same individuals might be due to different agents would turn out to be incorrect. Also incorrect was the speculation that a carrier state might be present in up to 8% of the general population. It is important, however, to emphasise that these were views of recognised experts and represented advanced thinking based on the data that CDC, reasonably in the circumstances, considered to be reliable.

**15.104** In 1985 Dr Alter of the NIH set out what was known, in his view, about post-transfusion hepatitis at that time.<sup>111</sup> His report provides an important point of reference on this topic. In relation to the natural history of NANB Hepatitis, he stated that the importance of the disease was not in its acute manifestations but in its chronic sequelae, the long-term abnormal conditions resulting from the disease. An 'astounding' number of cases progressed to chronic hepatitis, as judged by persistent ALT elevations. There was accumulating evidence that some cases progressed to severe chronic liver disease. At least 10% of patients who developed chronic ALT elevations following acute post-transfusion hepatitis progressed to cirrhosis. His view was that if these findings were validated, then the clinical implications of NANB Hepatitis were somewhat more serious than previously anticipated. This view was shared by some US specialists but was not universally endorsed by US haemophilia clinicians and other specialists.

**15.105** In August 1985 Louis Aledort and colleagues (from different disciplines in New York and other international centres) reported on the largest study at the time of liver biopsies and liver disease among patients with haemophilia.<sup>112</sup> Dr Aledort was one of the doyens of US haemophilia (and hence world haemophilia) specialists. The other authors represented some of the world's leading and best liver pathologists (from the USA, the UK, Belgium and Switzerland) and at least one leading US clinical liver specialist. Although this paper was published in August 1985, it is of interest that it was submitted for publication on 5 July 1983 and that parts of it were presented at a meeting towards the end of 1981, according to a note in the paper.<sup>113</sup> Liver samples and associated clinical data were collected from 155 patients from haemophilia centres in the USA and Western Europe. For 115 there were reports of liver biopsies and for the remaining 40 there were autopsy findings.

**15.106** The authors reported that in those subjects with haemophilia the incidence of cirrhosis (15%) and chronic active hepatitis (7%) was lower than previously reported. The frequency of severe liver disease (chronic active hepatitis or cirrhosis) in patients receiving large pooled concentrates was no greater than in patients treated principally with cryoprecipitate or plasma. This had not originally been predicted since patients receiving cryoprecipitate or plasma were exposed to far fewer donors per dose as compared to those receiving concentrate. The finding led the authors to conclude that there appeared

<sup>110</sup> Ibid [LIT.001.0465] at 0478

<sup>111</sup> Alter, 'Posttransfusion hepatitis: clinical features, risk and donor testing' in Liss, AR (ed) *Infection, Immunity and Blood Transfusion*, 1985, 47–61 [LIT.001.1822]. Preliminary Report paragraphs 7.70–7.75

<sup>112</sup> Aledort et al, 'A study of liver biopsies and liver disease among haemophiliacs', *Blood*, 1985; 66:367–372 [LIT.001.0505]. Preliminary Report paragraphs 7.83 and 7.84

<sup>113</sup> Presented in part at the American Society of Hematology meeting, San Antonio, Tex December 1981.

to be no indication to alter current therapy patterns because of concern over plasma product-related liver disease. It was acknowledged that the comparative lack of severity of the histopathological findings in the materials studied might not be entirely reassuring in the light of other recent findings.<sup>114</sup> In retrospect, the reservations underestimated the seriousness of the potential progression of the disease, but the assessment reflected a common view at the time among haemophilia specialists.

**15.107** The difference of opinion apparent in these reports reflected differences of experience and approach. Dr Aledort (and other haemophilia clinicians in the USA and Europe) had seen the transformative effect of factor concentrates on the lives of patients and had good reason to take a sanguine view of the possible adverse effects of NANB Hepatitis. Dr Alter, Dr Dienstag (two leading US authorities in their field) and others were, however, beginning to understand that what they saw of post-transfusion NANB Hepatitis in liver biopsies might represent a serious cause for concern.

**15.108** Dr Dienstag and Dr Alter reviewed the position reached in 1986, after the publication of hundreds of articles. Acknowledging at the outset that 'our understanding of NANB hepatitis is still unsettled and evolving...' and that '[s]trikingly clear is just how much we do not know about NANB hepatitis', they wrote presciently:

In the decade since its discovery, the concept of NANB hepatitis has evolved from that of a benign elevation of aminotransferase activity to that of a serious disease with significant long-term consequences. The longer patients are followed, the more obvious it becomes that [chronic active hepatitis] and cirrhosis are a very real part of the natural history of NANB hepatitis.<sup>115</sup>

**15.109** Since the recognition of NANB Hepatitis as a distinct form of viral hepatitis, studies had shown biochemical evidence of chronic hepatitis in approximately 50% of cases related to transfusion. Among those with chronic ALT elevations who were biopsied, approximately 60% had chronic active hepatitis, cirrhosis, or both. Overall, 10–20% of those with chronic ALT elevations had cirrhosis on initial or repeat biopsy.<sup>116</sup> Among cases described in published reports, of 20 patients in whom cirrhosis had developed after transfusion, five had died of liver failure. The finding in Dr Aledort's study<sup>117</sup> of liver biopsies from persons with haemophilia, that cirrhosis had developed in 15% of patients, a prevalence similar to that obtained in non-haemophilia, transfused populations, was said to be alarming. Dienstag and Alter commented:

Although there is a divergence of opinion as to the progressive nature of ... histologic abnormalities in hemophiliacs, a substantial proportion of these patients end up with cirrhosis, an unequivocal histologic diagnosis that leaves little room for argument....<sup>118</sup>

**15.110** The authors noted, furthermore, that indirect evidence for an association between NANB Hepatitis and hepatocellular carcinoma (liver cancer) was beginning to accumulate.<sup>119</sup>

<sup>114</sup> Aledort et al, 'A study of liver biopsies and liver disease among haemophiliacs', *Blood*, 1985; 66:367–372 [LIT.001.0505] at 0510

<sup>115</sup> Dienstag and Alter, 'Non-A, non-B hepatitis: Evolving epidemiologic and clinical perspective', *Seminars in Liver Disease*, 1986; 6:67–81 [LIT.001.1675] at 1679

<sup>116</sup> *Ibid* [LIT.001.1675] at 1680

<sup>117</sup> Aledort et al, 'A study of liver biopsies and liver disease among hemophiliacs', *Blood*, 1985; 66:367–372 [LIT.001.0505]

<sup>118</sup> Dienstag and Alter, 'Non-A, non-B hepatitis: Evolving epidemiologic and clinical perspective', *Seminars in Liver Disease*, 1986; 6:67–81 [LIT.001.1675] at 1682

<sup>119</sup> *Ibid* [LIT.001.1675] at 1682

**15.111** On 20 June 1986, the *MMWR* reported 13 cases of NANB Hepatitis among patients who had undergone cardiovascular surgery and, because of bleeding during surgery, had received Factor IX produced by Alpha Therapeutic Corporation.<sup>120</sup> The report noted that clotting factor preparations had frequently been linked to the transmission of NANB Hepatitis. In haemophilia patients who routinely received commercial factor preparations, episodes of NANB Hepatitis were common: as many as 50% were observed to go on to develop signs of chronic liver disease. Studies in first-exposed haemophilia patients and in surgical patients who received clotting factor preparations, suggested that the risk of NANB Hepatitis might be close to 100%.<sup>121</sup>

**15.112** The balance was moving towards the views of Dr Alter and his colleagues.

### *NANB Hepatitis aetiology and natural history: UK and other research*

**15.113** The discussion of reported research from sources other than those from the USA is necessarily more diffuse and it is difficult to form a view of the circulation and acceptability of other opinion from outside the UK in this period. As with the US source material, much of the relevant published research is described in Chapter 7 of the Preliminary Report and is not repeated in this chapter unless necessary.

### **Haemophilia**

**15.114** In the UK, Dr Gunson's report to the European Health Committee of the Council of Europe on 25 June 1982 commented that there appeared to be a low contamination rate of NANB Hepatitis in the UK in patients receiving cryoprecipitate but a high rate following transfusion of Factor VIII concentrates prepared from large pools.<sup>122</sup> He suggested that avoiding the use of large-pool fractions for those with mild coagulation defects was a practical way of reducing the incidence of post-transfusion NANB Hepatitis. The discussion that followed did not deal with the natural history of infection.

**15.115** Comment on the natural history of NANB Hepatitis came in September 1982 when Mannucci and colleagues published a follow-up to their 1978 report on liver disease in haemophilia patients.<sup>123</sup> One patient had died of gastrointestinal bleeding. Four of the remaining 10 patients continued to have chronic persistent hepatitis, two had developed chronic lobular hepatitis and there was spontaneous improvement of disease activity in three cases. The majority were asymptomatic. The emphasis in the authors' comments was similar to that reported by Aledort and colleagues. Progressive disease was not the rule in haemophilia patients with chronic NANB Hepatitis and only two patients had died from cirrhosis. This view was supported by data from the UKHCDO which showed that apparently only two haemophilia patients had died of cirrhosis in the UK between 1976 and 1980.<sup>124</sup>

**15.116** At that stage, it was thought that there was no evidence that chronic liver disease was a prominent cause of morbidity and death in haemophilia patients. The authors speculated that the course of chronic liver disease in those patients who had progressive

<sup>120</sup> 'Epidemiological notes and reports of non-A, non-B hepatitis associated with a Factor IX infusion during cardiovascular surgery – Arizona', *Morbidity and Mortality Weekly Report*, 1986; 35:391–394 [LIT.001.3782]

<sup>121</sup> *Ibid* [LIT.001.3782] at 3783

<sup>122</sup> Dr Gunson's report [SGF.001.1983] at 1985; Preliminary Report paragraph 7.19

<sup>123</sup> Mannucci et al, 'Nonprogressive course of non-A, non-B chronic hepatitis in multitransfused hemophiliacs', *Blood*, 1982; 60:655–658 [LIT.001.0543] Preliminary Report paragraphs 7.21 and 7.22

<sup>124</sup> Rizza et al, 'Treatment of haemophilia and related disorders in Britain and Northern Ireland during 1976-80: report on behalf of the directors of haemophilia centres in the United Kingdom', *British Medical Journal*, 19 March 1983 [LIT.001.0234]

disease might be unfavourably influenced by their continuous exposure to blood-borne viruses and by repeated and long-lasting challenge by allogenic plasma proteins transfused in the concentrates, a suggestion that was also to become prominent in relation to AIDS in the early stages of study of that disease.<sup>125</sup>

**15.117** An official from the Public Health Laboratory Service (PHLS) wrote to the DHSS on 10 January 1983, enclosing the terms of a letter which it was proposed to send to *The Lancet*.<sup>126</sup> The draft commented:

There is no evidence of which we are aware that indicates that re-exposure to non-A, non-B hepatitis viruses present in concentrates received by patients with severe coagulation defects predisposes them to a higher incidence of serious chronic liver disease than patients with mild disease who receive less frequent transfusions. If the 'hepatitis reduced' concentrates prove to be associated with a reduced risk of non-A, non-B hepatitis with an insignificant loss of factor VIII activity, then these products should be reserved in the first instance for patients with no prior exposure to factor VIII concentrates or those who have received less than 5 batches of factor VIII in the past. Similar considerations would apply to NHS factor IX concentrate, but we have as yet no accurate information concerning the risk of non-A, non-B hepatitis associated with NHS factor IX concentrate. Another study in patients undergoing open heart surgery reported an attack rate of 100% non-A, non-B hepatitis related to transfusions of factor IX concentrate, whereas an attack rate of 3% was reported in patients who received transfusions of whole blood only.<sup>127</sup>

**15.118** It appears that the cut-off point of five batches was an empirical idea not, at that stage, based on rigorous scientific analysis. In a practical sense it provided a ready test of whether a patient had been infrequently transfused. The official's comments were reasonably consistent with the predominant view among haemophilia doctors in the UK in 1982–83 (with the exception of Preston and colleagues).<sup>128</sup> Haemophilia doctors increasingly recognised the high frequency of NANB Hepatitis infection but still considered its clinical consequences to be benign.

**15.119** Among haemophilia experts, significant comment on the natural history of NANB Hepatitis was advanced with the publication in 1983 of the paper by Richard Stevens and others reporting on their study of 12 haemophilia patients in Manchester, 'Liver disease in haemophiliacs: an overstated problem?'<sup>129</sup> All patients were multi-transfused and all had persistently abnormal liver function tests. Otherwise, patient selection was random. The historical background that effectively set out the position challenged, as reported by Mannucci, Lesesne, Preston, Spero, Schimpf and others, was said to be:

The increasing use of plasma products has resulted in an improved quality of life for many haemophiliacs. However, over the past decade there have been reports of a high prevalence of abnormal liver function tests in multitransfused haemophiliacs. Liver biopsies carried out in such patients have been reported as

<sup>125</sup> The 'immune overload hypothesis' is discussed, in the context of HIV/AIDS, in Chapter 11, *AIDS Aetiology*.

<sup>126</sup> Covering letter dated 10 January 1983 [DHF.001.7106]

<sup>127</sup> Risk of Contracting Factor VIII Associated Non-A Non-B Hepatitis After First Exposure to Large Pool Concentrates – Implications for Trials of Hepatitis Reduced Factor VIII and IX [DHF.003.0064] at 0065

<sup>128</sup> Preston et al, 'Blood product concentrates and chronic liver disease', *The Lancet*, 6 March 1982 [LIT.001.0398]

<sup>129</sup> Stevens et al, 'Liver disease in haemophiliacs: an overstated problem?' *British Journal of Haematology*, 1983;55:649–655 [LIT.001.0008]; submitted 12 January and accepted for publication 3 June 1983. Preliminary Report paragraph 7.37

showing that up to half the cases are associated with abnormal liver histological appearances including chronic active hepatitis.<sup>130</sup>

**15.120** The outcome of the Stevens study was different. Only one patient showed evidence of severe chronic active hepatitis with progression to cirrhosis although a further four patients showed some evidence of mild chronic active hepatitis. On the basis of their findings, the authors stated that the results represented a much lower incidence of severe histological liver damage than many previous reports. They suggested that the true incidence of severe histological liver abnormality in multi-transfused haemophilia patients might be less than previously reported but similar to the more recent results of 115 liver biopsies carried out worldwide by Dr Aledort and colleagues.<sup>131</sup>

**15.121** At the beginning of 1983, pharmaceutical companies continued with practical preparations for the introduction to the market of modified products, reflecting the underlying view that the agent of transmission was a virus that was susceptible to inactivation. It was anticipated in government that the companies would seek to avoid the requirement for a formal clinical trial by the use of transfusions on a named patient basis (an expanded access programme for as-yet unlicensed drugs).<sup>132</sup>

**15.122** On 28 September 1983 Dr Craske produced the Annual Report for 1982–83 of the UKHCDO Hepatitis Working Party.<sup>133</sup> The report referred to the Oxford study, started in 1981, of hepatitis in infrequently treated haemophilia patients.<sup>134</sup> The findings had confirmed that the risk of contracting NANB Hepatitis from Factor VIII concentrates on first exposure was 100%, whether NHS or commercial Factor VIII was used. An internationally based trial of Hyland/Travenol's heat-treated Factor VIII (Hemofil T)<sup>135</sup> had commenced and an Armour heat-treated product (Factorate HT)<sup>136</sup> would soon be available for evaluation. Mannucci had already announced at the European Society of Haematology that the Hyland product transmitted NANB Hepatitis.<sup>137</sup> The problem of AIDS had begun to overshadow these developments, however. Directors required to consider the ethical problem of exposing persons with mild haemophilia to commercial material. The ethical problem was expressed as follows:

Since the only way of ensuring the susceptibility to non-A, non-B viruses is by using patients who have not previously received factor VIII or IX concentrate, a choice will have to be made between using heat treated products from commercial sources, which might carry a small risk of AIDS transmission, or using NHS concentrate which appears to carry a 100% chance of transmitting non-A, non-B hepatitis.<sup>138</sup>

<sup>130</sup> Stevens et al, 'Liver disease in haemophiliacs: an overstated problem?' *British Journal of Haematology*, 1983; 55:649–655 [LIT.001.0008]

<sup>131</sup> Aledort et al, 'A study of liver disease among haemophiliacs', *Blood*, 1981; 58:1 210a [LIT.001.0505]

<sup>132</sup> UK Haemophilia Centre Directors Hepatitis Working Party report: 'Factors to be Considered in the Selection of Hepatitis Reduced Products for Clinical Trial – Evaluation of Residual Inactivity for Hepatitis Viruses' [DHF.002.8965]

<sup>133</sup> Annual Report 1982/3 [SNF.001.0948]; Preliminary Report paragraph 7.45

<sup>134</sup> Subsequently reported by Fletcher et al, 'Non-A non-B hepatitis after transfusion of factor VIII in infrequently treated patients', *British Medical Journal*, 1983;287:1754–1757 [LIT.001.0239]

<sup>135</sup> Dry heat treated at 60°C for 72 hours.

<sup>136</sup> Dry heat treated at 60°C for 30/36 hours.

<sup>137</sup> Evidence of Professor Mannucci to the Lindsey Tribunal of Inquiry in Eire (noted at page 62 of the Tribunal's report) <http://health.gov.ie/blog/publications/report-of-the-tribunal-of-inquiry-into-the-infection-with-hiv-and-hepatitis-c-of-persons-with-haemophilia-and-related-matters/>. Travenol was part of the Baxter Group. The results were published in 1985: Colombo et al, 'Transmission of non-A, non-B hepatitis by heat-treated factor VIII concentrate', *The Lancet*, 1985; 2:1–4 [LIT.001.0369]

<sup>138</sup> UK Haemophilia Working Party Annual Report 1982/3 [SNF.001.0948] at 0952; Preliminary Report, paragraph 7.45

**15.123** The report also referred to the Behringwerke heat-treated product mentioned above (paragraph 15.48).

**15.124** A report of the Oxford study was published on 10 December 1983.<sup>139</sup> The factual information presented was the same in all material respects as Dr Craske's report to the UK Haemophilia Hepatitis Working Party on 28 September 1983.

**15.125** The Discussion section of the published study included the following observations:

This study shows a high incidence of non-A non-B hepatitis in patients treated with factor VIII who had either not received it previously or had received it only infrequently. All of those who received commercial concentrates developed hepatitis regardless of their transfusion history; those who received NHS factor VIII were less likely to develop hepatitis if they had been treated before. All nine patients who received NHS factor VIII for the first time developed hepatitis, while only eight out of the 15 who had received it previously did so .... It may be that the pool size of NHS concentrates has now increased to the point where the benefit conferred by using plasma from volunteer donors has been lost.<sup>140</sup>

**15.126** The discussion indicated the basis for many of the assertions of risk that were made at about this time and for some time thereafter. The fact that all nine 'virgin' patients developed NANB Hepatitis was the basis of the view that the exposure of new patients to Factor VIII concentrates, of UK origin or otherwise, carried a '100%' risk. The conjecture that the pool size of NHS concentrates may by then have increased to the point where the benefit conferred by using plasma from volunteer donors had been lost reflects the same attitude. These were important observations at the time.

**15.127** In an accompanying *BMJ* editorial,<sup>141</sup> Dr Jones (Newcastle Haemophilia Centre) stated that liver function tests were 'abnormal in most severely affected haemophiliacs who have had repeated transfusions'. Most post-transfusion hepatitis was now thought to be NANB. Despite the gloomy observations of others, he thought that probably most of the observed changes in liver function represented chronic persistent (perceived to be non-progressive) rather than chronic active (and progressive) hepatitis. Mortality from liver disease remained low. Life expectancy in haemophilia was near normal, due entirely to the widespread introduction of Factor VIII concentrates and comprehensive care.

**15.128** It is apparent that by the end of 1983 haemophilia specialists and the medical profession generally had been informed that UK Factor VIII concentrate was highly likely to transmit NANB Hepatitis virus(es) in a majority of those previously transfused and in every person transfused with Factor VIII for the first time. With the benefit of hindsight, however, some commentators were in error as to the long-term prognosis. Because they did not understand the natural history of NANB Hepatitis they thought that it could be inferred, from the observations over the year following infection which showed that most liver tests stabilised and no one remained very 'ill' with hepatitis, that NANB Hepatitis was unlikely to be a serious, long-term problem. That was despite the voices from Sheffield

<sup>139</sup> Fletcher et al, 'Non-A non-B hepatitis after transfusion of factor VIII in infrequently treated patients', *British Medical Journal*, 1983; 287:1754–57 [LIT.001.0239]. Preliminary Report paragraphs 7.50 and 7.51.

<sup>140</sup> Ibid [LIT.001.0239] at 0241

<sup>141</sup> Jones, 'Acquired immunodeficiency syndrome, hepatitis, and haemophilia', *British Medical Journal*, 1983; 287:1737–38 [LIT.001.0243]



suggesting that this might not be the case and the prevalence of chronic active hepatitis (known by liver doctors to carry a risk of progression), with or without cirrhosis, in 20–35% of the haemophilia patients whose biopsy results had been reported in the series of published studies.

### Post-transfusion hepatitis

**15.129** As in the USA, early reports of post-transfusion hepatitis in this period were associated with major surgical procedures. In 1982, a five-year study by Giuseppe Realdi and others (Padua, Italy) on post-transfusion hepatitis was reported as showing that five of 21 patients with post-transfusion hepatitis followed for five years or more developed cirrhosis.<sup>142</sup>

**15.130** In 1983 the 7th edition of Patrick Mollison's standard textbook on blood transfusion medicine in the UK was published.<sup>143</sup> In a discussion of NANB Hepatitis, it was noted that:

As a rule, non-A, non-B hepatitis is symptomatically mild. Patients seldom need to be admitted to hospital. Nevertheless, up to 60% of cases have abnormal [ALT] levels for more than 1 year; if a liver biopsy is taken, most of the cases show histological evidence of a significant chronic liver disease and approximately 10% show features of cirrhosis.<sup>144</sup>

**15.131** The textbook noted the results<sup>145</sup> of the USA-based TTV Study of 1981:

Although non-A, non-B hepatitis develops in some patients who have received only blood from donors with normal ALT levels, it can be deduced that at least 21% of cases of transfusion-associated hepatitis might be prevented by excluding only 3% of the present donor population ....<sup>146</sup>

**15.132** It was also noted by Mollison that the minimum carrier rate of the NANB Hepatitis virus in volunteer blood donors in the USA had been estimated to be 1.6% and in commercial blood donors to be 5.4%.<sup>147</sup> The textbook further noted that there was evidence that non-A, non-B viruses played a smaller part in the UK than in the USA.<sup>148</sup>

**15.133** At the meeting of the UK Blood Transfusion Services' Working Party on Transfusion Associated Hepatitis on 27 September 1983, there was discussion of 'apparent non-A non-B hepatitis-like illnesses' in patients receiving high doses of intravenous human normal immune globulin.<sup>149</sup> Incidence of infection was higher than in intramuscular infusion, the other standard route of delivery. The signs noted were early transaminitis. Dr Thomas

<sup>142</sup> Realdi et al, 'Long-term follow-up of acute and chronic non-A, non-B post-transfusion hepatitis: evidence of progression to liver cirrhosis', *Gut*, 1982; 23:270–275 [LIT.001.0528]. Preliminary Report, paragraph 7.10 gives further details

<sup>143</sup> Mollison, *Blood Transfusion in Clinical Medicine*, 7th edition, 1983, Blackwell Scientific Publications. This was to be the last edition edited by Mollison. The standard text has retained his name in subsequent editions.

<sup>144</sup> Ibid page 773. For this statement, Mollison cited Alter, 'The dominant role of non-A, non-B in the pathogenesis of post-transfusion hepatitis: a clinical assessment', *Clinics in Gastroenterology*, 1980;9:155–170 [LIT.001.3717]

<sup>145</sup> Aach et al, 'Serum alanine aminotransferase of donors in relation to the risk of non-A, non-B hepatitis in recipients: the transfusion-transmitted viruses study', *New England Journal of Medicine*, 1981; 304:989–994 [LIT.001.0753]; Holland et al, 'Post-transfusion viral hepatitis and the TTVS', *New England Journal of Medicine*, 1981; 304:1033–35 [LIT.001.1630]

<sup>146</sup> Mollison, *Blood Transfusion in Clinical Medicine*, 7th edition, 1983, Blackwell Scientific Publications, page 773

<sup>147</sup> Ibid page 774. Reference to Blum and Vyas, 'Non-A, non-B hepatitis: a contemporary assessment', *Haematologia*, 1982; 15:162–183 [LIT.001.1106]

<sup>148</sup> Mollison, *Blood Transfusion in Clinical Medicine*, 7th edition, 1983, Blackwell Scientific Publications, page 774; Preliminary Report, paragraphs 7.31–7.33

<sup>149</sup> Human normal immune globulin is a therapeutic product which provides antibodies to Hepatitis A, rubella, measles and other viruses for specific types of patient; broad-spectrum passive protection to premature babies; broad-spectrum protection for immunocompromised patients; and other beneficial uses. Importantly for this discussion, it is a product prepared from moderate-to-large plasma pools (often containing 1000 donations or more).

thought that the picture was similar to that seen of commercial Factor VIII concentrates from the USA.<sup>150</sup>

**15.134** There were several published reports on these patients.<sup>151</sup> The most relevant for present purposes is a paper by Dr Andrew Lever and others, published much later, on 10 November 1984.<sup>152</sup> They reported that the illnesses were acute NANB Hepatitis, clinically and histologically identical to the short-incubation NANB Hepatitis seen in haemophilia patients receiving Factor VIII concentrates. The comments made included the then common view that there were at least two parenterally transmitted NANB Hepatitis viruses with different incubation periods. In relation to the natural history of the postulated short incubation form of the disease, it was stated that the disease was usually mild during the acute phase but that a large proportion, usually greater than 80%, would go on to acquire chronic lesions, sometimes culminating in cirrhosis. Of the postulated long-incubation type, the paper stated that it was also a mild illness, but 20–40% of patients still had abnormal liver function progressing sometimes to cirrhosis.

**15.135** Leaving aside the distinction between the types, later disproved, the paper placed a new stress on the natural history of the disease and a growing appreciation in the UK of the potential for serious outcomes associated with NANB Hepatitis infection. Given the date of its publication, the paper may have had more significance for the general dissemination of knowledge in the next sub-period, 1984–1985, but the commentary is illustrative of the views of this group of UK experts at about the end of 1983. The paper made a further comment of some importance:

[T]he finding that the virus can be transmitted in [human normal immune globulin] concentrates suggests either that the general population has a very low level of antibodies to the putative virus or that such antibodies are not virus-neutralising.<sup>153</sup>

**15.136** The second proposition was correct and the first was not irrelevant to other work at the time. A prospective study of post-transfusion hepatitis in patients undergoing heart surgery, reported in November 1983, found that the incidence of post-transfusion NANB Hepatitis after cardiac surgery was low compared with similar studies in other countries, suggesting that blood transfusion using blood collected locally from volunteers rarely led to clinically significant chronic liver disease.<sup>154</sup>

### 1984–1985

**15.137** The next two years saw some convergence of opinion among experts from a number of groups. The National Institute for Biological Standards and Control (NIBSC) met on 9 February 1984 to discuss the infectious hazards of blood products.<sup>155</sup> This important body gave scientific advice to the UK licensing authority and to the Committee on the Safety of Medicines. The importance of the meeting lay in bringing together a range of

<sup>150</sup> Notes of the Minutes of the UK Working Party on Transfusion Associated Hepatitis Held at Edgware on Tuesday 27 September 1983 [SNB.001.3443] at 3444–45

<sup>151</sup> Preliminary Report paragraphs 7.44 and 7.47.

<sup>152</sup> Lever et al, 'Non-A, non-B Hepatitis Occurring in Agammaglobulinaemic Patients after Intravenous Immunoglobulin', *The Lancet*, 1984; 1062–64; [LIT.001.0449]

<sup>153</sup> Ibid [LIT.001.0449]

<sup>154</sup> Collins et al, 'Prospective study of post-transfusion hepatitis after cardiac surgery in a British centre', *British Medical Journal*, 1983; 287:1422–24 [LIT.001.0212]. The incidence was 14.6% in one study in the USA, in Italy 17.8%, in Sweden 18.9% and 30.4% in Japan. A study in the Netherlands had found a low incidence of post-transfusion NANB Hepatitis (3.4%) which was closely comparable with the results of the Newcastle study. Preliminary Report paragraph 7.48

<sup>155</sup> NIBSC Meeting Minutes [SNB.004.8628]; Preliminary Report, para 7.55

presentations by specialist contributors. There were a number of significant contributions from those whose views had already influenced opinion in specialist forums.

**15.138** Dr Thomas (NIBSC) commented on the finding that the first exposure to factor concentrate, from whatever source, was associated with 100% infectivity with NANB Hepatitis. Dr Craske (PHLS, Manchester) provided data on the incidence of jaundice in persons with haemophilia in the UK from 1969 to 1979, and on the prevalence of NANB Hepatitis in the haemophilia population. Dr McClelland (SNBTS, Edinburgh) presented statistical data on the risk to haemophilia patients of transmitting NANB Hepatitis by blood transfusion and factor therapy. In discussion, Dr Eibl (Imuno, Vienna) commented on European experience of managing the blood donation programme. Dr Lane (BPL, Elstree) and Dr Schild (NIBSC) gave information about current work by fractionators aimed at minimising infectious hazards. There were no executive decisions relating to NANB Hepatitis but the NIBSC had collected much relevant information which would be available to government and to the bodies the NIBSC advised. It was an important stage in the development of information available to inform decision-making bodies in the UK.

### Haemophilia

**15.139** On 9 January 1984 a report was prepared by the Blood Products Sub-Committee of the Haemophilia Society which reviewed the policy of the Society in relation to the supply of blood products in the UK.<sup>156</sup> It was recorded that the main ground for believing that British-made products were medically preferable to imported products had been the greater risk of hepatitis infection, particularly Hepatitis B infection, from imported products. Improved screening for anti-HBV and improved donor selection procedures employed by manufacturers had resulted in commercial material being of comparable standard to NHS material.<sup>157</sup> The report commented that:

- Hepatitis B remained a transfusion hazard.
- Regarding the risk of NANB Hepatitis, recent developments suggested that UK material was no better (and might be worse) than imported material.

**15.140** In light of the discussion, the Sub-Committee suggested that there was no continuing reason to prefer NHS products. A manuscript note on a copy of the report said that this view would not help convince Regional Health Authorities (in England and Wales) to use the NHS product.

**15.141** Trials of the new, possibly safer, imported products became an important topic for Haemophilia Directors. Details are set out in the Preliminary Report and need not be repeated in full.<sup>158</sup> On 29 March 1984, the Chairmen of the UKHCDO and its Hepatitis Working Party asked for cooperation between the Haemophilia Centre Directors in coordinating trials of the new heat-treated blood products.<sup>159</sup> The base-line information on transmission was that there was still a 63% infection rate of NANB Hepatitis on first exposure in patients who had not previously received Factor VIII concentrate.

<sup>156</sup> Haemophilia Society Blood Products Sub-committee Report [DHF.001.5151]

<sup>157</sup> This was a reference to the Oxford study: Fletcher et al, 'Non-A non-B hepatitis after transfusion of factor VIII in infrequently treated patients', *British Medical Journal*, 1983; 287:1754-57 [LIT.001.0239] Preliminary Report paragraph 7.54

<sup>158</sup> Preliminary Report, paragraphs 7.57, 7.58

<sup>159</sup> Memo [DHF.002.8963]

**15.142** On behalf of the UKHCDO, Dr Craske proceeded to coordinate a prospective study of hepatitis in previously infrequently treated haemophilia patients.<sup>160</sup> By that stage, clinical trials had been completed on only one product. A total of eight products were in preparation or available for trial, including two NHS Factor VIII concentrates. Dr Craske sought the cooperation of Directors in identifying suitable patients for coordinated trials.

**15.143** In reply to the UKHCDO's request for cooperation in entering suitable patients into trials, Professor Christopher Ludlam (Edinburgh Haemophilia Centre) replied that he wished to reserve places for any patients he might have, for testing Scottish product.<sup>161</sup> His patients constituted a group that had been treated consistently with PFC Factor VIII and he was unwilling to jeopardise the advantages of their selection for study exclusively in relation to the Scottish product by exposing them to imported products. Professor Cash was anxious to have a study carried out in the West of Scotland.<sup>162</sup> He wished to assess the incidence of hepatitis and transaminitis in 'virgin' (previously untreated) haemophilia patients who received SNBTS 'hepatitis reduced' Factor VIII by coordinated clinical trials. There were, however, few qualifying patients in Scotland as a whole at the time, or in any given period, available for the sort of study proposed by Professor Cash. The study was aimed at collecting information about what was clinically essential treatment for these patients. Most existing patients receiving factor concentrates for haemophilia therapy had by this date been infected with NANB Hepatitis. Only new patients requiring treatment by factor concentrates for the first time, might benefit if the modified product was effective in removing or reducing the risk of transmission. They constituted a small group at any given time.

**15.144** These studies and proposed studies treated NANB Hepatitis as a threat to the health of haemophilia patients that had to be dealt with. They were not primarily concerned with the natural history of the disease or with the analysis of its progression. At this stage, one way of tackling the risk was the development of effective virus-inactivated products. That depended on government funding and, in that context, the balancing of risk and benefit was relevant. The views of SHHD medical advisers were reflected in a memorandum by Dr Bell dated 23 May 1984, commenting on the Common Services Agency's case for funding the production of heat-treated Factor VIII.<sup>163</sup> Dr Bell noted that, at that time, nearly all newly-treated haemophilia patients became infected with NANB Hepatitis, though not usually of dramatic severity, and that about 40% also showed evidence of infection with Hepatitis B. He said that the longer-term effects of such infection in people with haemophilia were not known with certainty because, until relatively recently, haemophilia patients had little prospect of living into middle or old age. However, he thought that a significant proportion of non-haemophilia patients infected with Hepatitis B went on to suffer severe liver impairment which, apart from the personal aspect, made significant demands on health care resources. The clear implication was that the experience of haemophilia patients was likely to be similar.

**15.145** In 1985, reports were published that reflected the results of studies of the incidence of infection. The work of Peter Kernoff and others at the Royal Free Hospital, London, is dealt with in the Preliminary Report.<sup>164</sup> They found that all of their haemophilia

<sup>160</sup> Ibid [DHF.002.8963]

<sup>161</sup> Letter from Dr Ludlam to Miss Spooner, 10/04/1984 [SNF.001.3211]

<sup>162</sup> Letter from Dr Cash to Dr Crawford, 25/04/1984 [SNF.001.3212]; Preliminary Report, paragraph 7.59

<sup>163</sup> Mr Bell's memo [SGF.001.1986]; Preliminary Report, paragraph 7.60

<sup>164</sup> Preliminary Report, para 7.76; Kernoff et al, 'High risk of non-A, non-B hepatitis after a first exposure to volunteer or commercial clotting factor concentrates: effects of prophylactic immune serum globulin', *British Journal of Haematology*, 1985;60:469-479 [LIT.001.0800]

patients treated with commercial Factor VIII developed acute NANB Hepatitis. Ten out of 12 patients who were prescribed NHS concentrate also developed acute NANB Hepatitis. The results were not surprising given the size of the donor pools. The report by Massimo Colombo and others of their study of transmission of NANB Hepatitis by Hyland/Travenol's Hemofil T Factor VIII confirmed that NANB Hepatitis had an attack rate close to 100% in haemophilia patients not previously exposed to blood or blood derivatives who were given that commercial product.<sup>165</sup> Preston and others reported similar results in two previously untreated patients who were given Armour's heat-treated product, Factorate.<sup>166</sup>

**15.146** The focus of interest changed in June 1985 with the publication by Charles Hay and others (Sheffield) of 'Progressive liver disease in haemophilia: an understated problem?' The authors' discussion is informative. They stated:

Our observations show that progressive liver disease is a potentially serious problem in haemophilia. Of 79 haemophilic patients .... 17 had evidence of progressive liver disease (9 cirrhosis, 8 CAH). Serial liver biopsies showed progression of [Chronic Persistent Hepatitis] to [Chronic Active Hepatitis] and cirrhosis within a period of 2 – 6 years.

The prevalence of abnormal liver function tests in haemophiliacs increased rapidly with the widespread introduction of factor VIII and IX concentrates in the mid-1970s. These abnormalities are believed to arise as a sequel to viral infection transmitted by blood products .... Almost all previously untreated haemophiliacs acquire NANB hepatitis after administration of factor VIII concentrate, and regular users may have multiple attacks from more than one NANB agent.<sup>167</sup>

**15.147** As indicated in the Preliminary Report, Hay and others discussed their clinical findings and compared their results to those of Mannucci and colleagues in 1982, discussed above. The discussion continued:

Cirrhosis may take several years to develop and it is consequentially not surprising that cirrhosis was more common in our series than in earlier studies with shorter periods of follow-up. This is especially important in view of the fact that the high prevalence of liver disease probably dates from the introduction of factor VIII concentrates ....

A notable feature of our series is that 4 patients with CPH have shown progression to CAH and cirrhosis; this is at variance with the generally accepted view that CPH is benign and non-progressive and leads us to speculate that repeated exposure to hepatitis viruses may modify the usually benign course ....

Although few reports of death attributable to liver disease in haemophilia have appeared, we predict that this will become more common.<sup>168</sup>

<sup>165</sup> Preliminary Report, paragraph 7.81; Colombo et al, 'Transmission of non-A, non-B hepatitis by heat treated factor VIII concentrate' *The Lancet*, 1985;ii:1-4 [LIT.001.0369]

<sup>166</sup> Preliminary Report, paragraph 7.82; Preston et al, 'Non-A, non-B hepatitis and heat treated concentrates', *The Lancet*, 27 July 1985:213 [LIT.001.0464]

<sup>167</sup> Hay et al, 'Progressive liver disease in haemophilia: an understated problem?', *The Lancet*, 29 June 1985:1495-98 [LIT.001.0335] at 0336. The title was, as Dr Hay stated in testimony on Day 8 (page 5), in response to the 1983 publication by Stevens et al (Manchester) entitled 'Liver disease in haemophiliacs: an overstated problem?' *British Journal of Haematology*, 1983; 55:649-655 [LIT.001.0008]; Preliminary Report paragraphs 7.78-7.80

<sup>168</sup> Hay et al, 'Progressive liver disease in haemophilia: an understated problem?', *The Lancet*, 29 June 1985: 1495-98 [LIT.001.0335] at 0337

**15.148** Mannucci's response is set out in paragraph 7.85 of the Preliminary Report. Since this is an important juncture in the published debate, it is important to note the details:

[S]ince our patients had similar ALT pattern and length of follow-up as those investigated by Hay et al, we think that other factors must be considered to explain the different courses of liver disease. The fact that our patients were considerably younger than those studies by Hay et al ... suggests that the degree of liver damage might be inversely related to the age at which patients become infected. Children with chronic hepatitis B tend to have high levels of virus replication in the liver without severe liver disease. So, in view of the many epidemiological similarities between hepatitis B and non-A, non-B hepatitis, it is not surprising that children with non-A, non-B infection tend to have less progressive and more "tolerated" liver disease than adults with the same infection.<sup>169</sup>

**15.149** The findings by Hay's group were not challenged. A possible explanation of the different outcome was suggested. At least in the case of adult haemophilia patients, the risk of progressive liver disease had been shown to be greater than previously anticipated. In time, this was to become clearer and, as indicated in Chapter 13, *Knowledge of Viral Hepatitis Now*, paragraphs 13.68–13.73, it is now established that the rate of progression is related to age in patients infected with HCV.

### Post-transfusion hepatitis

**15.150** In 1984, 'Notes on Transfusion principles and practices' was published jointly by the DHSS, Scottish Home and Health Department (SHHD) and the Welsh Office on behalf of the NBTS and SNBTS.<sup>170</sup> The 'Notes on Transfusion' discussed Hepatitis A and Hepatitis B in the context of donor selection, and commented:

Very similar illnesses can also be caused by other viruses including the so-called 'non-A non-B' viruses. The latter are also transmissible by transfusion, but as yet no specific laboratory tests have been developed to identify them. The incubation period is also variable extending up to 70 days or more. The clinical course may be acute, or chronic leading to cirrhosis.<sup>171</sup>

**15.151** The notes concluded with instructions on the collection of samples and on the reporting duties of clinicians finding hepatitis. The notes were concerned with practical guidance but would have brought to the attention of any transfusion doctor that there was a risk of transfusion-transmission of viral hepatitis generally and NANB Hepatitis in particular.

**15.152** In its annual report to the Office of the Chief Scientist of the DHSS, lodged in May 1984 by the London School of Hygiene and Tropical Medicine, it was stated:

The development of specific serological tests for detection of markers of infection with parenterally-transmitted forms of non-A, non-B hepatitis continues to elude laboratory workers in this field. Similarly the viruses have not yet been identified.<sup>172</sup>

<sup>169</sup> Manucci and Colombo, 'Liver Disease in Haemophilia', *The Lancet*, 5 October 1985 [LIT.001.1656]

<sup>170</sup> Notes on Transfusion [DHF.003.0394]

<sup>171</sup> Ibid [DHF.003.0394] at 0412

<sup>172</sup> Annual Report to the Office of the Chief Scientist of the Department of Health and Social Security on the Work of the Hepatitis Laboratory [DHF.003.0101] at 0107

**15.153** The development of specific laboratory tests for NANB Hepatitis remained a matter of high priority.

**15.154** In marked distinction to the developments in haemophilia, there was less appreciation among those involved with transfusion, in the UK generally and in Scotland in particular, of the nature of the risks presented by NANB Hepatitis. In July 1984 Dr Follett (laboratory virologist at the Regional Virus Laboratory, Ruchill Hospital, Glasgow) and Dr Brian Dow (Senior Technician, SNBTS, Glasgow) presented the final report on a study of 'Non-A Non-B Hepatitis in the West of Scotland'. The first part of the report examined all notified clinical cases diagnosed as likely to be due to non-B post-transfusion hepatitis in the region over four years. Excluding four haemophilia patients who had been multiply transfused with Scottish and imported blood products, they concluded that there were nine likely cases. The second part of the report contained an examination of ALT levels, and the results of other serological tests, of 10,655 blood donations. They found elevated ALT levels in 367 individuals (3.4%), and markedly elevated levels in 96 cases (0.89%).<sup>173</sup>

**15.155** Interestingly, prison session donors (a number of whom recognised as intravenous drug users) showed 10 times more donations with grossly elevated ALT levels than among other groups of donor. These results discouraged SNBTS from continuing to hold donor sessions in prisons to collect blood for transfusion purposes.<sup>174</sup>

**15.156** The study was poorly funded, however, and limited in scope. There was no follow-up of the 10,655 blood donations. No valid conclusions could be drawn as to the frequency of post-transfusion NANB Hepatitis. Drs Follett and Dow concluded, however, that on the basis of the nine reported clinical cases, NANB Hepatitis was very rare in the region. The authors recognised that sub-clinical forms of post-transfusion hepatitis probably occurred but were not notified.<sup>175</sup> Like previous studies based on reported incidents, this work probably missed the vast majority of cases of post-transfusion NANB Hepatitis. The sub-clinical forms of infection were noted but not taken into account, although it later transpired that they were the dominant component in the actual pattern of transmitted infection.

**15.157** Most unfortunately, the report and the erroneous conclusion drawn, that NANB Hepatitis was very rare in the region, were firmly grasped by the SHHD and its medical advisors and held to be valid, until about 1987–88. This was to lead to a significant lack of understanding of the post-transfusion NANB Hepatitis problem and a marked reluctance to fund other studies.

**15.158** Dr McClelland (SNBTS, Edinburgh) presented a rather similar view to that of Drs Follett and Dow at the 18th Congress of the International Society of Blood Transfusion held in Munich in July 1984.<sup>176</sup> He stated that the risk of Hepatitis B following transfusion of blood or its components was extremely rare. Coagulation factor concentrates had a very high risk of transmitting NANB Hepatitis but clinically apparent post-transfusion NANB Hepatitis was a small problem. A few transfused patients developed asymptomatic elevations of liver enzymes but the importance of that remained undefined.

---

<sup>173</sup> Non-A Non-B Hepatitis in the West of Scotland [SGH.002.8040] at 8045

<sup>174</sup> Blood donation from prisoners is discussed in Chapter 26, *Donor Selection – Higher Risk Donors*.

<sup>175</sup> Non-A Non-B Hepatitis in the West of Scotland [SGH.002.8040] at 8042

<sup>176</sup> Abstracts of the 18th Congress of the International Society of Blood Transfusion [SNB.008.6696] at 6697. Preliminary Report paragraph 7.62

**15.159** Scottish blood transfusion experts were not alone in expressing such views in 1984. An article by Drs Barbara and Tedder (North London Regional Transfusion Centre and University College and Middlesex School of Medicine, London) published in October 1984<sup>177</sup> commented that most NANB Hepatitis infections were not apparent and were only detected by mild elevation of transaminase levels. It was noted that raised transaminase levels could be caused by other viruses or by factors such as drugs, alcohol, obesity and medications. There were major uncertainties about the consequences of NANB Hepatitis, according to these authors who stated that the usually mild acute NANB Hepatitis infections in haemophilia patients would have little significance but for their possible association with the development of chronic hepatitis. However, they stated, even that was frequently self-limiting and resolved within two years in most cases.

### Summary

**15.160** By the end of 1985, different views were beginning to emerge, especially among haemophilia clinicians and other experts such as Dr Lever and colleagues. It seems however, that the majority, reputable view from leading groups around the world, outside the USA, was that the likelihood was fairly remote that NANB Hepatitis would become a very significant long-term problem, with many individuals developing cirrhosis. Most reports had lacked any lengthy follow-up and had concentrated on the acute changes which researchers saw in blood tests and liver biopsies over the month or two of the initial illness. While there were a few voices suggesting that chronic liver disease/cirrhosis attributable to NANB Hepatitis was becoming, or likely to become, more and more of a problem, these were in a minority. However, to a great extent, the opinions expressed reflected the researchers' natural biases: differences were of the 'glass half full, glass half empty' variety.

**15.161** It seems reasonable to conclude that, until the end of 1985 at the earliest, it was a very tenable position to hold that infusion of Factor VIII concentrates presented a risk of significant long-term liver disease but that fatal liver disease was a very small risk. This position is exemplified by Dr Craske's remark that, to his knowledge, only two patients with haemophilia had died of cirrhosis in the previous 10 years.<sup>178</sup> It is likely that the view of the majority of these authorities (for most groups anyway) was that the relatively few deaths from cirrhosis among haemophilia patients during the 1970s and early '80s had been caused by the 'rump' of the Hepatitis B cases.

**15.162** At that time, commentators were all, to some extent, working in the dark. Research produced findings that could be, and were, described. However, the significance of the findings, in terms of the natural history of NANB Hepatitis, was often unclear.

**15.163** In the period between 1975 and 1985, increasingly sensitive tests for the Hepatitis A virus (HAV) and Hepatitis B virus (HBV) were developed. In particular, as the range of HBV viral markers improved, there was increasing understanding of which markers indicated present infection and infectivity and which indicated past infection and immunity. However, until the mid-1980s it was unclear what the various markers which commentators were describing for present infection with Hepatitis B in the blood signified in assessing the long-term prospects for the patient.

---

<sup>177</sup> Barbara and Tedder, 'Viral Infections Transmitted by Blood and Its Products', *Clinics in Haematology*, 1984; 13: 693–707 [LIT.001.3739]

<sup>178</sup> Meeting on the Infectious Hazards of Blood Products NIBSC, 9 February 1984 [SNB.004.8628] at 8630



**15.164** The significance of the various histological appearances of the liver – chronic persistent hepatitis, chronic lobular hepatitis, and chronic active hepatitis – in terms of likelihood of progression to serious liver disease or regression to normal, was also unclear at that time. Few of the patients studied in this period, either in the USA or in Europe, had any specific symptoms. Such evidence as had emerged on relatively long-term follow-up (up to five years) suggested that in most individuals chronic liver inflammation engendered by the putative NANB Hepatitis virus(es) would generally die down. It was only towards the later part of the period that suggestions began to emerge that, in perhaps 10% of those chronically infected, irreversible liver damage – cirrhosis – could develop.

**15.165** Although the vast majority, if not all, of the clinical studies of NANB Hepatitis associated with Factor VIII use, up to the end of 1985, had set out descriptions of liver disease acquired in real time before the arrival of HIV/AIDS, by late 1985 all major groups were preoccupied with HIV/AIDS and NANB Hepatitis was regarded as a less urgent problem. Furthermore, as was about to become apparent, co-infection with NANB Hepatitis and HIV/AIDS was to become relatively common and was to further complicate understanding of liver disease for the next two or three years.

**15.166** At the end of this period, there remained substantial deficits in knowledge of NANB Hepatitis and its natural history. The clinical dilemma as to whether to provide treatment with available human blood-derived therapeutic products remained but the perceived risks of infection had increased. At the meeting called by NIBSC on 9 February 1984, Dr Thomas expressed the problem clearly: 'The undoubted therapeutic benefit of Factor VIII concentrates was clouded by a well recognised side-effect, namely hepatitis, and also, more recently, by AIDS.'<sup>179</sup>

**15.167** There were, however, widely differing views at that meeting about the nature and the extent of the risks to patients. Dr McClelland's estimate of the risk of transmitting NANB Hepatitis by blood transfusion was 1 in 100 and he commented that the risks for haemophilia patients were much greater because of their exposure to large numbers of donors. In relation to hepatitis, Dr Craske reported that 30–40% of UK haemophilia patients had abnormal liver function tests, indicative of possible chronic liver damage. However, by 1983 only two haemophilia patients had died of liver disease in 10 years. Throughout this period the low mortality reported in haemophilia patients from complications of hepatitis had a significant impact on the assessment of risk/benefit for the patient receiving blood products.

**15.168** The 7th edition of Professor Sherlock's *Diseases of the Liver and Biliary System* was published in 1985. It provides a useful summary of the position regarding NANB Hepatitis in the UK at that time. At the end of the period discussed in this chapter, it can be taken to represent the information likely to have been available to the general body of clinicians and others in the UK concerned with liver disease at this time. Professor Sherlock noted four clinical types of NANB Hepatitis (among many).<sup>180</sup> Two were enterically spread and can be ignored for present purposes. The two parenterally spread types were (a) a blood transfusion related type with a relatively long incubation period, and (b) a type associated with the administration of blood products to haemophilia patients, distinguished by a short incubation period. The clinical course of infection was the same in each case. The acute attack was mild but could occasionally be fulminant (rapidly progressing). Approximately

<sup>179</sup> NIBSC Meeting on the Infectious Hazards of Blood Products, 9 February 1984 [SNB.004.8628]

<sup>180</sup> Sherlock S, *Diseases of the Liver and Biliary System*, 7th ed, Blackwell, Oxford, page 270

68% of patients developed chronic hepatitis. In 19%, this progressed slowly and almost without symptoms to cirrhosis. Fluctuating transaminases were said to be typical of the chronic state. It was commented, significantly, that a relationship to hepatocellular cancer had not been established. It was noted that there was no test for NANB Hepatitis and that there had been limited progress both in diagnosis and in assessing treatment.

**15.169** Professor Sherlock's preface was dated October 1985 and the text is likely to have been completed some months earlier. It is unlikely to have taken account of research in the second half of the year in which Professor Sherlock was not involved. Nevertheless, although it cannot be assumed that there was general knowledge of up-to-date research, the emerging position by the end of 1985, in both the USA and the UK, was that:

- There was increasing concern in some quarters about the potential seriousness of NANB Hepatitis, whether following blood transfusion, in relation to which there was more knowledge and more concern in the USA, or in haemophilia treatment.
- Almost all haemophilia patients who regularly received treatment with concentrates were likely to have been infected by the disease.
- First generation heated concentrates continued to transmit NANB Hepatitis.
- The debate over the benefits and drawbacks of screening blood donors for surrogate markers of NANB Hepatitis continued.

**15.170** The last two topics are discussed in Chapters 23 and 27. The next chapter takes up the developing story of NANB Hepatitis after 1985.

## CHAPTER 16

### KNOWLEDGE OF VIRAL HEPATITIS 3 – 1986 ONWARDS

#### Introduction

**16.1** This chapter continues the account of the development of knowledge of non-A, non-B Hepatitis (NANB Hepatitis) from 1986 through to the discovery of the Hepatitis C virus (HCV) and beyond. Some of the later developments described are also reflected in Chapter 13, *Knowledge of Viral Hepatitis Now*. They are repeated here for the context in which they arose and particularly to provide chronological references for developments in screening blood and testing blood donors, further developments in the treatment of blood components and products and other topics dealt with separately.

**16.2** As noted in the previous chapter (paragraphs 15.108–15.110), in 1986 expert opinion in the USA was moving towards general support for surrogate testing as a means of excluding from the donor pool as many donors infected with NANB Hepatitis virus(es) as possible.<sup>1</sup> That development resulted in the general introduction of surrogate screening of blood for alanine transaminase (ALT),<sup>2</sup> and testing of donors for antibodies to the Hepatitis B virus. That course was not to be followed in the UK however, although in other respects opinion in the UK began to change in the same period. Correspondence in *The Lancet* in February 1986 marked the beginning of a change in attitudes towards NANB Hepatitis.

#### Changing attitudes towards non-A, non-B Hepatitis

##### *Correspondence in The Lancet*

**16.3** A letter by Klaus Schimpf (Heidelberg, West Germany) published on 8 February 1986,<sup>3</sup> expressed agreement with the report in 1985 by Dr Charles Hay and his colleagues in Sheffield<sup>4</sup> that progressive liver disease in haemophilia patients was an understated problem. In Schimpf's study 52 biopsies were carried out on 45 patients between 1972 and 1985. There were signs of subsided hepatitis in 24% of the patients, of chronic persistent hepatitis in 27% and of progressive liver disease in 29% (16% chronic active hepatitis, 13% cirrhosis). Schimpf also noted that the multi-centre study by Louis Aledort and others had come to a similar conclusion regarding the frequency of cirrhosis.<sup>5</sup>

**16.4** The same edition of *The Lancet* contained an update on the condition of 12 patients who had developed NANB Hepatitis after treatment with a new intravenous gammaglobulin preparation produced by the Blood Products Laboratory, Elstree (BPL, the manufacturer of NHS blood products in England).<sup>6</sup> At least half of the patients had evidence of progressive liver disease, with cirrhotic changes in three. While specific to patients with primary hypogammaglobulinaemia (an immune deficiency characterised by

<sup>1</sup> A surrogate marker is a directly measurable physical entity (usually measured in a blood test) that has a statistical association (correlates) with a disease where it is not possible to test directly for the disease or where any direct test would be problematic. See Chapter 27, *Surrogate Testing of Donated Blood for non-A, non-B Hepatitis*.

<sup>2</sup> Proteins synthesised in liver cells, normally present in low levels in the blood, which become elevated when the liver is disordered by virus infection or other disorders of the liver.

<sup>3</sup> Schimpf, 'Liver Disease In Haemophilia', *The Lancet*, 1986; 323 [LIT.001.0341] at 0342

<sup>4</sup> Hay et al, 'Progressive liver disease in haemophilia: an understated problem?', *The Lancet*, 1985, 1495–98 [LIT.001.0335]

<sup>5</sup> Aledort et al, 'A Study of Liver Biopsies and Disease Among Haemophiliacs', *Blood*, 1985; 66:367–372 [LIT.001.0505]

<sup>6</sup> Webster et al, 'Non-A, Non-B Hepatitis After Intravenous Gammaglobulin', *The Lancet*, 1986:322 [LIT.001.0341]. First reported in 1984 by Lever et al (including Webster), 'Non-A, Non-B hepatitis occurring in agammaglobulinaemic patients after intravenous immunoglobulin', *The Lancet*, 1984; 1062–1064 [LIT.001.0449]

a reduction in gamma globulins and treated with blood products), the letter emphasised that NANB Hepatitis was a serious complication that should be controlled by discarding plasma donations with raised ALT levels.

**16.5** An editorial in *The Lancet* of 2 August 1986 stated:

The risk of contracting [NANB Hepatitis] from factor VIII and IX concentrates was first recognised ten years ago. The requirement for large pools of plasma, of up to 7000 donations in the UK ... and even larger pools with some commercial preparations, has produced attack rates approaching 100% in recipients after first exposure to unheated factor VIII. The acute illness was often mild .... Unfortunately, it is now clear that there is a substantial long-term risk of chronic sequelae, such as chronic active hepatitis and cirrhosis of the liver. Reports of serial liver biopsies in patients regularly treated with factor VIII and IX suggest that the risk of serious chronic liver disease may be as high as 16%.

....

Despite intensive research, the virus or viruses associated with non-A, non-B (NANB) hepatitis have not been isolated or characterised.<sup>7</sup>

**16.6** By the end of 1986, informed opinion in the USA (as typified by Alter and colleagues) and in parts of Europe had shifted decisively to reflect suspicion that the long-term progression of chronic NANB Hepatitis infection was not benign but severe, whether following blood transfusion or in haemophilia patients.

### *Increasing concern*

**16.7** In 1987, the 8th edition of the standard UK textbook on blood transfusion was published.<sup>8</sup> Post-transfusion NANB Hepatitis was said to be present when, between two and 26 weeks after transfusion, two consecutive blood samples showed a twofold increase in ALT levels – effectively the approach to diagnosis adopted in the USA. That method of diagnosis was described by Patrick Mollison, the author of this authoritative text, as ‘most unsatisfactory’ and was said to have led to ‘a great deal of uncertainty about the true incidence’ of post-transfusion NANB Hepatitis. It was estimated that NANB agents had caused 20–42% of sporadic cases of hepatitis in the USA,<sup>9</sup> compared with 13% within the UK.<sup>10</sup> Mollison wrote:

[NANB post-transfusion hepatitis] is usually mild and asymptomatic during the acute phase .... However, prospective studies in the USA have shown that the chronic sequelae of [NANB post-transfusion hepatitis] may be serious. Over 50% of patients develop chronic hepatitis as judged by persisting or fluctuating rises in [ALT] levels lasting for at least 1 year after onset of the disease and in most for more than 3 years .... Although the chronic phase of [NANB post-transfusion hepatitis], like the acute phase, tends to be mild,<sup>11</sup> some patients

<sup>7</sup> ‘Safer Factor VIII and IX’ *The Lancet*, August 2 1986 [LIT.001.3846]

<sup>8</sup> Mollison et al, *Blood Transfusion in Clinical Medicine*, 8th edition, 1987

<sup>9</sup> *Ibid* page 774. Reference to Alter et al, ‘Posttransfusion hepatitis: clinical features, risk and donor testing’ in *Infection, Immunity and Blood Transfusion*, 1985; 47–61 [LIT.001.0811]

<sup>10</sup> Mollison et al, *Blood Transfusion in Clinical Medicine*, 8th edition, 1987, page 774. Reference to Farrow et al, ‘Non-A, non-B hepatitis in West London’, *The Lancet*, 1981: 982–984 [LIT.001.3904]

<sup>11</sup> Mollison et al cited Alter et al, ‘Posttransfusion hepatitis: clinical features, risk and donor testing’, *Infection, Immunity and Blood Transfusion*, 1985, 47–61 [LIT.001.0811] in support of this statement.

develop severe chronic liver disease and 10% of these patients progress to cirrhosis which is generally milder than alcoholic cirrhosis.<sup>12</sup>

**16.8** It was noted that the available data were based on biopsies in very small numbers of patients.<sup>13</sup>

**16.9** In a letter to the *British Medical Journal (BMJ)* published on 14 February 1987, Dr John Gillon and Dr Brian McClelland (both of the Edinburgh and South East Scotland Blood Transfusion Service) commented that only one study of the long-term consequences of post-transfusion NANB Hepatitis infection had been reported.<sup>14</sup> This was a reference to the Alter study.<sup>15</sup> The letter narrated that of the 50% of cases which became chronic as evidenced by raised ALT levels persisting for more than six months, 10–15% might be expected to show evidence of clinically important liver disease. As noted in the Preliminary Report,<sup>16</sup> applied to the UK these figures were almost certainly an overestimate. However, it is of greater importance that at this time the authors did not have locally relevant data to draw on. There was still considerable uncertainty but some growing understanding. At an international symposium on viral hepatitis and liver disease held in London in May 1987, Dr Alter said:

NANB remains a frustrating and perplexing dilemma. Nonetheless we know a little more about its physical properties, we know considerably more about its clinical outcome, and we know of multiple ways in which it can be inactivated. What we do not know exactly is where to go next, or what can be done to create the breakthrough that will allow progress with NANBH to parallel that with hepatitis B and hepatitis A.<sup>17</sup>

**16.10** There were other international meetings at the time, reflecting increasing concern. As noted in the Preliminary Report, the European Health Committee of the Council of Europe held its 21st meeting between 29 June and 1 July 1987.<sup>18</sup> The prevailing uncertainty was reflected in the extract of a report of the 10th meeting of the Committee of Experts on Blood Transfusion and Immunohaematology circulated for that meeting.<sup>19</sup>

### *Scientific developments: discovery of the Hepatitis C virus*

**16.11** The scientific background was about to change. On 10 May 1988, the Chiron Corporation announced that:

Scientists at Chiron Corporation have identified, cloned and expressed proteins from a long-sought blood-borne hepatitis non-A, non-B virus, and have developed a prototype immunoassay that may lead to a screening test for hepatitis non-A, non-B antibodies ....<sup>20</sup>

<sup>12</sup> Mollison et al, *Blood Transfusion in Clinical Medicine*, 8th edition, 1987; 774–75

<sup>13</sup> Ibid page 775

<sup>14</sup> Gillon and McClelland, 'Autologous blood transfusion', *British Medical Journal*, 1987; 294:441 [LIT.001.0218]

<sup>15</sup> Alter et al, 'Posttransfusion Hepatitis: Clinical Features, Risk and Donor Testing' in *Infection, Immunity and Blood Transfusion*, 1985, 47–61 [LIT.001.0811]

<sup>16</sup> Preliminary Report, paragraph 9.47

<sup>17</sup> Alter, 'Transfusion-associated [NANB] hepatitis: the first decade', *Viral Hepatitis and Liver Disease*, 1988; 537–542, Alan R Liss, New York [PEN.018.1551] at 1555. See the Preliminary Report paragraphs 9.54 and 9.55 for further material relating to this symposium

<sup>18</sup> Preliminary Report paragraphs 9.61 to 9.65

<sup>19</sup> Extract from the Report of the Committee of Experts on Blood Transfusion and Immunohaematology -SP-HM- 10th Meeting – Rome 19-22 May 1987 [SNB.001.9445]

<sup>20</sup> News Release dated 10.05.88 from Chiron Corporation announcing the cloning of the NANB Hepatitis virus [PEN.016.0290]

**16.12** Scientific details were not published at that time,<sup>21</sup> although the report of the Chiron discovery in *Nature* said: 'The search for the elusive viral agent responsible for [NANB] hepatitis may be over.'<sup>22</sup> Throughout the remainder of 1988 there was little in the way of published material on HCV and no technical support for the claim. In the UK public sector, research was focused on virus inactivation. There was powerful support for that approach. In an article published in *The Lancet* in December 1988, Dr Alter and others stated:

Because [of] the increasing number of direct and indirect donor screening measures required to protect the blood supply, the most promising approach to the reduction of transfusion-associated disease is the biophysical removal or biochemical inactivation of hepatitis and other blood transmitted viruses ...<sup>23</sup>

**16.13** Work in that area is discussed in Chapters 23 and 24.

**16.14** In the short term, the Chiron report was scarcely noted in published statements by commentators who remained pre-occupied with the natural history of the disease. Although there was growing appreciation that there were risks associated with the use of plasma products, the prevailing view among Scottish Home and Health Department (SHHD) medical staff remained that NANB Hepatitis was generally benign – a view that would have received support from the 7th edition of Professor Sherlock's book (discussed in the last chapter at paragraph 15.168). In Scotland, there had been a report of four cases of infection that might have been transmitted by intravenous immunoglobulin manufactured at the Protein Fractionation Centre (PFC, the manufacturer of NHS blood products in Scotland), Edinburgh, during 1987.<sup>24</sup> In an internal memorandum to Mr Hamish Hamill at the SHHD dated 30 August 1988, Dr John Forrester noted that the product was under suspicion of transmitting NANB Hepatitis, but concluded:

[T]his particular hepatitis is so benign, at least in the short term, that evidence of transmission has to be specially sought, the patient not being ill at all in the ordinary sense.<sup>25</sup>

### *Progressive disease as an aspect of the natural history of non-A, non-B Hepatitis*

**16.15** There were still differences of view among medical practitioners generally about the seriousness of NANB Hepatitis infection. An editorial in *The Lancet* in December 1988 summarised the recent history of 'Chronic liver disease and haemophilia'.<sup>26</sup> The editorial noted that while acute post-transfusion hepatitis and chronic increases in liver enzyme concentrations had long been associated with both Factor VIII and Factor IX infusion, those caring for haemophilia patients were slow to accept chronic progressive liver disease as an important complication. It was noted that few haemophilia patients had any signs or symptoms of liver disease, deaths from hepatic failure were rarely reported and raised ALT levels were attributed to chronic persistent hepatitis rather than chronic active hepatitis. The results from studies of early series of patients undergoing liver biopsy

<sup>21</sup> Scientific details of the discovery were not published until April 1989: Choo et al, 'Isolation of a cDNA clone derived from a blood-borne non-A non-B viral hepatitis genome', *Science*, 1989; 244:359–362 [LIT.001.0629] and Kuo et al, 'An assay for circulating antibodies to a major etiological virus of human non-A, non-B hepatitis', *Science*, 1989; 244:362–364 [PEN.017.2764]

<sup>22</sup> 'Candidate cause identified of non-A, non-B hepatitis', *Nature*, 19 May 1988 [SGH.002.8036]

<sup>23</sup> Alter et al, 'Photochemical decontamination of blood components containing hepatitis B and non-A non-B virus', *The Lancet*, 1988; 1446–50 [LIT.001.3984]

<sup>24</sup> See Preliminary Report paragraphs 9.98 and 9.99 for further information on this issue.

<sup>25</sup> Memo [SGH.002.4672] at 4673

<sup>26</sup> 'Chronic liver disease and haemophilia', *The Lancet*, 1988; 1465–66 [LIT.001.3838]

were generally reassuring in that most of them showed either chronic persistent hepatitis or mild chronic active hepatitis, with little to suggest severe liver damage.<sup>27</sup> However, as noted in paragraph 16.3 above, Hay and colleagues (1985) had documented a significant progression from chronic persistent hepatitis to chronic active hepatitis to cirrhosis.<sup>28</sup> Their assessment was echoed by Schimpf (paragraph 16.3, above).<sup>29</sup>

**16.16** Similar figures were provided in a contemporaneous report from Dr Elizabeth Miller and colleagues in London (1988).<sup>30</sup> The editorial stated:

The evidence that chronic progressive liver disease is an important complication of haemophilia treatment is therefore becoming increasingly persuasive. Furthermore, experience with other types of viral hepatitis suggests that cirrhosis and hepatocellular carcinoma may first appear decades after infection.<sup>31</sup>

**16.17** Opinion was moving towards acceptance of more progressive disease as an aspect of the natural history of NANB Hepatitis.

### Reactions to the Chiron announcement and further scientific developments

**16.18** There were mixed responses to the initial announcements of Chiron's discoveries. The American Association of Blood Banks (AABB) reported that, while there remained some scepticism about the results, a leading expert in the field, Harvey Alter (US National Institutes of Health) had said that Chiron's identification of the NANB Hepatitis protein was 'what we've been looking for for 10 years... one has to be skeptical but the data I've seen looks very good'.<sup>32</sup> The AABB commented:

Because Chiron has not yet published its results some scepticism remains about their findings....

Health experts agree that further testing still needs to be performed because the protein identified may be one of several capable of causing non-A, non-B hepatitis.<sup>33</sup>

**16.19** At the end of 1988 publication of scientific analysis of Chiron's work was still awaited.

**16.20** Dr Brian Dow, at the time a Senior Grade Scientific Officer at the West of Scotland Blood Transfusion Service, gave evidence that he thought he had been aware of Chiron's discovery at this time but had been unwilling to believe it was true until the first generation tests were available.<sup>34</sup> It appears that this was a common attitude.

<sup>27</sup> Reference was made to the following reports: (1) Lesesne et al, 'Liver biopsy in hemophilia A', *Annals of Internal Medicine*, 1977; 86:703–707 [LIT.001.3712]; (2) Preston et al, 'Percutaneous liver biopsy and chronic liver disease in haemophiliacs', *The Lancet*, 1978; 592–594 [LIT.001.0387]; (3) Spero et al, 'Asymptomatic structural liver disease in hemophilia', *New England Journal of Medicine*, 1989; 293:1373–78 [LIT.001.0177]; (4) Mannucci et al, 'Nonprogressive course of [NANB] chronic hepatitis in multitransfused hemophiliacs', *Blood*, 1982; 60:655–658 [LIT.001.0543] and (5) Stevens et al, 'Liver disease in haemophiliacs: an overstated problem?', *British Journal of Haematology*, 1983; 55:649–655 [LIT.001.0008]

<sup>28</sup> Hay et al, 'Progressive liver disease in haemophilia: an understated problem?', *The Lancet*, 1985; 1495–98 [LIT.001.0335]

<sup>29</sup> Schimpf, 'Liver disease in haemophilia', *The Lancet*, 1986; 323 [LIT.001.0341] at 0342

<sup>30</sup> Miller et al, 'Non-invasive investigation of liver disease in haemophiliac patients', *Journal of Clinical Pathology*, 1988; 41:1039–43 [LIT.001.3840]

<sup>31</sup> 'Chronic Liver Disease and Haemophilia', *The Lancet*, 1988; 1465–66 [LIT.001.3838]

<sup>32</sup> Quoted in 'Hepatitis non-A, non-B virus discovered', *Blood Bank Week*, 13 May 1988 [SNB.002.4411]

<sup>33</sup> 'Hepatitis non-A, non-B virus discovered', *Blood Bank Week*, 13 May 1988 [SNB.002.4411] at 4412

<sup>34</sup> Day 67, page 90

**16.21** Details of Chiron's discovery and resulting test were not published until the following year when, on 21 April 1989, Qui-Lim Choo and others published scientific details of the isolation of the genome of HCV.<sup>35</sup> At the same time, George Kuo and others (Chiron, US National Institutes of Health and others) published details of an assay to detect antibodies to HCV.<sup>36</sup> The test had been developed by Ortho Diagnostics Systems (Ortho) in conjunction with Chiron.

### *The science of discovery*

**16.22** Chiron had inoculated a chimpanzee with a serum sample<sup>37</sup> from a patient with post-transfusion hepatitis and had cloned the putative virus. Serum was taken from another patient who had recovered from post-transfusion NANB Hepatitis and was assumed to have produced antibodies to the NANB agent. The antibodies were 'labelled' and introduced to the putative virus. An appropriate reaction was observed which showed the connection required to verify the hypothesis that the cloned material was, or included, the agent of transmission of NANB Hepatitis.<sup>38</sup>

**16.23** It is appropriate to set out the story a little more fully to indicate why the discovery had such an impact on understanding of the infection. At the outset of the process, the subject, a patient who was known to have had a transfusion, was believed to have become ill with NANB Hepatitis about three weeks after the procedure. To test that hypothesis, serum from the patient was injected into a chimpanzee called Rodney. Rodney developed hepatitis, an essential step in removing any doubt whether the episode in the patient was due to an infectious agent, since it demonstrated transmissibility.<sup>39</sup>

**16.24** A sample of serum was taken from Rodney and RNA and DNA were extracted. At that stage it was not known whether the postulated transmissible agent was an RNA or DNA virus.<sup>40</sup> Reverse transcriptase, an enzyme that allows RNA to convert into DNA, was added to the genetic material extracted from Rodney's serum, with the result that the whole genetic material present was DNA. The DNA would include chimpanzee DNA but it would also include the DNA of the putative virus if it were present. That material was then put into plasmids, a vehicle that enabled the expression (synthesis) of the DNA code of whatever proteins had been introduced, in the case of a virus in the same way as the virus would normally synthesise proteins.<sup>41</sup> The product of that exercise was then put into E-coli for propagation in the hope that, as the bacteria reproduced, the introduced DNA from the chimpanzee and the putative virus would also reproduce genetically in the bacterial cells. This was the only way in which the viral DNA would encode for the protein which was part of the structure of the putative virus.<sup>42</sup>

**16.25** At that stage, serum was taken from a patient who was known to have had post-transfusion NANB Hepatitis and who was assumed to have developed antibodies to the virus. Using an appropriate ligand, a radioisotope or an enzyme label that creates a coloured substrate, the antibodies were labelled as human virus antibodies. When introduced to

<sup>35</sup> Choo et al, 'Isolation of a cDNA clone derived from a blood-borne non-A, non-B viral hepatitis genome', *Science*, 1989; 244:359–362 [LIT.001.0629]

<sup>36</sup> Kuo et al, 'An assay for circulating antibodies to a major etiologic virus of human non-A, non-B hepatitis', *Science*, 1989; 244:362 [PEN.017.2764]

<sup>37</sup> Serum is plasma with the clotting factors removed to avoid complications of clotting during the viral extraction process.

<sup>38</sup> Professor Thomas' report on Hepatitis C [PEN.017.1071]

<sup>39</sup> Professor Thomas – Day 52, pages 21–22

<sup>40</sup> Ibid pages 22–23

<sup>41</sup> Ibid page 29

<sup>42</sup> Ibid pages 22–24



the material propagated in *E. coli*, the labelled antibodies were expected to differentiate and bind to any human virus protein or DNA present and not to chimpanzee DNA. Such a reaction would be identified radioactively or by chemi-luminescence.<sup>43</sup> The reaction was observed in a tiny minority of the wells into which the samples were dispensed but showed the necessary connection.

**16.26** Chiron's overall procedures and approach to finding the virus and its procedures were not fundamentally unique: many researchers had tried similar approaches, but without success. There may have been many reasons for failure, including the use of virus material that did not include an antigenic component common to all the genotypes of the virus.<sup>44</sup> However, so much effort had been expended in searching for the putative virus in so many centres worldwide that by 1987–88 many people had given up believing that there was a virus, preferring the explanation that a chemical reaction caused the transaminase rise in patients in much the same way as some drugs used in medication can cause hepatitis.<sup>45</sup> Chiron's advantages were having 'well-pedigreed' chimpanzee sera to establish the transmission of hepatitis through passage (the sequential process from the initial patient through two chimpanzees in succession which proves the existence of a transmissible agent); and sera containing a large amount of virus. The infective serum from the first chimpanzee was diluted until it no longer transmitted hepatitis,<sup>46</sup> enabling Chiron to calculate the amount of virus in the initial sample.<sup>47</sup> For this work Chiron was granted a patent and lengthy and complex litigation followed. So far as is material, the challenge to the patent failed.<sup>48</sup>

**16.27** The publication of details of the Chiron discoveries marked the beginning of a period of research, both into the characteristics of HCV and into the effectiveness of markers of HCV infection and corresponding developments in treatment. The term 'Hepatitis C' almost entirely supplanted 'NANB Hepatitis' in the discussion of liver disease following Chiron's breakthrough in the understanding of NANB Hepatitis. The terms have never, however, been truly synonymous.

**16.28** The articles by Choo and others and Kuo and others referred to above were highly technical. The identification of the virus depended on the characterisation of the clones produced. The conclusions, and claims, were significant:

Thus, our data indicate that clones 5-1-1 and 81 are derived from the genome of a blood-borne NANBH virus that we now term the hepatitis C virus (HCV) ... Our present data showing that the virus contains a positive-stranded RNA molecule of at least 10,000 nucleotides is consistent with it being related to the togaviridae or flaviviridae .... The cDNA clones reported here were obtained in the absence of prior knowledge concerning the virus, the viral genome, and the presence of circulating viral antibodies. As such, this represents cloning without prior characterization of the infectious agent.<sup>49</sup>

<sup>43</sup> Ibid pages 24–26; Professor Tedder – Day 49, page 40 for terminology

<sup>44</sup> Professor Thomas – Day 52, page 36

<sup>45</sup> Ibid page 28

<sup>46</sup> The process referred to as 'titration'.

<sup>47</sup> Professor Thomas – Day 52, pages 26–28

<sup>48</sup> *Chiron Corporation and Others v Murex Diagnostics Ltd and Others and Chiron Corporation and Others v Organon Teknika and Others* (1996) R.P.C. 535. The scientific background to the discovery is more fully set out in Lord Justice Morritt's judgment, from page 589. Professor Thomas, who gave evidence at the trial, commented on the novelty of granting a patent for a natural sequence: Day 52, pages, 28–29. He also expressed reservations about claims extending the scope of the patent to the whole virus, since the Chiron artefact lacked the 3 prime coded region essential for replication: Day 52, pages 37–38. However, detailed analysis of the validity of the patent is beyond the scope of this Report.

<sup>49</sup> Choo et al, 'Isolation of a cDNA clone derived from a blood-borne non-A, non-B viral hepatitis genome', *Science*, 1989; 244: 359–362 [LIT.001.0629] at 0631

**16.29** In retrospect, the Chiron discovery was to prove more significant than was appreciated at the end of the 1980s and into the early 1990s. Other topics continued to attract attention. The scientific basis for the work was not readily understood and general understanding only developed over time. The background to Chiron's work set out above helps to explain the difficulties. Professor Thomas encapsulated the discovery in a brief, and somewhat concentrated, statement:

[Chiron] reported the cloning of HCV in 1989, by antibody probing of an expression library made from a reverse transcribed RNA extract of the serum of an infected chimpanzee initially inoculated with a serum sample from a patient with post-transfusion hepatitis (PTH). The antibody source was a serum specimen from a subject who had recovered from post-transfusion NANB hepatitis and was assumed to have produced antibodies to NANB agent.<sup>50</sup>

**16.30** The concepts, and the language, reflect a highly sophisticated knowledge of the biology of virus replication. The current understanding of the position has been set out in Chapter 13, *Knowledge of Viral Hepatitis Now*. However, this would have been science understood by only a few at the end of the 1980s.

**16.31** Chiron had achieved a significant, and inventive, development in knowledge of HCV infection but the work was incomplete: the whole virus had not been identified. In Chiron's experiments, the antigen recognised by the antibody in the recovered patient's serum was in the region NS4, one of the enzymes known as proteases that came, in time, to be targeted by protease inhibitors which increase substantially patients' response rates to treatment by impairing the ability of the virus to reproduce. Not all genotypes of HCV<sup>51</sup> have NS4 proteins, however, and this was to affect the usefulness of early forms of the assay developed. Without a sophisticated knowledge of cell biology, incomplete research findings were almost bound to leave even the most interested and careful commentators with reservations about the discovery.

**16.32** In the context of transfusion-related transmission and blood product therapy, post-transfusion Hepatitis C now appears to explain most if not all cases of what was NANB Hepatitis viral infection. Before the discovery of HCV, however, many people infected with the virus would not have been labelled as 'non-A, non-B' patients: there were few NANB Hepatitis diagnoses.<sup>52</sup> Alcohol and alcoholic liver disease were often associated with hepatitis and many patients were labelled as having 'alcoholic liver disease' alone, where two (or possibly more) risk factors would now be recognised, giving rise to much of the stigma associated with infection.<sup>53</sup>

### Unresolved issues in non-A, non-B Hepatitis

**16.33** The balanced view of the state of knowledge in 1989, as reflected in the eighth edition of Sherlock's *Diseases of the Liver and Biliary System*, published that year but continuing to reflect to a considerable extent views expressed in earlier editions, was that NANB Hepatitis was still 'ill defined'.<sup>54</sup> As regards the parenteral type of NANB Hepatitis, Professor Sherlock stated:

<sup>50</sup> Professor Thomas' report on Hepatitis C [PEN.017.1071]

<sup>51</sup> As noted in Chapter 13, *Knowledge of Viral Hepatitis Now*, HCV exhibits considerable genetic heterogeneity. Seven distinct genotypes of HCV have been identified.

<sup>52</sup> Professor Hayes – Day 78, pages 46–47

<sup>53</sup> Ibid pages 47–48

<sup>54</sup> Sherlock, S. *Diseases of the Liver and Biliary System*, 8th edition, 1989, page 301

The causative agent has not hitherto been identified ... [although] a viral genomic clone has been isolated from infected plasma and liver. This encodes the antigen associated with non-A, non-B viral hepatitis in man and chimpanzees.<sup>55</sup>

**16.34** It is likely that the text was written before publication of the more definitive Chiron papers in 1989 and Professor Sherlock's comment reflects information provided in the original *Science* announcement. Chiron's discoveries were not presented in her text as resolving the aetiology of NANB Hepatitis.

**16.35** On the other hand, Professor Sherlock's analysis of the clinical manifestations of infection with NANB Hepatitis presented a more serious and accurate picture than before. It was now thought that 60% of patients would have raised serum transaminases one year after infection. In 68% the disease became chronic and cirrhosis developed in 20%.<sup>56</sup> She stated that prognosis was very variable. In some cases, the diseases were benign with spontaneous biochemical improvement over one to three years. In others, chronic persistent hepatitis and chronic active hepatitis could convert to more serious disease and even go on to cirrhosis. In general, however, despite biochemical evidence of disease, the patient was asymptomatic and the development of hepatic failure was rare. Hepatocellular cancer had been recorded but was exceedingly rare.<sup>57</sup> In contrast to the seventh edition, a relationship to hepatocellular cancer was now acknowledged.

**16.36** Another insight into the perception of NANB Hepatitis among virologists in the UK at the end of 1988 was provided in a paper entitled 'Unresolved issues in non-A, non-B hepatitis' delivered by Professor Arie Zuckerman (Professor of Microbiology, Royal Free Hospital School of Medicine, London), presented at the Second International Symposium on Viral Hepatitis and Hepatocellular Carcinoma in Taipei in December 1988.<sup>58</sup>

**16.37** Professor Zuckerman stated that NANB Hepatitis was the most common form of hepatitis occurring after blood transfusion in some parts of the world (possibly 90% where blood donations were screened for HBsAg by sensitive tests) and that there was evidence of at least two transmissible agents.<sup>59</sup> It occurred in haemodialysis and other units and could be transmitted by therapeutic plasma components. He noted that there was preliminary information of an association with hepatocellular carcinoma, and commented generally on NANB Hepatitis:

Although in general the illness is mild and often subclinical or anicteric, severe hepatitis with jaundice does occur and the infection is a significant cause of fulminant [rapidly progressing] hepatitis. There is considerable evidence that the infection may be followed in many patients ... by prolonged viraemia and the development of a persistent carrier state. Studies of histopathological sequelae of acute non-A, non-B hepatitis infection revealed that chronic liver damage, which may be severe, may occur in as many as 40 – 50% of the patients.<sup>60</sup>

<sup>55</sup> Ibid page 326

<sup>56</sup> Ibid page 327

<sup>57</sup> Ibid page 367

<sup>58</sup> Zuckerman, A, 'Unresolved Issues in Non-A Non-B Hepatitis' [SNB.001.9490]

<sup>59</sup> Ibid [SNB.001.9490] at 9492–93

<sup>60</sup> Ibid [SNB.001.9490] at 9493

**16.38** Professor Zuckerman said that clinical evidence of more than one type of the disease was based on observation of multiple attacks of hepatitis in individual patients and experimental laboratory research. He dismissed argument based on incubation periods. His own explanation of the occurrence of multiple attacks was subsequently shown to be wrong. It later transpired that multiple attacks of Hepatitis C could occur because of insufficient host immunity to different genotypes of HCV rather than because of the existence of more than one viral species. However, that knowledge depended on advanced genetic research that still lay in the future. Like Professor Sherlock in the eighth edition of her book, Professor Zuckerman was writing before publication of the scientific data supporting Chiron's claims. It appears that neither Professor Sherlock nor Professor Zuckerman was willing at that stage to arrive at final conclusions on what was known of Chiron's discoveries.

**16.39** It is apparent that, despite the novelty of Chiron's science, or perhaps because of it, there was not immediate and universal acceptance of its validity. The initiative, in terms of fundamental research into HCV, continued to lie with Chiron and the US Centers for Disease Control.

**16.40** The second meeting of the Advisory Committee on the Virological Safety of Blood (ACVSB) took place on 22 May 1989.<sup>61</sup> Professor Zuckerman's Taipei paper was circulated along with a second paper, from an unidentified but clearly official source,<sup>62</sup> and members were given the results of the Council of Europe questionnaire prepared by Dr Gunson and the report of the Committee of Experts on Blood Transfusion and Immunohaematology from May 1987. In addition, scientific data from Chiron was available. The article published by Choo and others in *Science* was referred to and the accompanying paper noted:

The data suggests that NANB hepatitis agent is similar to the togaviridae or flaviviridae. The authors refer to this virus as hepatitis C virus.<sup>63</sup>

**16.41** The discussion of NANB Hepatitis was brief, so far as reported in the minute of the meeting. It was recorded that members had advised that, although colleagues in the USA considered that only one virus caused NANB Hepatitis, there might be two or more. The question whether there was more than one agent of transmission continued to arise. An editorial in *The Lancet* on 5 August 1989, 'Will the real hepatitis C stand up?', discussed the question whether there was a distinct short incubation agent with reference to reports of observations of apparently different incubation periods.<sup>64</sup>

**16.42** However, in general, interest came increasingly to focus on the Chiron/Ortho test. It was in that context that political interest was aroused by articles in *The Guardian*<sup>65</sup> and *The Scotsman*<sup>66</sup> in August 1989 that were likely to cause public concern. The article in *The Guardian*, for example, stated that '6000 people last year may have received blood transfusions contaminated with hepatitis C'. There was official reaction to the media comment.

<sup>61</sup> Minutes [SNB.001.9416]. The background to the setting up of ACVSB is set out in Chapter 31, *The Introduction of Screening for Hepatitis C*, paragraphs 31.28–31.40

<sup>62</sup> 'Non-A, Non-B Hepatitis' ACVSB 2/7 [SNB.001.9483]

<sup>63</sup> Ibid [SNB.001.9483]

<sup>64</sup> 'Will the real hepatitis C stand up?', *The Lancet*, 1989: 307–308 [LIT.001.3848]

<sup>65</sup> 'Dilemma on Virus Blood Test', *The Guardian*, 24 August 1989[SGH.002.8010]

<sup>66</sup> 'Doctor Says Hepatitis Blood Tests Could Cost Millions', *The Scotsman*, 25 August 1989 [SGH.002.8007]

**16.43** On 23 August Mr George Tucker (SHHD) sent a memorandum to Mr Michael Forsyth, MP, then Under-Secretary of State in the Scottish Office with responsibility for health: 'Testing of blood donations – test for Hepatitis C'.<sup>67</sup> Mr Tucker dealt with the claim in *The Guardian*: the statement was said to be 'unnecessarily alarmist', as it assumed that one per cent of all donations came from donors who were infectious (and not simply carriers) and that they passed on the antigen, and not just the antibody, in their donation. It also said that only a minority of those infected with Hepatitis C displayed any symptoms either in the short or long term. The memorandum further noted that the prevalence of HCV in the population had not been established and nor had the role of blood in its transmission. The UK Health Departments, along with the UK blood transfusion services, were said to be examining all the available data. The main focus of the memorandum was the position of the SHHD and the DHSS on testing, and that may explain the brevity of the information provided on the prevalence and consequences of infection.

**16.44** From the position adopted by Professor Zuckerman at the end of 1988 through to September 1989, expert opinion was consistent in the UK and more widely. Dr Ruthven Mitchell (SNBTS, Glasgow) attended and produced a report of proceedings at an international meeting on HCV, organised by Ortho and held in Rome on 14–15 September 1989.<sup>68</sup> There had been discussion at the conference on the prevalence and sequelae of NANB Hepatitis. Dr Mitchell's report stated that about 10% of persons transfused developed NANB Hepatitis, which could be of two forms, an acute form and a chronic form.<sup>69</sup> The incubation time varied from a few weeks to months. About 90% of post-transfusion hepatitis was due to the NANB Hepatitis virus or viruses. About 50% of those would become chronic and, of those, 20% would develop cirrhosis or some long-term liver impairment. Prevalence of the Hepatitis C antibody (anti-HCV) varied among different countries. Patients in the highest risk categories had the highest prevalence of anti-HCV. People with haemophilia had an anti-HCV prevalence of 60–80%.

**16.45** Dr Gunson reported the proceedings of the Rome meeting to the meeting of the Advisory Committee on Transmission Transmitted Diseases (ACTTD)<sup>70</sup> on 9 October 1989. His report included a recommendation in the following terms:

The Committee is asked to approve the routine testing of blood donations for anti-HCV in principle and request the National Directors in England and Scotland to arrange for the simultaneous introduction of the tests at an appropriate time when a policy for handling the seropositive donors has been defined.<sup>71</sup>

**16.46** It would be almost two years before the simultaneous introduction of testing of blood donations for anti-HCV was introduced throughout the UK. This delay is discussed in Chapter 31, *The Introduction of Screening of Donated Blood for Hepatitis C*.

<sup>67</sup> Memo [SGH.002.8012]

<sup>68</sup> Report of Meeting [SNB.001.8678]. Dr Mitchell produced a further report [SNB.002.4553]. Dr Gunson also prepared a report on the Rome meeting. Dr Gunson's original report [SNB.006.1456] was considered at the 3rd meeting of the ACTTD on 9 October 1989 and a revised version of his report was considered at the 4th meeting of the ACVSB on 6 November 1989 [SNF.001.1383] at 1401.

<sup>69</sup> Dr Mitchell's report of the incidence of NANB Hepatitis at 10% was grossly inflated, if intended. A more accurate estimate would have been 1%.

<sup>70</sup> The background to the setting up of ACTTD is set out in Chapter 27, *Surrogate Testing for non-A, non-B Hepatitis*.

<sup>71</sup> Report [SNB.006.1456] at 1460

**16.47** After this time, there was a change in the proportions of individuals reported to be affected by adverse sequelae of infection. On 8 January 1991 at the sixth meeting of the ACTTD, a paper prepared by Dr Gillon (SNBTS, Edinburgh) on counselling of donors was also discussed.<sup>72</sup> Dr Gillon was a member of the SNBTS Working Party on Donor Counselling for HCV, along with Drs R Crawford, G Galea and J Davidson. The fourth draft of their report<sup>73</sup> found that there were thought to be at least two NANB Hepatitis viruses, but that Hepatitis C was almost certainly the most common form, thought to be responsible for around 70% of post-transfusion hepatitis. This misapprehension occurred because first generation antibody tests detected only part of the variable 'non-structural' part of the virus – NS4 – which was only present, in this form, in about 70% of HCV cases overall (see paragraph 16.31 above). Once subsequent antibody tests to less variable parts of the virus had been developed, it was realised and accepted that almost all post-transfusion NANB Hepatitis could be ascribed to HCV. The report stated that most people with NANB Hepatitis would be asymptomatic but that some would go on to develop long-term liver damage: around 10–15% of those with post-transfusion NANB Hepatitis might eventually develop significant liver disease. The prevalence of carriage of NANB Hepatitis in the general donor population was not known. The prevalence of confirmed anti-HCV in UK donors was likely to be around 1 in 1000 (0.1%). Preliminary studies on Scottish blood donors showed that approximately 0.5% were repeatedly positive.

**16.48** By this stage, however, expert opinion was moving towards adopting HCV screening and the numerical data on prevalence came to be discussed in that context. Effective HCV testing of blood donors was introduced on 1 September 1991 and formed a new setting for study of the infection. Material became available to assess the prevalence of disease and prospective studies of the progress of infection became more practicable. The introduction of testing did not, however, resolve the question of the historic prevalence of infection nor of the numbers of patients likely to survive with the infection.

**16.49** In the 1990s, many countries initiated 'look-back' studies to identify patients who had received infected blood,<sup>74</sup> in an attempt to assess the prevalence of HCV infection in their populations. Work in south east Scotland found that look-back for Scottish patients would be feasible and practicable. After review on 11 January 1995, UK Ministers announced a national look-back following the East of Scotland Blood Transfusion Service model.<sup>75</sup> This topic is discussed in Chapter 35, *An Investigation into the Steps Taken to Identify the Individuals who were Infected (Look-back)*.

**16.50** The UK national HCV look-back exercise carried out between 1995 and 1998 resulted in the creation of the National Hepatitis C Register as a research tool at the Health Protection Agency (HPA), Colindale, in 1998. The initial UK exercise was closed to new entrants in 1998.

**16.51** Anonymised data from all patients identified by the look-back exercise as having contracted Hepatitis C as a result of transfusion were entered into the central register at the HPAs Centre for Infections. Systematic collection of clinical data using standardised report forms allowed data to be gathered in a uniform way approximately every two years.

<sup>72</sup> Minutes [SNB.001.8770] at 8772; Draft Report [SNB.001.8779]

<sup>73</sup> Fourth Draft Report (extracts) [SNB.001.8803]

<sup>74</sup> Professor Thomas – Day 53, page 38. The purpose of look-back was to trace NHS patients who had received blood, blood components or blood products derived from donations by donors who tested positive for Hepatitis C antibodies after 1 September 1991, when screening was introduced, and who had previously donated blood which was found by retrospective testing also to have been infective. See Chapter 35, *An Investigation Into the Steps Taken to Identify the Individuals who were Infected (Look-back)*.

<sup>75</sup> Press release [SNF.001.2191]

The data, along with mortality data for patients on the register and for controls, allowed the clinical course of HCV infection to be established and risk factors for progressive disease to be investigated.

**16.52** The Scottish exercise continued formally until 1998. On 10 June that year Dr Aileen Keel, Senior Medical Officer, SHHD, wrote to Professor Ian Franklin, Medical and Scientific Director, SNBTS.<sup>76</sup> Dr Keel informed Professor Franklin that the Advisory Committee on the Microbiological Safety of Blood and Tissue for Transplantation had resolved that all reasonable measures had been taken to trace components and recipients in Scotland and that the tracing exercise could stop.

**16.53** As the look-back exercises were coming to an end, constitutional change was implemented, with the Scottish Executive (now the Scottish Government) and Scottish Parliament convened on 1 July 1999. Description of the next stages in the developing knowledge of HCV needs to take account of the changes brought about by devolution. The differing courses of action followed in England, Wales and Scotland were described in the report of a meeting of the All-Party Parliamentary Hepatology Group on 18 November 2008.<sup>77</sup> Professor David Goldberg, Chair of the Action Plan Governance Board, gave evidence on the Hepatitis C Action Plan of the Scottish Government.<sup>78</sup> Phase I of the Plan comprised evidence gathering, which disclosed that an estimated 38,000 people were living with the virus in Scotland, of whom 14,800 had been diagnosed and only 2000 had ever received antiviral treatment. Cases of liver failure were increasing. HCV-related mortality had overtaken HIV mortality in the mid-1990s. Part II of the Plan detailed actions aimed at prevention of infection, diagnosis and treatment and care.

**16.54** The prevalence of HCV infection in the blood donating population in both England and Scotland in the first six to 12 months after the introduction of screening was low, particularly in the case of repeat donors, among whom patients with higher risk factors had already been excluded by other means. Effective heat treatment of PFC coagulation products, which was achieved by the PFC in October 1985 for Haemophilia B patients and in April 1987 for Haemophilia A therapy, made a major contribution to the protection of those patients.<sup>79</sup> However, it transpired that the majority of batches of clotting factor concentrates made from volunteer blood donations before effective heat treatment was introduced were indeed infected and the frequency of transmission was similar following use of English and Scottish NHS and commercial material, as had already been inferred.<sup>80</sup> Screening of donations, from 1 September 1991, provided substantial protection for all recipients of blood, blood components and blood products.<sup>81</sup>

**16.55** Most of the current knowledge of Hepatitis C (discussed in Chapter 13, *Knowledge of Viral Hepatitis Now*) developed after September 1991. With routine screening added to viral inactivation the threat of transmission of HCV infection by transfusion or by blood product therapy was substantially removed. Since then, new cases have been largely confined to needle sharing, mother to child transmission and medical procedures.<sup>82</sup>

<sup>76</sup> Letter [SGH.003.1055]

<sup>77</sup> APPHG paper *Divided Nations: Tackling the hepatitis C challenge across the UK* [LIT.001.4538]

<sup>78</sup> Ibid [LIT.001.4538] at 4549. Professor Goldberg is a Consultant Epidemiologist at Health Protection Scotland and Honorary Professor of Public Health at Glasgow University.

<sup>79</sup> Chapter 24, *Viral Inactivation of Blood products for Haemophilia Therapy 1985–1987*, paragraph 24.9 and paragraphs 24.157–24.159.

<sup>80</sup> Professor Thomas – Day 52, page 80

<sup>81</sup> Chapter 31, *The Introduction of Screening of Donated Blood for Hepatitis C*, paragraph 31.248

<sup>82</sup> *Confronting the silent epidemic: a critical review of hepatitis C management in the UK* [LIT.001.4801] at 4814

Practical implementation of Phase II of the Scottish Action Plan has been discussed in relation to the management of prisoners by the Western General Hospital, Edinburgh.<sup>83</sup> However, Professor Goldberg's view remains generally pessimistic:

Maintaining the current level of response is not an option if we are to interrupt the UK's relentless escalation in serious disease and death caused by hepatitis C. Action Plans without muscle have suboptimal impact. There is no time to lose.<sup>84</sup>

### Perception of the severity of NANB Hepatitis/Hepatitis C

**16.56** Professor Goldberg's comment is a reflection of the contemporary view of HCV infection. In the late 1980s there was a material change in the general perception of the severity of the sequelae of NANB Hepatitis infection. The stages in developing thought have been noted but, in order fully to appreciate the extent of the change, it is appropriate to summarise the main points.

**16.57** From about 1978 doctors had monitored haemophilia patients' ALT levels more or less as a matter of course, but in the UK liver enzyme abnormalities without clinical signs of infection were not thought to be indicative of hepatitis. Probably, during the period 1980–88, there developed a general recognition among haemophilia doctors of the existence of NANB Hepatitis but most would have perceived the disease to have a generally benign prognosis.

**16.58** Histology obtained by conventional biopsy was thought by the middle and later 1980s to be the most reliable way of monitoring the severity of liver disease.<sup>85</sup> Earlier misconceptions, based on the histological changes observed in patients with Hepatitis B infection and which had contributed to the inference that NANB Hepatitis was a disease with a generally benign prognosis, were set aside. It came to be appreciated that it was wrong to suppose that chronic persistent and chronic active hepatitis would follow the same clinical course in Hepatitis C as it does in Hepatitis B.<sup>86</sup> In the mid-1980s views had begun to change towards recognising NANB Hepatitis as a more serious condition: chronic persistent hepatitis in haemophilia patients was not as benign as hitherto supposed.<sup>87</sup>

**16.59** Professor Howard Thomas<sup>88</sup> said that this was when views were changing.<sup>89</sup> His evidence is accepted as a reflection of the state of knowledge among experts at the cutting edge of research and clinical practice; general knowledge would develop more slowly. Two relevant conclusions follow. In the first place, there was no generally accepted view prior to 1985 that NANB Hepatitis had more than the generally benign prognosis described by Professor Sherlock before the 8th edition of her book. Secondly, from publication of the 8th edition in 1989 it was generally understood that NANB Hepatitis infection could be associated with serious disease. The development of generally accepted opinion in the second half of the 1980s is likely to have been subject to individual clinicians' access to, and understanding of, the latest developments in the field. It will not have been uniform and it will be likely to have been patchy until 1989.

<sup>83</sup> Ibid [LIT.001.4801] at 4819

<sup>84</sup> Ibid [LIT.001.4801] at 4823

<sup>85</sup> Professor Thomas – Day 53, pages 9–10

<sup>86</sup> Professor Thomas – Day 52, page 119

<sup>87</sup> Professor Thomas – Day 53, pages 41–43; Hay et al, 'Progressive liver disease in haemophilia; an understated problem?', *The Lancet* 1985; 1:1495–97 [LIT.001.0335]

<sup>88</sup> Currently Emeritus Professor in Hepatology at Imperial College, London.

<sup>89</sup> Professor Thomas – Day 52, page 146



**16.60** By 1989, Professor Sherlock and others (including Professor Thomas) were engaged in studies, based on biopsy findings, which demonstrated that patients with chronic NANB Hepatitis had disease that covered the whole spectrum of acute and chronic hepatitis, including cirrhosis.<sup>90</sup> Professor Sherlock's view, as expressed in the 8th edition of her textbook in 1989, was changing towards recognition that NANB Hepatitis was a disease with a variable prognosis, ranging from a benign condition with spontaneous biochemical improvement after a few years to a chronic disease associated with cirrhosis in a significant proportion of patients, and hepatic failure and hepatocellular cancer in rare cases.

**16.61** It is a material fact that early forms of treatment with Interferon became available for clinical testing in about 1989, soon after the announcement of the Chiron discoveries.<sup>91</sup> Interferon A was first used in England in 1989 and in Scotland in 1990–91. It would be some years before the grant of a licence and approval for use in England and Wales and before equivalent regulatory approval was given in Scotland, in November 1994. However, with the identification of the virus and the arrival of the first forms of therapy (initially thought to be more effective than events were to prove) there was an incentive to further develop knowledge of the disease.

### Developments since 1991

**16.62** Since effective viral inactivation, the infusion of blood products has not been associated with the transmission of Hepatitis C to any material extent. Largely retrospective research demonstrated that until then the frequency of transmission of HCV by Factor VIII concentrates, as shown by raised ALT levels, was similar in both commercial materials and the products of the UK public service fractionators.<sup>92</sup> More generally, transfusion of blood and blood components has not been associated with transmission of Hepatitis C since 1991 when screening of donated blood for HCV became universal practice in the UK. These events superseded the debate which had persisted between 1970 and 1990, as to whether volunteer blood donations were safer than those derived from paid donors, in particular blood products imported from the USA.

**16.63** Current known cases of infection among NHS patients, and cases yet to be diagnosed, generally have their origins in treatment before those critical dates. Unless the infection is picked up incidentally during health screening or following detection of abnormal liver biochemistry in a blood test taken for an unrelated reason, and because the clinical course of NANB Hepatitis/HCV infection is asymptomatic in most cases, the infection may not come to medical attention for many years until late-stage disease is reached. At that stage the patient presents with signs of chronic liver disease or a complication of cirrhosis, such as variceal haemorrhage, ascites or the development of hepatocellular carcinoma. Estimates of undiagnosed cases cannot be substantiated. An unknown number of individuals may currently be infected but remain asymptomatic. Some may be destined never to develop complications; others will progress. Knowledge of the cohort currently infected, and their prognoses, is necessarily incomplete.

**16.64** Professor Thomas emphasised that doubt remained about the progression of the disease generally:

<sup>90</sup> Bamber et al, 'Clinical and histological features of a group of patients with sporadic non-A non-B hepatitis', *Journal of Clinical Pathology*, 1981; 34:1175–80 [LIT.001.0759]

<sup>91</sup> Professor Thomas – Day 53, page 40

<sup>92</sup> Professor Thomas – Day 52, page 76; Professor Thomas' report [PEN.017.1071] at 1077. And see, for example, Yee et al, 'The natural history of HCV in a cohort of haemophilic patients infected between 1961 and 1985', *Gut*, 2000; 47:845–851; [LIT.001.4318]

[S]ome would say, even now, we do not really know the factors that determine the rate of progression and, for instance, in Italy Hepatitis C has a much worse prognosis to what you see in northern Europe ... and ... that's arguably related to all the other factors ... how much alcohol you take, the genetic factors, whether there is co-infection with other viruses, all manner of things.

So I don't think this uncertainty about the natural history that was prevalent between 1978 and 1985 has changed massively. I think we are still wondering: is it 20 per cent or 40 per cent that will develop cirrhosis? All we can deduce from these studies is that some people in the context of normal life ... where we eat and drink ... some people have severe liver disease. But how many, that's an open question still because none of the studies ... are statistically significant. There isn't a large enough sample of unselected cases.<sup>93</sup>

**16.65** There have, however, been advances in knowledge of HCV infection, as shown in Chapter 13, *Knowledge of Viral Hepatitis Now*. Developments since about 1997 have involved laboratory research, by Dr Graeme Alexander and others, on the effect of ageing (measuring people's biological age)<sup>94</sup> and outcome for patients. 'Telomeres', pieces on the ends of DNA which act a bit like the piece of plastic on the end of a shoelace, prevent the DNA from 'fraying' and being damaged. There is a relationship between progressive degradation of DNA, as the telomeres shorten with age, and the development of age-related diseases such as cancer, cardiovascular disease and strokes. It is now known that the same mechanism affects HCV-positive patients, once they reach a certain biological age. They become unable to mount an immune response to infection. The immune system begins to be impaired at around age 60 and cannot cope with Hepatitis C as the virus takes a stronger grip.<sup>95</sup>

**16.66** On the basis of the evidence as a whole on this topic, one would anticipate that a person, infected with HCV after attaining an age at which deterioration in the structure of DNA had progressed sufficiently to damage the DNA's capacity to defend itself against disease, will progress relatively rapidly from infection to cirrhosis and then to liver failure. The 'biological age' of an individual is likely to vary, and Dr Alexander's reference to age 60 might be unduly alarmist in many cases. After that age, however, the epidemiological evidence appears to be clear.

**16.67** In epidemiological terms, Hepatitis C is known to have affected people to some extent in the mid-20th century. However, there is now scientific evidence that it affected the general population in many parts of the world long before that.<sup>96</sup> Since the mid-1980s there has been intensive research into its history and genetics. Research into the genetics of HCV by Professor Peter Simmonds of Edinburgh University has developed methods of classifying sub-types of the virus and effectively constructing an evolutionary tree for the virus showing how the various genotypes and sub-types now recognised have developed and diverged over time. His research has now demonstrated that HCV is a member of a very ancient group of viruses.<sup>97</sup> The characteristics of the disease caused by this virus were, however, quite unknown until the end of the twentieth century.

<sup>93</sup> Professor Thomas – Day 52, pages 138–139

<sup>94</sup> 'Biological age' is a measure of how well or poorly a given individual's body is functioning relative to their calendar ('chronological') age. It measures how old a person's body is compared to what we would expect from an 'average' body at that age.

<sup>95</sup> Dr Alexander – Day 4, pages 42–44 and 46–47

<sup>96</sup> Professor Goldberg – Day 6, page 96

<sup>97</sup> Dr Gillon – Day 6, page 20

**16.68** At the beginning of the oral hearings of this Inquiry in March 2011, the isolation and culture of one type of the complete Hepatitis C virus had been reported.<sup>98</sup> The position in 2011 was explained by Professor Willem van Aken when he gave evidence.<sup>99</sup> Almost 100% of the genomic composition of the virus had been identified by the end of the 1980s but the virus as a whole had not been isolated. It could not be reproduced by culturing (growing in appropriate nutrient substances) and one could therefore not add a known quantum of virus to plasma and submit it to inactivation to see how much virus was destroyed. However, knowledge of almost the whole genomic composition of HCV enabled scientists to make comparisons with other viruses and to select viruses with similar genomic characteristics, such as pestiviruses and togaviruses. These could be used as 'indicator viruses' or proxies for HCV. Knowledge of the genomic composition of HCV sufficient for this purpose was not achieved until around 2000. Reports of the isolation of specific sub-types of particular genomes have been published in the last ten years and there have been significant developments in the treatment of HCV infection as a result.<sup>100</sup>

### Summary

**16.69** The state of knowledge of HCV, and the natural history of the disease, discussed in Chapter 13, *Knowledge of Viral Hepatitis Now*, had not reached maturity in the early 1990s. Professor Thomas' evidence relating to the scientific basis of Chiron's discoveries reflected the results of continuing research over many years.

**16.70** It can be concluded, however, that:

- There was no generally accepted view prior to 1985 that NANB Hepatitis had other than a generally benign prognosis.
- 1985 was a turning point: this was when information began to emerge that would lead to changing views.<sup>101</sup>
- From 1985 it became increasingly understood that NANB Hepatitis infection could be associated with serious disease, progressing to cirrhosis in a significant proportion of cases, and to liver failure and ultimately hepatocellular cancer, albeit rarely.
- The introduction of Interferon therapy from 1989 provided a focus for wider understanding of the characteristics and natural history of HCV infection.
- The science of genetics has been fundamental to the discovery of characteristics of HCV.
- Diagnostic techniques, using model viruses based on genetic analysis, became available at the end of the twentieth and the beginning of the twenty-first century.

**16.71** The current understanding of Hepatitis C is necessary background to a proper appreciation of the accounts of patients and witnesses of experiences of infection with the virus. Depending on the route of transmission, recipients of blood and blood component transfusions are highly likely to have been infected before September 1991 and haemophilia patients to have been infected before October 1984 (patients treated with Factor IX) or April 1987 (patients treated with Factor VIII).

---

<sup>98</sup> See Chapter 13, *Knowledge of Viral Hepatitis Now*, paragraph 13.20.

<sup>99</sup> Day 2, pages 29–34

<sup>100</sup> See Chapter 13, *Knowledge of Viral Hepatitis Now*, generally for discussion of the progress in treatment.

<sup>101</sup> Professor Thomas – Day 52, page 146

© Crown copyright 2015

An online version of the report is available at [www.penroseinquiry.org.uk](http://www.penroseinquiry.org.uk)

**ISBN: 978-0-85759-022-0 (Volume 2 of 5)**

**This Inquiry Report comprises an Executive Summary (ISBN: 978-0-85759-023-7), five volumes and a DVD**

Published on behalf of The Penrose Inquiry by APS Group Scotland, 21 Tennant Street, Edinburgh EH6 5NA  
DPPAS43828 (03/15)

THE  
PENROSE  
INQUIRY

# Final Report

**Volume 3:  
Blood and Blood Products**

THE  
PENROSE  
INQUIRY

# Final Report

**Volume 3:  
Blood and Blood Products**

Laid before the Scottish Parliament by the Scottish Ministers  
under section 26 of the Inquiries Act 2005.

March 2015  
SG/2015/15

© Crown Copyright 2015



This publication is licensed under the terms of the Open Government Licence v3.0 except where otherwise stated. To view this licence, visit [nationalarchives.gov.uk/doc/open-government-licence/version/3](https://nationalarchives.gov.uk/doc/open-government-licence/version/3) or write to the Information Policy Team, The National Archives, Kew, London TW9 4DU, or email: [psi@nationalarchives.gsi.gov.uk](mailto:psi@nationalarchives.gsi.gov.uk).

Where we have identified any third party copyright information you will need to obtain permission from the copyright holders concerned.

This publication is available at [www.penroseinquiry.org.uk](http://www.penroseinquiry.org.uk).

ISBN: 978-0-85759-022-0  
(Volume 3 of 5)

Published on behalf of The Penrose Inquiry by APS Group Scotland, 21 Tennant Street, Edinburgh EH6 5NA  
DPPAS43828 (03/15)

## CONTENTS

<b>Volume 3: Blood and Blood Products</b>		Page
17	Blood and Blood Products Management	709
18	Collection of Blood – General	735
19	Production of Blood Products – Facilities	763
20	Haemophilia Therapy – The Period up to the Early 1980s	785
21	Haemophilia Therapy – Use of Blood Products	805
22	Haemophilia Therapy – Use of Blood Products 1985–1987	897
23	Viral Inactivation of Blood Products for Haemophilia Therapy up to 1985	933
24	Viral Inactivation of Blood Products for Haemophilia Therapy 1985–1987	1013



## CHAPTER 17

### BLOOD AND BLOOD PRODUCTS MANAGEMENT

**17.1** This part of the report deals generally with questions related to the collection of blood and its adaptation for clinical use. Some information about the administrative and management structures set up for the provision of blood services in Scotland is required, as background to that discussion, to introduce relevant bodies and to provide an indication of the scope of their responsibilities. It is not necessary for the purposes of the Inquiry, however, to attempt to provide a comprehensive account of the history of these bodies or their legal background. For the early stages in the history the Inquiry has drawn on two monographs describing the organisation of blood collection and management: Dr W N Boog Watson's *The Scottish National Blood Transfusion Association 1940 – 1965*<sup>1</sup> and Professor Ronald Girdwood's *Fifty Years of an Organised Blood Transfusion Service in Scotland*<sup>2</sup> written in the early 1990s. Together these provide fascinating insights into aspects of the story which cannot be developed in this report.

#### **Early history of blood organisation: the SNBTA**

**17.2** The Scottish National Blood Transfusion Association (SNBTA) was formally constituted on 5 March 1940. The need for a national organisation had been advocated by the Blood Transfusion Sub-Committee of the Department of Health's Scientific Advisory Committee, which had been set up at the beginning of 1939 as part of a review of emergency medical preparations in Scotland in anticipation of war following the Munich crisis in 1938.<sup>3</sup>

**17.3** The remit of the Blood Transfusion Sub-Committee had included review of existing facilities and the consideration of necessary changes in securing the provision of blood for emergency use. More particularly the Sub-Committee was instructed 'to advise on the storage of blood in selected centres'. The practice of storing blood in blood banks was novel. It had started in Madrid in 1937 during the Spanish Civil War. Spanish experience influenced the sub-committee and led to a preliminary recommendation, before publication of its report, that stores of blood should be established in the principal population centres. By 3 September 1939, when war was declared, small blood banks had been established at the Royal Infirmary of Edinburgh (RIE) and Stobhill Hospital, Glasgow.<sup>4</sup>

**17.4** The start of the war coincided with other changes in blood transfusion that pointed to a need for central administration of the service. Professor Girdwood recalled:

[T]he situation was that there was a major war in progress just at the time when knowledge about blood transfusion problems and techniques was increasing and clearly some form of Scottish national organization was speedily required.<sup>5</sup>

<sup>1</sup> Boog Watson, WN. *The Scottish National Blood Transfusion Association, 1940–1965*, 1965, E&S Livingstone Ltd, Edinburgh and London [PEN.019.1359]

<sup>2</sup> Girdwood, RH. *Fifty Years of an Organised Blood Transfusion Service in Scotland* (undated) [SNB.010.1836]

<sup>3</sup> Boog Watson, WN. *The Scottish National Blood Transfusion Association, 1940–1965*, 1965, E&S Livingstone Ltd, Edinburgh and London [PEN.019.1359] at 1364–5

<sup>4</sup> Ibid [PEN.019.1359] at 1365; Girdwood, RH., *Fifty Years of an Organised Blood Transfusion Service in Scotland* (undated) [SNB.010.1836] at 1837

<sup>5</sup> Girdwood, RH. *Fifty Years of an Organised Blood Transfusion Service in Scotland* (undated) [SNB.010.1836] at 1838

**17.5** Donor centres had already been set up in Edinburgh and Glasgow. The Edinburgh operation had started in 1929 and had grown over the intervening period as a result of a number of initiatives, the last of which, in 1936, had been promoted by the Lord Provost. In Glasgow, the Lord Provost convened a meeting in June 1939 which led to the organisation of a panel of donors and, shortly thereafter, to the establishment of a regional donor centre. In other areas practice was less developed. Following on the sub-committee's report, letters were sent to the Lords Provost and civic leaders throughout the country urging the development of transfusion services. Against the background of enthusiastic but varying response, it was decided that a national council was required to take central control and form a more permanent Blood Transfusion Association. On 9 February 1940, the Department of Health for Scotland invited Lord Rosebery to chair the national organisation in Scotland.<sup>6</sup>

**17.6** From the outset it was intended that the transfusion service would remain a voluntary service, supported by voluntary donations, but it was anticipated that generous central government grants would be required to support the range and scope of services the Association would be expected to provide. During the war, the service was enthusiastically supported by members of the public, both as donors and in raising funds by collections, fairs and other events. That changed after the war. Dependence on the Exchequer grant grew rapidly, to the extent that by 1952 voluntary donations accounted for less than 0.5% of the SNBTA's revenue.

### **A step change in service provision**

**17.7** Over the war period there were major changes in the scope of the blood transfusion service. The SNBTA took over a miscellany of local services including the blood banks in Edinburgh and Glasgow, and small lists of donors in other areas. It also set about establishing some common policies. Five regional centres were established at Dundee, Edinburgh, Glasgow, Aberdeen and Inverness.

**17.8** The introduction of blood banks was a major development. Until 1939 some districts had no storage facilities at all. In some smaller hospital areas relatives were called in when a transfusion was required and, subject to compatibility, were bled immediately before treatment of the patient. Some hospitals had lists of professional donors who would give blood for a fee. Some favoured voluntary donation, recruiting donors by public appeal or with the help of charitable organisations.<sup>7</sup> The SNBTA developed new procedures for the organisation of blood collection and new facilities for handling and processing the blood collected. In the future, only exceptionally would a volunteer be called on to provide blood for a single patient. Donor sessions would be organised and blood collected to build up and replenish blood banks. Blood banks would store whole blood or plasma to be called down by hospitals in the region for clinical use. Storage required refrigeration equipment and support services. Funds were required immediately and were raised with such efficiency that by July 1940, the chairman of the SNBTA technical committee could claim that the various services could cope with any demands which might be made on their resources.<sup>8</sup>

<sup>6</sup> Boog Watson, WN. *The Scottish National Blood Transfusion Association, 1940–1965*, 1965, E&S Livingstone Ltd, Edinburgh and London [PEN.019.1359] at 1364–5

<sup>7</sup> Ibid [PEN.019.1359] at 1365

<sup>8</sup> Ibid [PEN.019.1359] at 1366

**17.9** However, technological changes were imminent. It became clear that plasma had considerable value since it obviated the need for cross-matching in an emergency situation, and was particularly effective in treating shock. There was a considerable demand from the armed forces. Unrefrigerated plasma was shipped from the United States (before the USA entered the war), but often arrived with bacterial contamination. Casualties in the war brought home the need for local supplies to be available.<sup>9</sup> In August 1941, central depots were organised in Edinburgh and Glasgow, to prepare raw material collected locally and from other regions of Scotland and to store plasma for use. This removed the risk of contamination associated with imported plasma. It was agreed that a predetermined quantity of blood for processing would be regularly provided from each blood bank in the country.<sup>10</sup>

**17.10** It was then shown in England that plasma could be dried and reconstituted. In its dried state plasma could be preserved for a much longer period. There arose a great demand for the product, especially from the armed forces, but also for emergency use in civilian practice.<sup>11</sup> A unit for the production of dried plasma was required. The necessary apparatus was installed in Edinburgh at the beginning of 1943 to meet all Scottish needs. Edinburgh was thought to be in less danger of bombing than the west of Scotland. For the next 12 years, it continued to be the processing centre for the whole of Scotland for the production of dried plasma.<sup>12</sup>

**17.11** In the meantime, in the early months of the war, the Department of Health (DoH) funded the provision of a 'saline infusion fluids centre' for the preparation of saline glucose and other solutions used for intravenous injection. It had been located in Glasgow where the clinician selected by the Department to take charge of the operation worked. These early decisions were reflected in the location of the major laboratory and production facilities in the Glasgow and Edinburgh regions as they developed. The laboratory at Edinburgh was expanded to handle the fractionation of plasma when that process was introduced in 1952, initially for the production of immunoglobulin.<sup>13</sup> As demand grew for the specialist services provided in Glasgow, civil defence considerations led to the relocation of its facilities to Law Hospital, Carluke. The western service became responsible for plasma drying in 1956 for the whole of Scotland except the Edinburgh and south-east region.<sup>14</sup> The provision of laboratory and other facilities required for the development of the service is discussed in Chapter 19, *Production of Blood Products – Facilities*.

**17.12** The war years saw huge changes in the transfusion service, in its organisation and in its facilities and, more particularly, in the scope and range of the blood and blood components it managed and provided. There were also changes in the relationships between the service and its donors.

<sup>9</sup> Girdwood, RH. *Fifty Years of an Organised Blood Transfusion Service in Scotland* (undated) [SNB.010.1836] at 1839

<sup>10</sup> Boog Watson, WN. *The Scottish National Blood Transfusion Association, 1940–1965*, 1965, E&S Livingstone Ltd, Edinburgh and London [PEN.019.1359] at 1367

<sup>11</sup> *Ibid* [PEN.019.1359] at 1367

<sup>12</sup> *Ibid* [PEN.019.1359] at 1374–5

<sup>13</sup> Foster, 'Plasma Fractionation in Scotland', *Blood Letter*, Spring 2008 [PEN.017.2468]

<sup>14</sup> Boog Watson, WN. *The Scottish National Blood Transfusion Association, 1940–1965*, 1965, E&S Livingstone Ltd, Edinburgh and London [PEN.019.1359] at 1367

## Donor organisation

**17.13** Before March 1940, donor organisation was a strictly local concern and policies varied across the country. Small payments and other forms of reward had been made to donors in some areas of Scotland. The newly formed SNBTA favoured the use of voluntary donations and decided to bring an end to payments. This was one of the first acts of the new body and helped to bring about consistency in the practice of recruiting and dealing with donors throughout Scotland. It came to characterise the Scottish system in popular perception and in the representations made about the system domestically and internationally. In *The Gift Relationship*,<sup>15</sup> published in 1970, Richard Titmuss, a United Kingdom social scientist, described the British system of blood management as following the social welfare model, with blood treated as a free community resource, collected and distributed by the State. In Scotland the State provided financial support, but did not have a significant managerial role before the National Health Service was established on 5 July 1948, when the National Health Service (Scotland) Act 1947 (the 1947 Act) came into force.<sup>16</sup>

**17.14** The SNBTA took over a service that had grown in a piecemeal fashion. Operational units had a strong sense of local identity. The SNBTA developed a network of blood transfusion centres and panels of volunteer blood donors, in the modern sense, that reflected practice throughout the United Kingdom after the Second World War.<sup>17</sup> In general, however, Titmuss's characterisation applied to Scotland from 1940: the developing service conformed to the social welfare model.

**17.15** From 1940, the service continued to be based on the voluntary donor. War conditions affected the operation of the service. Many potential donors were on active service in the armed forces. Others were employed in occupations remote from collection centres. Mobile collection teams were necessary in some areas to meet the growing demand for blood in 1943 and 1944. There was a strong public response. In 1943 the number of donors rose from 43,000 to 57,000 and in the first half of 1944, as 'D-Day' approached, a further 10,000 donors were recruited. The invasion of France created increased demand in the third quarter of 1944. However, after the war the transition to peace was difficult. Staff changes followed the return of personnel to civilian life. Premises had to be returned to civilian use. Public enthusiasm waned and donor attendances at sessions fell.<sup>18</sup>

**17.16** The wider environment had changed with peace. The requirements of hospitals treating service personnel decreased after the war. However, changes in the therapeutic application of blood and blood components and products in civilian hospitals continued to increase with the growing importance of the use of blood in maternity work and in the treatment of burns and other accident damage. Transfusion was no longer a near-desperate measure in the face of emergency: it had become a well-established form of treatment with ever widening possibilities. The incentive to support the service financially by private donation had changed. In the meantime, the work of the SNBTA was made more difficult by uncertainty about its future. It was increasingly dependent on public funding and, as a corollary, exposed to the influence of government policy. There was a

<sup>15</sup> Titmuss, RM. *The Gift Relationship: From Human Blood to Social Policy*. 1970, Allen & Unwin, London

<sup>16</sup> The voluntary principle is discussed more fully in Chapter 18, *Collection of Blood – General*, paragraphs 18.3 to 18.20.

<sup>17</sup> Dr Derek Norfolk – Day 7, page 60

<sup>18</sup> Boog Watson, WN. *The Scottish National Blood Transfusion Association, 1940–1965*, 1965, E&S Livingstone Ltd, Edinburgh and London [PEN.019.1359] at 1367–8

possibility in 1948 that the Association would be merged with the National Health Service. That did not happen.

**17.17** The Association's property and staff were transferred to the Secretary of State when the National Health Service was established but the SNBTA itself continued as an independent body.<sup>19</sup> A proportion of the officers and members of the Association were now nominated by the Secretary of State or by regional hospital boards. But the regime established by agreement with the Secretary of State provided the stability the Association required to get on with its work. An early task was revision of the lists of donors in every region to reduce the registered donors to those who were 'live', who could be expected to attend donor sessions when asked to do so. The work of recruiting new 'live' donors was vigorously pursued.<sup>20</sup>

**17.18** The need for review of the donor system varied across the individual regions. Before the war, Edinburgh was the only place in Scotland with an established blood transfusion service. In other places some hospitals had worked with small lists of donors. The drive to recruit more donors had been managed in various ways across Scotland. In certain areas the population was concentrated around major settlements, while in others the scattered population led to a greater reliance on mobile teams that often had to travel considerable distances. The western service, based round Glasgow, had been able to recruit many donors from the work forces of large industrial employers. An early task for the SNBTA had been to establish a suitable network of blood banks, taking account in some regions of the need to equip smaller, more remote, hospitals that could not easily be served by the larger regional centres.

**17.19** The heterogeneity of the regions was largely a reflection of geography, population spread and employment. This did not change after the war, nor with the establishment of the National Health Service. Blood collection had to take account of the realities. Regional organisers, appointed in each region in 1940 with responsibility for raising the money required to maintain the service, to recruit donors and to arrange blood donation sessions, depended for success on voluntary local organisers. Dr Boog Watson said:

In every rural parish, country town and city district in which donors were recruited the regional organisers by personal search and personal approach secured their local organisers, often through such channels as the Red Cross, W.V.S., or Women's Rural Institutes.<sup>21</sup>

This produced a diverse group of men and women from all walks of life who maintained contact with donors. The collection of blood had the character of a voluntary charitable activity. Effective organisation depended on the goodwill of the organisers and the donors and their personal commitment. These characteristics would continue.

### **The role of ministers**

**17.20** The National Health Service (Scotland) Act 1947 provided that it would be a function of the Secretary of State to promote the establishment of a comprehensive health service and provide or secure the provision of services, which necessarily included the provision of blood for clinical use. Accordingly:

<sup>19</sup> Ibid [PEN.019.1359] at 1368

<sup>20</sup> Ibid [PEN.019.1359] at 1369

<sup>21</sup> Ibid [PEN.019.1359] at 1377-8

- From 1948, the principal duty of providing effective health care in Scotland, including promoting the effective provision of blood transfusion services, has been the responsibility of the Secretary of State for Scotland and now the Scottish Ministers.
- The Secretary of State assisted by Scottish Office Health Ministers, and now Scottish Ministers and in particular the Health Ministers, supported by their respective civil servants, have operational control of health care policy.

**17.21** Central government provided increasing funding of the SNBTA's operations by Exchequer grant. The sum provided in 1944 was £7250. By 1964 that had risen to £363,368.<sup>22</sup> There was ever-increasing need for funding of the service, including the funding of major capital projects. These included facilities for the production of coagulation factor products for the treatment of haemophilia and other coagulation disorders. It was probably inevitable that the SNBTA's role would be reduced.

**17.22** Professor Girdwood commented:

When the war ended the need for Government financing became much greater and the coming of the National Health Service necessitated a complete reconsideration of the organization of blood transfusion services in Scotland. It was decided not to make this a responsibility of Regional Hospital Boards .... The notion that the Association could continue to administer the Service was not realistic ....<sup>23</sup>

However, change did not come as quickly as it might. Legislation was not in place until 1972.

**17.23** Section 19 of the National Health Service (Scotland) Act 1972 provided for the constitution of the Common Services Agency for the Scottish Health Service (the CSA) with effect from 1 April 1974.<sup>24</sup> It provided that:

(2) The Secretary of State may by order delegate to the Agency such of his functions as he considers appropriate.

And

(8) In carrying out its functions the Agency shall act subject to and in accordance with such directions as may be given by the Secretary of State.

## The CSA

**17.24** The functions of the CSA were initially set out in the National Health Service (Functions of the Common Services Agency) (Scotland) Order 1974<sup>25</sup>. Article 3 of the Order, as regards blood, provided:

<sup>22</sup> Ibid [PEN.019.1359] at 1381

<sup>23</sup> Girdwood, RH. *Fifty Years of an Organised Blood Transfusion Service in Scotland* (undated) [SNB.010.1836] at 1843

<sup>24</sup> National Health Service (Scotland) Act 1972 s 19(3) and National Health Service (Functions of Common Services Agency) (Scotland) Order 1974 (SI 1974/467) Article 3(a). From 28 May 2004 the CSA adopted the name 'NHS National Services Scotland': <http://www.nhsns.org/uploads/publications/AnnualReportandAccounts0304-for%20website.pdf>. This change had no legal effect and the statutory name is used in this Report.

<sup>25</sup> SI 1974/467

It shall be the duty of the Agency to undertake the following functions:—

....

(e) the provision of supplies of human blood for the purposes of carrying out blood transfusion and related services, including the production of blood fractions.

Formally, the CSA took over most of the functions of the SNBTA in 1974. In structural terms, the CSA operated through a management committee and a series of sub-committees including, in time, the (CSA) Blood Transfusion Sub-Committee.

**17.25** Accordingly, in terms of the successive Health Acts and subordinate legislation:

- From 1974, the CSA had delegated responsibility for the operational management of blood services.
- The CSA was subject to, and was obliged to act in accordance with, such directions as might be given by the Secretary of State.

**17.26** The 1947 Act was repealed by the National Health Service (Scotland) Act 1978 (the 1978 Act) which continued the general duties of the Secretary of State, including the provision or securing the provision of services. The CSA was reconstituted under the 1978 Act and section 19 of that Act repeated the provisions of section 19 of the 1972 Act as quoted above. Under the 1972 and 1978 Acts the members of the Management Committee of the CSA were appointed by the Secretary of State.

**17.27** That remained the position until, with effect from 1 October 2008, the 1974 Order was revoked by the National Health Service (Functions of the Common Services Agency) (Scotland) Order 2008.<sup>26</sup> So far as relevant for present purposes, the 2008 Order removed the production of blood fractions from the functions of the CSA, but continued to provide for delegation of the provision of supplies of human blood for transfusion and related services.

### **The CSA and the Blood Transfusion Service**

**17.28** Scottish Home and Health Department (SHHD) circular HSR(72)C2<sup>27</sup> which dealt specifically with the CSA, narrated under the heading 'Functions' that the purpose of the new organisation was to provide the SHHD and the Health Boards with a variety of services which could be provided most efficiently by a single agency. It also stated, under the heading 'Central Organisation' that:

The main responsibility for the day to day running of each service within the allocated expenditure and in accordance with broad policies will fall to the chief officer or director of that division of the CSA; and he will in most cases be directly responsible to the Management Committee or to any sub-committee which may be set up for the particular service. It is unlikely that the Management Committee as such will normally have to concern itself with the detailed running of any of the services provided by its operational divisions or that it could attempt to do so over a wide range of services.

<sup>26</sup> SSI 2008/312

<sup>27</sup> SHHD circular HSR(72)C2, *Common Services Agency*, 3 November 1972 [PEN.019.1477]

....

As indicated, regulations made by the Secretary of State may provide, where appropriate, for sub-committees which include persons not members of the Management Committee. It will be open to the Management Committee to propose such sub-committees for those services where it seems necessary to do so....<sup>28</sup>

**17.29** The government's intention to transfer responsibility for the Blood Transfusion Service to the CSA was set out in the Scottish Home and Health Department (SHHD) circular HSR(73)C40. It stated under the heading 'Reorganisation';

On the appointed day, the Blood Transfusion Service will become a division of the CSA; operational arrangements, based on the five centres and the Protein Fractionation Centre will not be affected. Staff employed by the Association will transfer to the employment of the CSA, although this will not affect the work or organisation of the centres.<sup>29</sup>

**17.30** That operational control was intended to remain with the SNBTS was recognised by the CSA Management Committee as reflected in an extract from the minutes of its second meeting on 14 March 1974:

It was noted that the operational responsibility for the Blood Transfusion Service would rest with each Regional Director within his region. So far as operational problems affecting Scotland as a whole were concerned it was agreed that a Co-ordinating group should be set up consisting of the National Medical Director, the five Regional Directors, the Scientific Director of the Protein Fractionation Unit, and the Administrative Officer. The National Medical Director would act as spokesman for the group to the Management Committee.

**17.31** SHHD circular HSR(73)C40 was greeted with concern among transfusion specialists. They were worried that the CSA would lack the technical competence to manage the highly specialised transfusion service that was envisaged as the replacement for the SNBTA and that the Regional Directors would lose the autonomy they had enjoyed under the SNBTA.

**17.32** These concerns were expressed by a member of the South-East Scotland Regional Blood Transfusion Service (probably Dr Robert Cumming),<sup>30</sup> in a paper circulated on 29 November 1973 commenting on the circular. His concern was that circular HSR(73)C40 lacked information about future arrangements. It did not show 'evidence of policy', nor did it make adequate provision for 'representation by those who best understand the clinical, scientific and technical complexities of blood transfusion practice'.<sup>31</sup>

**17.33** From a different point of view, Mr John Watt, Scientific Director of the Protein Fractionation Centre (PFC), sent proposals for restructuring the service to all Regional Transfusion Directors in December 1973.<sup>32</sup> He proposed a centralised management arrangement, which he argued would be compatible with the new overall organisation, but would operate through a committee comprising administrators, transfusion and

<sup>28</sup> Ibid [PEN.019.1477] at 1478

<sup>29</sup> SHHD circular HSR(73)C40, *Common Services Agency – The Blood Transfusion Service*, 26 October 1973 [SNB.011.0587]

<sup>30</sup> Dr Cumming was at the time Regional Director of the SNBTS (Edinburgh and South-East Scotland Region), but about to retire. See his letter of the same date to Dr Wallace and others [SNB.011.0589]

<sup>31</sup> *The Blood Transfusion Service: Common Services Agency – (HSR(73)C40)* [SNB.011.0592] at 0592–3

<sup>32</sup> *The Scottish National Blood Transfusion Service: A Future in the Common Services Agency?* [SNB.011.0602]



scientific directors, donor representatives, and representatives of user interests. The bias in his proposals was towards management by experts and those intimately concerned with the quality of delivery.

**17.34** Writing on the eve of the restructuring of the Blood Transfusion Service in January 1974, Dr John Wallace, Glasgow and West of Scotland BTS, said:

S.N.B.T.A., apart from its financial control, has allowed each regional director comparative freedom in developing the transfusion service within his region. I am now afraid that we are likely to feel the iron hand of central management, unless we exert professional influence.<sup>33</sup>

Dr Wallace was concerned that integration would undermine community health at local level, in view of the wide diversity of the service requirements within individual regions.

**17.35** Differences of approach among the Directors were resolved early in 1974. On 16 January the Regional Transfusion Directors and Mr Watt wrote to the secretary of the SNBTA commenting on the restructuring of the service.<sup>34</sup> They repeated concern about the information in circular HSR(73)C40. They drew attention to the far-reaching changes taking place in the clinical, scientific, technical and organisational spheres of blood transfusion practice; proposed that the arrangements for the transfer to CSA be held in abeyance; and argued that SNBTA should continue in office pending an acceptable solution for the effective management of the Blood Transfusion Service. They asked for more time to be given to the development of proposals, and for discussion.

**17.36** Meetings followed that letter,<sup>35</sup> but the government's policies were implemented against the opposition of the Directors. It was an inauspicious start to new arrangements intended to provide an integrated service. Some practical steps were taken. The service had been transferred. A National Medical Director had been appointed.

**17.37** Even after the establishment of the CSA and the SNBTS, Transfusion Directors continued to be exercised by the lack of transfusion expertise on the CSA's Management Committee and to press for alternative arrangements. During the later part of 1976 the Directors were in touch with Dr McIntyre, SHHD.<sup>36</sup> They reiterated their initial anxiety and stated:

The anxiety... has been realised. The Management Committee does not have within, or available to, it, such independent specialist and other advice as was available within its predecessor, the Executive Committee of SNBTA. This lack of professional expertise and clinical user involvement is considered by the Transfusion Directors to be a retrograde step in the management of the service.<sup>37</sup>

They proposed the transfer of the management of the Blood Transfusion Service to a management committee, independent of the CSA and directly responsible to the Secretary of State, with a wide representative membership including transfusion specialists, donor interests and user interests.<sup>38</sup>

<sup>33</sup> Letter to Dr Charles Cameron dated 4 January 1974 [SNB.011.0596] at 0598–9

<sup>34</sup> Letter [SNB.011.0610]

<sup>35</sup> See *Future Management of the Blood Transfusion Service in Scotland* [SGH.001.2758] at 2759

<sup>36</sup> Letter of 22 October 1976 from Miss Corrie to Dr McIntyre [SGH.001.2758]; Letter of 15 November 1976 from Dr Wallace to Dr McIntyre [SGH.001.2738]

<sup>37</sup> *Future Management of the Blood Transfusion Service in Scotland* [SGH.001.2758] at 2759

<sup>38</sup> *Ibid* [SGH.001.2758] at 2760

**17.38** Regional Directors continued to be apprehensive that the centralised management arrangements of the CSA were in conflict with what they understood to be the 'responsibilities and authorities' of their roles.<sup>39</sup>

**17.39** The Directors' proposals and representations were given short shrift in a reply by Dr McIntyre dated 2 December 1976. He wrote:

It is only fair to say ... that the SNBTS is now formally a part of the NHS and can therefore only be administered in the existing health service framework. On a number of occasions General Jeffrey<sup>40</sup> raised with officers of the Department the question of the SNBTS being taken outside the framework of the CSA and on each occasion it was made quite clear that there would be no question of this.<sup>41</sup>

General Jeffrey was formerly Chairman of the SNBTA, and was appointed the first National Medical Director of the SNBTS in 1975. He served in that post until his death in 1977. Dr Cash was appointed to replace General Jeffrey in October 1979.

**17.40** Dr McIntyre's letter was not the end of the matter. The Regional Directors had understood that there might be a review of management after three years. A meeting of Regional Directors and the SHHD took place on 18 May 1977 at which there appears to have been a frank exchange of irreconcilable views.<sup>42</sup> Leaving aside personal comments, there were two complaints: the CSA management structure was costly, inefficient and counter-productive; and there was a lack of professional expertise on or available to the CSA committees which had responsibility for the management of the Blood Transfusion Service. The Inquiry has not investigated and cannot form or express views on the detailed complaints and comments made on behalf of the Directors, principally by Professor John Cash. It is sufficient to note that they were extensive, and appeared to reflect the apprehensions the Directors had expressed in 1974, and were further reflected in a loss of harmony, and acute disquiet. From the Directors' point of view, there appeared to be no progress.

**17.41** On 15 June 1977, however, a step was taken towards establishing a framework for managing the service. The CSA Management Committee agreed to establish an ad hoc committee, 'to examine and report to the Management Committee on the management arrangements for the Blood Transfusion Service within the Common Services Agency'. The ad hoc committee in turn set up a working party in which representatives of the SNBTS Directors participated.<sup>43</sup>

**17.42** On 20 December 1977, Professor Cash reported to the SNBTS Directors Co-ordinating Group that the CSA Management Committee had proposed a remit for a blood transfusion sub-committee of the Management Committee. He reported:

This met most of the aims which the Directors had sought in their meetings before the Working Party began and the Director representatives hoped that further progress would be made.<sup>44</sup>

The Working Party met and made proposals to the ad hoc committee.

---

<sup>39</sup> Dr McClelland's statement on collection of blood from 'higher risk' donors [WIT.003.0072] at 0073

<sup>40</sup> Former Chairman of SNBTA

<sup>41</sup> Dr McIntyre's letter [SNB.003.4499]

<sup>42</sup> Note of meeting [SGH.001.2587]

<sup>43</sup> Minute of meeting of CSA Management Committee, 26 April 1978 [PEN.012.1745]

<sup>44</sup> Minutes of SNBTS Co-ordinating Group, 20 December 1977 [SNB.003.4712] at 4715

**17.43** Thereafter a draft report of the ad hoc committee's proposals was circulated and reported to the Co-ordinating Group on 14 March 1978. At this stage, there was concern that the proposals departed in some respects from the Working Party's report to the ad hoc committee. Among representations agreed to be made on the proposals, the following were material:

- The National Medical Director should be a non-voting member of the proposed blood transfusion sub-committee.
- Transfusion Directors should receive sub-committee papers and have the right to attend if they wished.
- The National Medical Director was to receive the agenda for meetings of the Management Committee and its sub-committees.
- The National Medical Director should be able to nominate a deputy to attend meetings of the proposed sub-committee.<sup>45</sup>

**17.44** After further discussion, the ad hoc committee reported its recommendations that a sub-committee of the Management Committee should be set up specifically to deal with Blood Transfusion Service matters with specified terms of reference. These recommendations were accepted by the Management Committee on 26 April 1978. The Regional Directors also accepted the recommendations.<sup>46</sup>

**17.45** The terms of reference of the CSA Blood Transfusion Service Sub-Committee defined as at July 1978 included:

(1) The review of the operational activity of the Blood Transfusion Service to ensure that the services provided are efficient and economic and within approved financial allocations.

(2) The formulation of proposals for the development and improvement on the services given by the Blood Transfusion Service and to make recommendations of the priority and proposed programming of such developments and improvements.

(3) Liaison with other authorities on developments in the Blood Transfusion Service and on operational matters.

....

(8) The provision of medical and operational equipment required for the efficient and economic operation of the Blood Transfusion Service.

(9) The preparation of a capital programme (including accommodation and vehicles) for the Blood Transfusion Service...

....

(10) The appointment of such ad hoc advisory committees and working parties as may be necessary to advise on specific matters relating to the services provided by the Blood Transfusion Service.

---

<sup>45</sup> Minutes of SNBTS Co-ordinating Group, 14 March 1978 [SNB.003.4753] at 4754-5

<sup>46</sup> Minutes of CSA Management Committee special meeting on 26 April 1978 [PEN.012.1745]

(11) Any other matters relating to the Blood Transfusion Service which the Management Committee [of the CSA] may refer from time to time.<sup>47</sup>

In formal structural terms there was significant delegation to the sub-committee of the functions listed, and this would continue to be the case.

**17.46** The membership of the sub-committee was specified. The Management Committee was to be represented by six members. In addition there were to be two specialists in clinical medicine, two specialists in laboratory medicine, one SHHD medical officer, and one representative of donor interests. The National Medical Director was not to be a member of the sub-committee. It was provided that that officer should receive the agenda and all papers for each meeting of the sub-committee and be entitled to attend or be represented at meetings. Other Transfusion Directors might attend with the agreement of the Convenor. Three of the four representations listed in paragraph 17.43 above were met.

**17.47** The terms of reference of the sub-committee delegated control of the establishment, appointment and dismissal of staff, with the following exceptions: the National Medical Director and Regional Directors, the Scientific Director of the Protein Fractionation Centre, and other consultant medical staff. The National Medical Director was to be responsible to the Management Committee for the efficient operation of the service, including the Protein Fractionation Centre, and, within the resources available to the CSA, for the implementation of national policies with regard to the supply of blood and blood products to the National Health Service.<sup>48</sup> The job description of the National Medical Director agreed on 26 April 1978 outlined the duties and responsibilities of the office, including:

1. Ascertainment of the needs of clinicians for blood products and for ensuring in consultation with the Regional Directors and the Scientific Director of the [PFC] that adequate supplies of plasma are made available and processed accordingly at the [PFC] to meet these needs.
2. Co-ordination of the distribution of supplies of blood products.
- ....
5. Advising the [SHHD] on national policy questions affecting the development of the Blood Transfusion Service.<sup>49</sup>

Various administrative matters also formed part of the job description. There was no definition of any relationship between the National Medical Director and the sub-committee.

**17.48** The constitution of the CSA Blood Transfusion Service sub-committee went a considerable way towards meeting the objections to the lack of expertise available to the Management Committee in relation to blood transfusion matters. However, neither the sub-committee nor the National Medical Director had executive control of the management of the service. By inference, that was left with the Regional Transfusion Directors and the Scientific Director of the PFC. The reasoning of the Management Committee in specifying the role of the National Medical Director was set out in the minutes of the meeting of 26 April 1978, as an aspect of the constitutional arrangements for the sub-committee:

---

<sup>47</sup> Minute of Blood Transfusion Service Sub-Committee meeting, on 19 July 1978 [PEN.012.1751] at 1755

<sup>48</sup> Minutes of CSA Management Committee special meeting, on 26 April 1978 [PEN.012.1745] at 1750

<sup>49</sup> Ibid

[T]o provide the most suitable management structure for maintaining and developing the highest standards within the Blood Transfusion Service, the National Medical Director should be responsible to the Management Committee for the efficient operation of the Blood Transfusion Service in Scotland, including the Protein Fractionation Centre ....<sup>50</sup>

**17.49** The National Medical Director's direct responsibility to the Management Committee for the efficient operation of the service was not qualified by any requirement for reference to the sub-committee. The sub-committee's overview role included review of activities falling within the job description of the National Medical Director, however, as an officer of the Management Committee. Relationships among the several participants in the management structure were poorly defined, from a modern perspective. One element in the job description of the National Medical Director should be noted. It was part of the duties of the office to advise the Scottish Home and Health Department on national policy questions affecting the development of the Blood Transfusion Service, apparently directly and without involving the Management Committee or its sub-committee.

### **CSA oversight of the Blood Transfusion Service: the formal position**

**17.50** The formal arrangements for CSA oversight of the SNBTS that were established in 1978, continued throughout the remainder of the reference period and beyond. In 2002 a review was undertaken of 180 public bodies including 49 NHS bodies, one of which was the CSA. The review of the CSA looked at all aspects of its role, including its management of the SNBTS and the management structures in place.<sup>51</sup> The conclusions of that Review noted general satisfaction with the CSA:

[A]part from SNBTS where stakeholders and staff alike feel relocation of SNBTS to another organisation is preferred.<sup>52</sup>

**17.51** The narrative of the report identified three causes of dissatisfaction, two of which related to strategic planning and finance in 1999, and a third which is of greater relevance for present purposes:

A perception in SNBTS that the performance of the organisation is managed by the Medicines Control Agency, the Clinical Pathology Association and SNBTS Clinical User group, and CSA is not qualified to manage the performance of SNBTS.

**17.52** The report commented that the critical views identified in the course of the review perhaps reflected:

[A]n inadequate understanding of the role of the NHS Boards across Scotland in supporting, developing and holding to account specialist services to ensure they meet the needs of the public. Whatever organisational arrangements apply, there needs to be a proper system of corporate and clinical governance, and

<sup>50</sup> Ibid [PEN.012.1745] at 1747

<sup>51</sup> Scottish Executive *Public Bodies: Proposals for Change*, June 2001, available at <http://www.scotland.gov.uk/Resource/Doc/158633/0043032.pdf> (accessed 8 December 2014); Scottish Executive, *Review of Public Bodies: Discussion Paper*, January 2001, available at <http://www.scotland.gov.uk/Resource/Doc/156334/0041936.pdf> (accessed 8 December 2014); Scottish Executive, *Public Bodies Review: Review of the Common Services Agency for NHS Scotland*, 2002, available at <http://www.sehd.scot.nhs.uk/publications/DC20021002csa.pdf> (accessed 8 December 2014)

<sup>52</sup> Scottish Executive, *Public Bodies Review: Review of the Common Services Agency for NHS Scotland*, 2002, at p17, available at <http://www.sehd.scot.nhs.uk/publications/DC20021002csa.pdf> (accessed 8 December 2014)

a Board providing a focus for efficient, effective and accountable governance and strategic leadership and direction.<sup>53</sup>

**17.53** The SNBTS plea for re-organisation, which had been repeated, was dismissed, but it was observed in the conclusions of the Review:

There is some justification for their concerns because of the lack of a developed system of clinical governance in CSA; a lack of clarity about the role and purpose of the Board, and therefore a lack of clarity about how CSA and its component Divisions support and add value to each other's activities.<sup>54</sup>

**17.54** It is not part of the remit of this Inquiry to provide a critique of the management or management structure of the CSA in relation to the SNBTS. It is, however, helpful when looking at the work of the SNBTS during the reference period to understand the views of senior SNBTS staff at the time, given the conclusion of the Review concerning the CSA's lack of a developed system of clinical governance and its failure to establish a clear understanding of its role and purpose in the minds of SNBTS staff and other stakeholders.

**17.55** Whether justified or not, there was a deep-rooted view among transfusion professionals until at least 2002 that the CSA did not make a positive contribution to the delivery of the service.

**17.56** The 2002 Review reflected the reality of (a) the statutory framework governing the NHS, and (b) the importance of public accountability, as factors underlining the existing governance structures. The Scottish Government has submitted that:

While the utility of CSA in the management structure was at some stages questioned, it is important to emphasize that its role was part of the general arrangements under which both special and territorial health boards exercised the principal responsibility for the day to day running of the health service in Scotland. Those arrangements devolved responsibility from SHHD as the central department and distanced the NHS from political interference.<sup>55</sup>

**17.57** For present purposes, it is sufficient to note this view. The Transfusion Directors' concern that the management structure lacked specialist membership and advice necessary for effective clinical governance clearly continued notwithstanding the 1978 changes. The authority of the National Medical Director was less well defined than his responsibilities. Those background factors may throw light on some of the events that will be discussed in this report.

### **CSA oversight of the Blood Transfusion Service: the factual position**

**17.58** The delivery of the service in the 1970s had become challenging. The activities of the SNBTS at or about the beginning of the reference period were described in evidence submitted to the Royal Commission on the National Health Service, in January 1977.<sup>56</sup> In relation to management, the evidence was perhaps aspirational rather than reflective of practical reality. In the 1970s, and perhaps reflecting its limited role, the SNBTS

<sup>53</sup> Scottish Executive, *Public Bodies Review: Review of the Common Services Agency for NHS Scotland*, 2002, at page 7, <http://www.sehd.scot.nhs.uk/publications/DC20021002csa.pdf> (accessed 8 December 2014)

<sup>54</sup> *Ibid* at page 17

<sup>55</sup> Submission to the Inquiry on behalf of the Scottish Government [PEN.019.0274] at 0280

<sup>56</sup> Evidence from the SNBTS to the Royal Commission on the NHS [SNB.003.4592]

headquarters was a tiny organisation comprising the National Medical Director, one national administrator, a secretary and a clerical assistant, with little practical influence over regional operations.<sup>57</sup> But the evidence of the regional services operated from regional transfusion centres provided a clear explanation of the scope of the work done at that period:

The Protein Fractionation Centre is sited in Edinburgh ... It serves the whole of Scotland, and at some future date may serve part of England. Its principal function is the fractionation of human blood plasma supplied by the regional services and the return of finished blood products to them.<sup>58</sup>

The National Headquarters, [responsible for the co-ordination of work within the SNBTS,] is also based in Edinburgh.<sup>59</sup>

The functions of the SNBTS ... the following are carried out by all or some of the regional services, in conjunction with the PFC:

- (a) Donor recruitment and the organisation of blood-collecting sessions.
- (b) Medical selection of blood donors and the collection of blood, either as single donations, or by plasmapheresis.
- (c) Collection of blood from selected donors for the preparation of blood-grouping anti-sera; and the immunisation of animals to provide other laboratory reagents.
- (d) Immunisation of volunteers for the production of anti-D immunoglobulin.
- (e) Tests on each donation to determine its blood groups, and tests for transmissible disease.
- (f) Compatibility testing of donations for transfusion to individual patients.
- (g) Antenatal and neonatal blood group serology in relation to the prevention and treatment of haemolytic disease of the newborn.
- (h) Blood group serological reference services, including the investigation of cross-matching problems and transfusion reactions.
- (i) Leucocyte and platelet typing; compatibility testing for organ transplantation.
- (j) Separation of blood into its cellular elements; and the fractionation of plasma to produce a wide range of therapeutic substances (below).
- (k) Clinical blood transfusion, including the management of haemostatic defects, the use of cell separators, and advice on the use of blood and blood products.
- (l) Research and development, and participation in training programmes for postgraduates, undergraduates, medical laboratory technicians, and nurses.

<sup>57</sup> Dr McClelland – Day 9, page 16; Dr McClelland’s statement on collection of blood from ‘higher risk’ donors – [WIT.003.0072] at 0073–74

<sup>58</sup> Evidence from the SNBTS to the Royal Commission on the NHS [SNB.003.4592]

<sup>59</sup> The BTS HQ was established in 1974 at the time of the transfer to CSA: see *Future Management of the Blood Transfusion Service in Scotland* [SGH.001.2758] at 2759

The products prepared for transfusion include:

Whole blood

Concentrated red cells:

- fresh
- frozen

Platelets

Plasma:

- dried
- fresh dried
- fresh frozen

Albumin solution

Stable plasma protein solution

Normal immunoglobulin

Specific immunoglobulins:

- anti-D
- anti-tetanus
- anti-vaccinia
- anti-hepatitis B
- anti-varicella/zoster
- anti-rubella

Coagulation factors:

- fibrinogen
- factor VIII – as cryoprecipitate (frozen)
  - as 'intermediate factor' (dried)
- factors II, IX, X
- factors II, VII, IX, X<sup>60</sup>

**17.59** This was the range of activities at about the start of the reference period that were, at least nominally, delegated by the Secretary of State to the CSA to manage. It had developed against the background of significant and sometimes dramatic changes in the therapeutic application of blood and blood products, in the scientific and technological developments that enabled their production, and in the facilities provided for research and development and for the manufacture of blood products. That would continue throughout the reference period: scientific and technological change drove changes in the use of blood and in the production and application of blood products.

**17.60** While the management structures put in place by the CSA clearly generated considerable debate, it is reasonably clear that they did not have the significant impact on the autonomy of local transfusion directors that had been feared. Taking over practical responsibility for the wide-ranging activities of the service would have been a major logistical exercise. In the event, notwithstanding the formal structural changes, the Blood Transfusion Service would continue to be characterised by a high degree of local autonomy, until substantial restructuring of the SNBTS on a national functional basis began in the late 1990s, long after the period in which the events of importance in this Inquiry had happened.<sup>61</sup>

<sup>60</sup> Evidence from the SNBTS to the Royal Commission on the NHS [SNB.003.4592] at 4593–5

<sup>61</sup> Professor Turner – Day 7, pages 11–12



**17.61** Before the CSA was established and the management structures described above had been put in place, the SNBTS Regional Directors and the Scientific Director of the PFC had met on a regular basis with representatives of the SHHD to discuss operational matters. The work of the Regional Directors as a group continued after the developments in 1978. In addition, as noted in paragraph 17.47 above, the National Medical Director's role as specified in the job description of 26 April 1978 expressly included advising the SHHD on national policy questions affecting the development of the Blood Transfusion Service.

**17.62** Regional autonomy was maintained among the Regional Directors, In the course of the Inquiry Professor Cash, who was appointed National Medical Director, commented on what he perceived to be deficiencies in his position. He commented that he had no authority over the Regional Directors. For example, in relation to a topic discussed later, the collection of blood from prisons, on which consensus was not achieved, he said:

My main recollections were that I was not the boss, that all consultants are equal, that I was merely there to co-ordinate and chair; that individual regional directors had the authority to stick to their view and so on and so forth.

....

So I was there chairing a meeting, and if we didn't get consensus and all agreeing there was no way on a particular issue we could go forward.<sup>62</sup>

**17.63** The view of an operational director was expressed by Dr Perry, the Scientific Director of PFC. He commented on the CSA situation as he found it:

[I]n terms of giving any direction to a strategy for producing products ... they had no role in that at all and had very little knowledge – I think they almost totally deferred to SNBTS managers and also the Scottish Home and Health Department, where they did have medics and scientists that really understood to an extent what we were doing.<sup>63</sup>

The regular meetings of SNBTS Regional Directors were attended by representatives of the SHHD, substantially reflecting the reality of Dr Perry's views.

**17.64** In one area, the control of expenditure, delegated management appears to have been effective at least in formal terms. The SNBTS Management Sub-Committee made an application for funding as part of the CSA's bid in the course of the annual Public Expenditure Survey (the PES). The SNBTS bid, supported by the best evidence available to the Sub-Committee and by information and submissions from the SNBTS Directors and the National Medical Director, was passed to the CSA Management Committee. There it was subjected to scrutiny and amalgamated, so far as acceptable, with other applications, before submission to the SHHD. In practice, recurrent expenditure was generally inflated annually by a percentage uplift. New expenditure required more particular justification. Accountability for expenditure followed the same route. However, this appears to have been more of a paper exercise than a reflection of substantial financial control.

---

<sup>62</sup> Professor Cash – Day 10, pages 42–43

<sup>63</sup> Dr Perry – Day 45, pages 7–8

**17.65** Dr Perry said that, in addition to matters of finance, the CSA took an interest in recruitment, promotion and discipline of staff, ensuring compliance with Whitley Council<sup>64</sup> rules, for example.<sup>65</sup> But that interest did not extend to review of performance. Dr Perry said that his contract required him to report to a committee of management, but ‘in practice very little reporting went on’.<sup>66</sup> He looked on the National Medical Director as the closest he had to an operational manager, a de facto relationship.<sup>67</sup> He said:

[A]s far as the CSA is concerned, I had no experience of – either personally or as group – of the CSA being closely involved in any of the complex decision-making that accompanied the operational management of a blood transfusion service.<sup>68</sup>

**17.66** Dr Perry commented further on contact with SHHD officials:

I think there was quite a regular dialogue between particularly the national medical director but also to an extent regional directors as well if there was a specific topic. There would have been a direct discussion between managers in the SNBTS and officials from the Scottish Home and Health Department particularly if there was a major area of funding that was required or a building development or a major new development, such as heat treating of Factor VIII that required significant funding. Then the Scottish Home and Health Department will have discussed that directly with experts within the Scottish Blood Transfusion Service. And those discussions would not necessarily have included managers or officials from the Common Services Agency. My impression at the time was that the Common Services Agency, if there had been an agreement reached between the Scottish Home and Health Department and the SNBTS on a particular issue, then the CSA would not have interfered or intervened in that because they did not have the expertise or knowledge.<sup>69</sup>

**17.67** Dr Perry’s evidence reflects the position adopted by other SNBTS officials. The CSA and its committees and sub-committees were not involved in any significant way in the delivery of the service over the major part of the period with which the Inquiry is concerned. It appears clear that their independence of active CSA management in the operational aspects of the service continued notwithstanding the structural changes of 1974, 1978 and later years.

**17.68** In substance, central government delegated responsibility to the CSA for certain management functions that, in the event, fell short of operational control over the technical aspects of the delivery of the Blood Transfusion Service. Since the SHHD, and therefore Ministers, controlled funding and health policy, devolution would never have been complete. SHHD officials were involved in technical discussions throughout the period, and those took place in direct contact with the National Medical Director and the Regional Directors. In addition, from 1973 the SHHD organised and chaired annual meetings with Scottish Haemophilia Centre Directors and SNBTS Directors to consider the provision of blood products for the treatment of people with haemophilia. Those meetings provided opportunities to influence decisions. The SHHD also maintained close links with the Department of Health and Social Security (DHSS) and its predecessors in London.

<sup>64</sup> Whitley Councils are joint councils of employers and trade unions, providing a forum for consultation on pay and conditions.

<sup>65</sup> Dr Perry – Day 45, pages 7–8 and 65–66

<sup>66</sup> *Ibid.*, pages 2 and 4

<sup>67</sup> *Ibid.*, page 3

<sup>68</sup> *Ibid.*, pages 8–9

<sup>69</sup> *Ibid.*, pages 9–10

**17.69** In the course of the reference period, decisions were taken and implemented that had important consequences for the delivery of the service, wholly without the participation of the CSA, its committees or sub-committees. Two examples illustrate this in relation to scientific developments, which will be discussed in greater detail later. In November 1984, scientists from the PFC heard at a conference in Groningen that HIV could be inactivated by being dry heated to 68°C for one hour. On return to Scotland they implemented the process changes necessary to test the suggestion, found that the Scottish product would sustain heating at 68°C for two hours and proceeded to implement the changes, with great advantage to National Health Service patients dependent on Factor VIII therapy. At the end of 1985, PFC scientists abandoned research on pasteurisation of Factor VIII concentrate, and adopted a dry heat-treatment process for virus inactivation. They were again successful. Objectively, the process changes involved real and significant policy decisions relating to the delivery of the service. They were implemented without reference to the CSA and its committees.

**17.70** In relation to medical matters, in 1991–93 the Edinburgh and South-East Scotland Region undertook a look-back exercise relating to the transmission of Hepatitis C, that was not referred to the CSA or its committees, and was arguably a direct challenge to SHHD policy. It proved the practicality of look-back, and contributed significantly to the UK Government's decision in 1995 to adopt look-back for the whole country.

**17.71** These are examples only and do not tell the whole story. Some elements of the blood transfusion function have changed over time, and central policies have had a direct impact. For example, fractionation of human blood and the production of coagulation factors ended in 2006. That was the result of a strategic review by the Board of NHS National Services Scotland on the future of the Protein Fractionation Centre and Diagnostics Scotland which was initiated in 2004. The review resulted in the closure of the Protein Fractionation Centre in 2007 and the removal of the production of blood fractions from the functions of the CSA in 2008. Other functions have been added, some reflecting technological changes in the use of human cells and tissue which are not relevant to the Terms of Reference. Again, policy decisions have played a part in such innovations. However, as expressed on its web page 'Meeting the transfusion needs of patients in Scotland', the SNBTS perceives its role to be comprehensive:

Our key priority is to ensure that NHS Scotland has enough blood to meet the transfusion needs of patients in Scotland. It is our responsibility to make sure that blood tissues and cells are available when patients need them.<sup>70</sup>

**17.72** Delegation of the functions of the Secretary of State, and later the Scottish Ministers, for the provision of blood for transfusion remains in place, much as it was under the 1974 Order. But until the end of the last century the reality of SNBTS management was often very different from what the formal structures would have suggested. Apart from a few specific situations, which will be noted in context, the formal management structure was irrelevant to the functioning of the service. That structure provided a route for setting budgets and for financial accounting, but did not impinge on the medical, scientific or technical operations of the SNBTS. On one view, it cloaked an underlying failure to integrate fully the operational activities of the Blood Transfusion Service in Scotland, perhaps until the re-organisation in the late 1990s. On another, it was a

<sup>70</sup> Scottish National Blood Transfusion Service, 'About Us: Meeting the transfusion needs of patients in Scotland', <http://www.scotblood.co.uk/about-us.aspx>

pragmatic response to the reality that while governance required a management structure within NHS norms, effective delivery of the transfusion service depended on the regional and functional autonomy of the specialist directors and staff of the SNBTS.

**17.73** In considering, the role and structure of the CSA from its formation onwards, and, in particular, its oversight of the Blood Transfusion Service, it has to be borne in mind that the concept of corporate governance did not start to develop in the UK until reports such as the Cadbury Report and the Nolan Report on Standards in Public Life were issued in 1992 and 1995, respectively. Clinical governance also began to develop around the same time. Its introduction into the NHS in Scotland was announced in 1998 in NHS MEL (1998) 75 as one of the commitments contained in the 1997 White Paper, *Designed To Care*. The 2002 Review of the CSA made a number of recommendations including that the purpose, function and structure of its Board should emulate that of NHS Boards. Those changes were implemented and are reflected in current governance arrangements. Blood, Tissue and Cells (SNBTS) is one of the six Strategic Business Units of the CSA. The Strategic Business Units incorporate most of the divisions that were part of the CSA (now renamed NHS National Services Scotland) since its inception, along with others that have joined or been established over the years. The Board's Clinical Governance Sub-Committee provides strategic oversight and scrutiny of the SNBTS. SNBTS has a Clinical Governance and Safety Group to ensure effective clinical governance at a tactical and operational level. It reports to the Board's Clinical Governance Committee and its role is to ensure the safety and consistent quality of blood, tissues and cells and that service requirements are being met.

**17.74** The Scottish Government's Closing Submission to the Inquiry about the functioning of the system was:

The formal lines of communication were followed in so far as submission of funding bids was concerned. It does not appear from the evidence, however, that there was strict adherence to the formalities in relation to issues of medical or scientific policy; nor indeed was there rigidity about the level at which communications took place between SHHD and CSA .... [T]he reporting system ought to have led from SNBTS to the managing committee of CSA, and the formal position was that SNBTS directors were responsible to the Blood Transfusion Service subcommittee of the CSA management committee. But in practice this route was evidently not always taken .... Thus while there were clearly established lines of communication, these were not slavishly adhered to, ensuring that where appropriate matters could be raised and resolved with reasonable speed and at the appropriate level.<sup>71</sup>

**17.75** It is not clear that SNBTS directors were formally responsible to the Blood Transfusion Service sub-committee of the CSA until the later 1990s. Otherwise, it is a masterly and restrained summary. How far it reflects the realities of the situation will best be seen in relation to the disposal of particular issues relating to management which will be discussed in context. At this stage it is sufficient to note that in some contexts, the formal structure was ignored as irrelevant to the delivery of the service, and SHHD officials were complicit with SNBTS professionals in the development of practical expedients which implicitly acknowledged the unsuitability of the formal structure for management of a highly specialised service.

---

<sup>71</sup> Submission to the Inquiry on behalf of the Scottish Government [PEN.019.0274] at 0280–0281

**17.76** However, the problems that arose were not wholly attributable to the management structure of the CSA. There were other issues that arose from the independence of the Regional and National Directors.

### **The role of the Transfusion Director and the National Medical Director**

**17.77** The scope of the Regional Transfusion Directors' responsibilities was described by Dr Brian McClelland.<sup>72</sup> Dr McClelland held a number of progressively more senior posts in Edinburgh and the South-East of Scotland BTS and at Edinburgh University from 1977 to 2001.<sup>73</sup> In 1979 he was appointed Regional Director. Dr McClelland's job description as Regional Director contained no reference to managerial accountability. It imposed overall responsibility for ensuring that the full range of the service was efficiently carried out. It stated that in practice the responsibility for the administration of budgets was delegated to Regional Transfusion Directors. In terms of national management of the service, it was stipulated that the director would be expected to share with the other Transfusion Directors the responsibilities involved in coordinating the national service as a whole. The director was expected to attend the regular meetings of the Transfusion Directors to discuss matters of common interest, usually under the chairmanship of the National Medical Director.

**17.78** The job description did not require the post holder to report to or accept review by a line manager. Subject to the obligation to co-ordinate the service with other Regional Transfusion Directors, each director was autonomous to a significant degree.

**17.79** Dr McClelland pointed to change from the mid-1980s. The appearance of AIDS, the commencement of regulatory inspections of the transfusion services, the enactment of the European Directive on consumer protection and the development of the guidelines for the transfusion services in the UK led to progressive convergence of practices among the UK transfusion centres.<sup>74</sup> Until then the service was characterised by its history: it was composed of distinct regional services, each with a strong sense of local identity and under its own director. Dr McClelland noted that:

Despite the reassignment of management of SNBTS from the SNBTA to the CSA, the Regional Transfusion Centres (RTCs) remained largely autonomous entities. In respect of blood donor selection, the Region Transfusion Director (RTD) and his/her consultant colleagues determined their own local policies and issued guidance to medical and nursing staff ....

Discussions between RTD's at national level were just that, and they often agreed to disagree. Moreover, the concept of clinical freedom was sacrosanct  
....<sup>75</sup>

Dr McClelland said:

[I] would simply like to explain that ... looking at it now, it does seem rather odd that an organisation which calls itself a national organisation did appear to be behaving in many respects as a series of regional organisations. And you know, the truth is that at this period, at the time that I joined it, it very much

<sup>72</sup> Dr McClelland's statement on collection of blood from 'higher risk' donors [WIT.003.0072] at 0073

<sup>73</sup> Dr McClelland – Day 9, page 2

<sup>74</sup> Dr McClelland's statement on collection of blood from 'higher risk' donors [WIT.003.0072] at 0074

<sup>75</sup> Ibid [WIT.003.0072] at 0072–3

was a series of regional organisations and that was where it had come from and the level of sort of autonomy that at that time rested with the regional directors was not actually particularly unconventional. The health service in its totality was a very different place in the 70s and 80s from what it is now.<sup>76</sup>

**17.80** From 1979 Dr, later Professor, John Cash held the post of National Medical Director.<sup>77</sup> His views on his role have already been noted. In addition to the comments already quoted he said:

[T]here are documents, plenty of documents, available .... in which I write to the CSA and the department and we have letters back from them. In actual fact, trying to get clarification as to my management role in the SNBTS at that time, and what clearly came back -- and I had long discussions with .... the deputy chief medical officer -- was that I was the first among equals.

Eventually, I took the view -- this is much later in the 1980s -- that this wasn't .... going to work and we needed a general manager and they changed the management structure .... So I was there chairing a meeting, and if we didn't get consensus and all agreeing there was no way on a particular issue we could go forward. Looking back, the wonderful thing is in the main we nearly always did get consensus, as a result of which we were enormously successful in many .... areas.<sup>78</sup>

**17.81** Notwithstanding Professor Cash's view of the practical success of the service, which differed to some extent from Dr McClelland's, it is clear that for much of the reference period the service lacked a coherent strategic control structure and the guidance that might reasonably have been expected to flow from that. Given prevailing opinion on clinical autonomy, devising and enforcing an effective structure would have been challenging at any time in the 1970s and early to mid 1980s. The arrival of AIDS changed attitudes, and provision of guidance on practice became more acceptable. However, there was lack of a developed system of clinical governance, as found by the 2002 Review, and the issue was never put to the test.

**17.82** As is clear from the selection of written comments referred to above, from the beginning those with professional responsibilities for delivering the service had reservations about the management structure. By 1990, when the radical changes already mentioned were introduced, many of the events that gave rise to the issues related to the transmission of infection with which the Inquiry is concerned had largely passed into history.

### The role of the clinician

**17.83** RTC medical staff did not have direct clinical responsibility for the care of patients and were not clinically responsible for the transfusion of patients before or after the inception of the SNBTS. Those responsibilities remained with the individual consultants who had under their care patients requiring transfusions of blood or blood products. The concept of clinical freedom was important to the medical and surgical consultants. A surgeon, for example, would decide on the likely need for transfusion for a given procedure, without reference to a transfusion specialist. The transfusion specialist or haematologist would

<sup>76</sup> Dr McClelland – Day 9, pages 16–17

<sup>77</sup> Professor Cash – Day 10, pages 2–3: Professor Cash's job title was changed in 1989 to 'Medical and Scientific Director' of the SNBTS, without change in function.

<sup>78</sup> Professor Cash – Day 10, page 43

give advice, if asked, on difficult cases, either in difficult serological or difficult clinical cases.<sup>79</sup> As history was to unfold, clinical freedom extended to the choice of therapeutic blood product, which was to become an issue.

## PFC

**17.84** The main functions and functional departments of the PFC are described in Chapter 19, *Production of Blood Products – Facilities*. In addition to its manufacturing function, the PFC had a research function. The Director of the PFC and other senior personnel provided information and advice on matters of plasma fractionation requested by the SHHD, DHSS and other national and international bodies, as required.

**17.85** The Scientific Director of the PFC, who was responsible for the management of all the activities of the PFC, was accountable to the Management Committee of the CSA until 1991. Thereafter the post was accountable to the SNBTS General Manager/National Medical Director. The PFC Scientific Director was independent of the National Medical Director (for most of the material time Professor Cash). As Dr Robert Perry indicated, accountability was not enforced in review of the Scientific Director's operations. The effective independence of the scientists at the PFC will be discussed in context.

## The modern service

**17.86** It is unnecessary to trace in detail the development of the modern service. All administrative organisations change. Issues for the Inquiry that emerge from the position in the 1970s and early 1980s as it has been described here will include whether the characteristics of the organisation increased risk to NHS patients. For example, the collection of blood in prisons, and the approach to donor selection with regard to high risk donations generally, provide a focus for part of this discussion which is dealt with separately in Chapter 26, *Donor Selection – Higher Risk Donors*. But it is appropriate to note that there have been significant changes over the reference period, and that the service as it exists today is rather different from the service in the 1970s and 1980s.

**17.87** From the beginning of the reference period until 1990, the SNBTS National Medical Director/National Medical and Scientific Director and the Regional Transfusion Directors were not formally accountable to the CSA Blood Transfusion Service Sub-Committee of the CSA Management Committee. In 1990 the post of SNBTS General Manager was created and the directors were made accountable to the General Manager on managerial aspects, and were professionally accountable to the National Medical and Scientific Director. There was one central body, the Management Board, through which all policy and strategic decisions passed.<sup>80</sup> The Management Board comprised the General Manager, the National Medical and Scientific Director, the Regional Directors, the Director of the PFC, the Director of the National Science Laboratory, the National Finance Manager, the National Donor Services Manager and the National Administrator.<sup>81</sup> The CSA Management Board met for the first time on 19 June 1990 to finalise its remit in the new structure.<sup>82</sup> A Medical and Scientific Committee (the MSC) was established to provide a scientific and professional forum for the SNBTS.<sup>83</sup> The MSC would present its recommendations on medical and

<sup>79</sup> Professor Turner – Day 7, pages 4–5

<sup>80</sup> *Management of the SNBTS in the '90s* Report by the General Manager, 7 May 1990 [SNB.002.4674]

<sup>81</sup> *Ibid* [SNB.002.4674]

<sup>82</sup> Minute of Meeting [SNB.002.4726]

<sup>83</sup> Minute of Extra-ordinary Meeting of the Medical and Scientific Committee, 14 August 1990 [SNB.002.4930]

scientific matters to the Management Board, reducing the need for detailed discussion of such matters by the Board. From this time on there was a greater degree of centralised management.

**17.88** Re-structuring of the SNBTS into a national functional organisation was put in the hands of the National Director, Angus Douglas, in about 1997–98, soon after he took up office. Public consultation followed in 1998, and a major re-organisation of the SNBTS was implemented.<sup>84</sup> The five regional centres continue, but with less autonomy than before, and some services are now managed on a national basis, such as red cell preparation, tissues and the clinical directorate. The directors of the national services are accountable to the SNBTS National Directorate and the Management Board.<sup>85</sup> Part of the reasoning behind the changes was:

[To] allow clinicians to concentrate on closer working with local hospitals in delivering more effective clinical care via the use of blood and blood products ....<sup>86</sup>

**17.89** As a result of the re-organisation, overall coordination, strategy, senior staff appointments, succession planning, representation within CSA and some external relationships, audit and quality audit became the responsibility of the National Director. The National Medical and Scientific Director became responsible for clinical services, blood bank management, clinical apheresis, clinical laboratory services, research and development, and relationships with external medical organisations. Other national directorates, as set out in the SNBTS Annual Report for 1999–2000 were:

- Blood Supply Chain
- Plasma Products (PFC)
- Diagnostics Scotland
- Bone and Tissue Products
- Products and Clinical Services<sup>87</sup>

**17.90** The Regional Transfusion Directors were re-designated Clinical Directors reporting to the National Medical and Scientific Director. Some services remained local. Hospital blood banking, the provision of advice and information on transfusion medicine to hospitals and some diagnostic services remained based in the regional centres, but generally the service was centrally controlled.

**17.91** The Directorates have changed from time to time. For present purposes it is unnecessary to trace these changes. They continued to reflect changing demands for effective management structures within the SNBTS, starting from the 1998 re-organisation. For present purposes, the importance of these developments lies in the contrast they provide with the situation that obtained throughout the material part of the reference period — when decisions were required that had an impact on the functioning of the Blood Transfusion Service in face of many and fundamentally changing demands.

<sup>84</sup> Scottish National Blood Transfusion Service, Strategic Proposals Consultation Document [SGH.007.2327] Consultation began on 27 May 1998 and ended on 26 August 1998.

<sup>85</sup> Professor Turner – Day 7, pages 11–12

<sup>86</sup> Scottish Office press notice, 28 October 1998 [SGH.003.8451] at 8454

<sup>87</sup> SNBTS Annual Report 1999/2000 [SNB.010.6719] at 6730



**17.92** The management structure of the Blood Transfusion Service inevitably forms part of the context in which the delivery of blood, blood components and blood products for clinical use has to be discussed. The critical period arising from the Terms of Reference ends in the early 1990s, by which time blood for clinical use was effectively screened for infection with HIV and HCV and blood products were effectively treated to inactivate virus infection.

### **Conclusions**

**17.93** From the inception of the National Health Service:

- The Secretary of State for Scotland, Scottish Health Ministers, and Scottish Home and Health Department civil servants had control of health care policy.
- Until 1974 operational control of the delivery of the service was not exercised in relation to the operations of the SNBTA which provided blood transfusion services as an independent body, increasingly funded by Exchequer grant.
- In 1974 the Secretary of State delegated to the CSA responsibility for the provision of supplies of human blood for the purposes of carrying out blood transfusion and related services, including the production of blood fractions.
- In practice, the CSA did not exercise operational control over the Blood Transfusion Service.
- Both before and after 1974 the Regional, and latterly the National Medical and PFC Scientific Directors, of the Service had largely autonomous control of their respective operations, exercised independently of the CSA.
- In general, in relation to operations of the Blood Transfusion Service requiring specific funding or policy decisions, there was much direct contact between Regional, Medical and the PFC Scientific Directors of the Service and officials of the SHHD that did not involve the CSA.



## CHAPTER 18

### COLLECTION OF BLOOD – GENERAL

**18.1** As discussed in Chapter 25, *Screening of Donated Blood for Hepatitis B*, the development and application of screening tests for the presence of Hepatitis B antigen and antibody, perceived at the time to be increasingly effective, had a central role in mitigating the risks of transmission of viral infection during the first decade of the reference period. The limitations of the technology available were noted at the time. Though the predicted effectiveness of the screening tests available improved over that period, tests never achieved detection rates for Hepatitis B of more than about 50% even in the best circumstances. Other means had to be relied on as they became known, not only for detection of Hepatitis B infection, but for other risks of transmission of viral infection. This chapter examines the procedures adopted. It is important to note, however, that in the perceptions of the time, reliance on screening technology defined the context in which other measures were put in place, at least from the end of 1972 when screening for Hepatitis B surface antigen (HBsAg) became general throughout the UK. Whatever their limitations, they were the best tools available.

**18.2** This chapter discusses blood donation collection practice generally, leaving topics relating to the acceptance of blood from 'higher risk' donors for separate discussion. Inevitably, increasing knowledge of the risks of transmission of disease was a further factor in changes in practice. Most of the chapter will deal with the earlier part of the reference period, taking account of changes in practice related to specific risks and noting technological change relevant to those changes, where appropriate.

#### **Blood collection: the voluntary principle**

**18.3** Well before the beginning of the reference period, both within the UK and internationally, there was a widely held view among government and specialist organisations, that purchased blood carried a relatively high risk of transmitting hepatitis. The report of the World Health Organization Scientific Group on Viral Hepatitis, *Viral Hepatitis*, Number 512 of the Technical Report Series in 1972, recognised a wider range of factors relating to the risk of transmission of the Hepatitis B virus (HBV):

Great variations in the prevalence of hepatitis B antigen in apparently healthy blood donors have been found in different parts of the world. Prevalence also varies with such factors as the socioeconomic status and sex of the donor, whether he is a volunteer or paid, and whether he lives privately or in an institution. Antigen has been detected most frequently in males in the younger age-groups.<sup>1</sup>

Some of these factors, in particular gender and socioeconomic status, would have been unlikely to have influenced donor selection in the UK at any period. However, payment was a factor that could be dealt with as a matter of general policy.

---

<sup>1</sup> 'Viral Hepatitis: Report of a WHO Scientific Group', *World Health Organization Technical Report Series*, 1973, No. 512 [SGH.002.9746] at 9761

**18.4** As noted in Chapter 17, *Blood and Blood Products Management*, paragraph 17.13, with the formation of the Scottish National Blood Transfusion Association (SNBTA) in 1940, voluntary donation became the rule throughout Scotland, and funding and collection procedures took on the character of voluntary charitable activities. In war time, voluntary donation was an obvious response to the call to assist the blood transfusion service. The programme had considerable success: see Chapter 17 at paragraph 17.15.

**18.5** By 1975–76, when the Scottish National Blood Transfusion Service (the SNBTS) had largely superseded the SNBTA in the collection and supply of blood for clinical use, the scale of the activities had increased dramatically, and a high level of blood collection was maintained thereafter.

**18.6** At the beginning of the reference period, the voluntary nature of blood donation was universally accepted and admired. Dr Brian McClelland reflected a common view among Blood Transfusion Service personnel:

I think people in the UK were extremely proud of the voluntaryism [sic] and the voluntary system and they knew it was morally better and they probably felt also that it was microbiologically safer. It was safer.<sup>2</sup>

**18.7** The World Health Organization (WHO) was a prominent supporter of the voluntary principle internationally. It published guidance in 1971: *Guide to the Formation and Operation of a Transfusion Service*, aimed specifically at countries lacking a developed blood transfusion service.<sup>3</sup> According to its preface:

The present book is intended to help physicians and pathologists who, after receiving a basic training in blood transfusion, are entrusted with the responsibility of establishing and developing transfusion services in their own countries, either under the ministry of health or through the agency of a voluntary organization, such as a Red Cross Society.<sup>4</sup>

The relevance of the book to developing knowledge of hepatitis is discussed in Chapter 14, *Knowledge of Viral Hepatitis 1*.

**18.8.** The *Guide* encouraged voluntary donation, identifying concealment of previous illnesses like jaundice as a risk associated with paid donation, implicitly recognising that a history of jaundice was a contra-indication to receiving blood from individuals who had been infected.<sup>5</sup> The guidance commented that paid donors were mostly ‘from the lowest social strata where alcoholics and drug addicts are often found’. That, and the risk that paid donors might form syndicates and from time to time demand an increase in financial recompense, were said to have brought paid blood donations into disrepute in many places.<sup>6</sup> As regards voluntary unpaid donors, the *Guide* stated:

‘The voluntary unpaid blood donation is a humanitarian act towards the sick by the healthy .... Under this system it is easier to verify the donor’s state of health, since – unlike some paid donors – he has no reason to try to conceal illness’.<sup>7</sup>

<sup>2</sup> Dr McClelland – Day 9, page 72

<sup>3</sup> *Blood Transfusion: a Guide to the Formation and Operation of a Transfusion Service* [PEN.002.0462]. The guide was edited by CC Bowley, KLG Goldsmith and W d’A Maycock on behalf of the International Society of Blood Transfusion and the League of Red Cross Societies, with contributions from experts from England, Canada, France, the Netherlands and Switzerland.

<sup>4</sup> Ibid [PEN.002.0462] at 0466

<sup>5</sup> Ibid [PEN.002.0462] at 0472

<sup>6</sup> Ibid [PEN.002.0462] at 0472

<sup>7</sup> Ibid [PEN.002.0462] at 0473

**18.9** In May 1975, the WHO passed Resolution 28.72: *Utilization and Supply of Human Blood and Blood Products*.<sup>8</sup> The resolution urged Member States to promote the development of national blood services based on voluntary non-remunerated regular blood donation; to enact effective legislation governing the operation of blood services; and to take other actions necessary to protect and promote the health of blood donors and of recipients of blood and blood products. In January 1987, the 79th session of the WHO at Geneva reiterated its support for resolution WHA28.72.<sup>9</sup> Subject to qualifications relating to developing countries, from the outset of the reference period the WHO advice was consistent: Member States should adopt the voluntary principle and take steps to embed it in effective legislation. The picture that emerges is of consistent support for the voluntary principle.

**18.10** There is perhaps no better way of characterising the voluntary donor in the systems in place in the UK at about the beginning of the reference period than by reference to what Professor Richard Titmuss, author of *The Gift Relationship*, said in a presentation to a joint symposium held by the Royal Society of Edinburgh and the Royal College of Physicians in February 1972:

[T]he primary characteristics of the voluntary donor ... [are]: the absence of tangible immediate rewards in monetary or non-monetary forms; the absence of penalties, financial or otherwise, for not donating; and the knowledge among donors that their donations were for unnamed strangers without distinction of age, sex, medical condition, income, class, religion or ethnic group.

No donor type can, of course, be said to be characterised by complete, disinterested, spontaneous altruism. There must be some sense of obligation, approval and interest; some awareness of need and of the purpose of the blood gift; perhaps some organised group rivalry in generosity; some knowledge that fellow-members of the community who are young or old or sick cannot donate, and some expectation and assurance that a return or reciprocal gift may be needed or received at some future time. Nevertheless, in terms of the free gift of blood to unnamed strangers there is no formal contract, no legal bond, no situation of power, domination, constraint or compulsion, no sense of shame or guilt, no gratitude imperative, no need for penitence, no money and no explicit guarantee of or wish for a reward or a return gift however many donations are made. They are acts of free will; of the exercise of choice; of conscience without shame.

Virtually all donors in Britain ... fall into this category.<sup>10</sup>

**18.11** As is clear from international guidance, the generally accepted view was that blood collected from unpaid volunteers was inherently safer than blood collected from individuals paid for their blood. While it was logically indefensible to infer that blood collected from unpaid volunteers was safe, adherence to the voluntary principle gave a high degree of confidence in the safety of donated blood, and that clearly had an influence on the practices adopted in the management of the collection process.

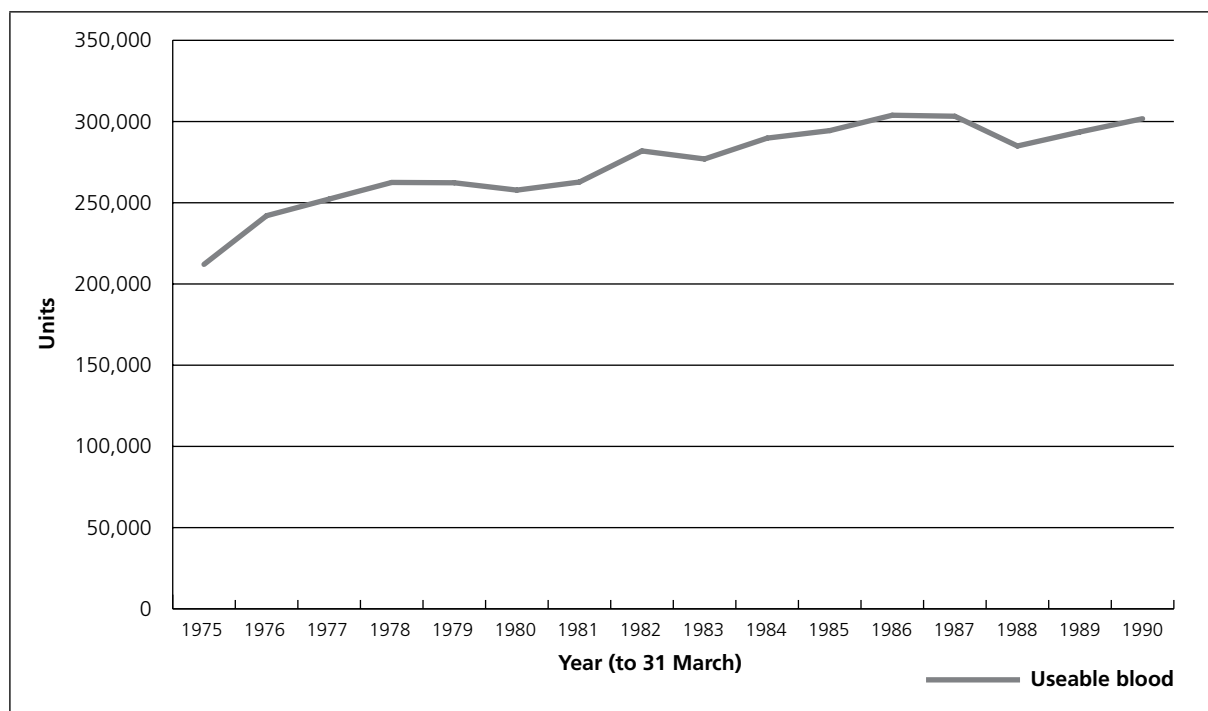
<sup>8</sup> Twenty-Eighth World Health Assembly, Geneva, 13–30 May 1975, WHA28.72 [DHF.003.0764]

<sup>9</sup> World Health Organization Executive Board, Seventy-Ninth Session, Geneva, 12–23 January 1987: EB79.R1 Blood and Blood Products [PEN.019.1382]

<sup>10</sup> Titmuss, 'The Blood Donor' *Proceedings of The Royal Society of Edinburgh*, section B (Biology) 1972; vol 71 Supplement. s. 59 at s. 61 [PEN.002.0570] at 0571. Professor Titmuss was Professor of Social Administration, The London School of Economics and Political Science.

**18.12** The events that created the risks of transmission of the infections with which the Inquiry is concerned (HIV/AIDS and HCV) happened during the period up to 1991 when there was continuing growth in the volume of donations. The pattern of blood collection in Scotland from 1975–1990 is shown in Figure 18.1.<sup>11</sup> The data reflected in this graph are net of rejections or deferrals.<sup>12</sup> The values in the graph rose from 212,061 usable donations of blood in the year ended 31 March 1975 to 301,741 usable donations in the year ended 31 March 1990. The picture overall is one of steady growth. Technological innovations contributed to the developing picture. Plasmapheresis helped boost total blood collection. Data on plasmapheresis are not available on a consistent basis across this period, but there was a steady rise throughout the 1980s, reaching over 15,000 donations in 1990.

**Figure 18.1 Blood Donations 1975 to 1990**



**18.13** For immediate purposes, Figure 18.1 illustrates the success of the SNBTS in recruiting donors and maintaining growth in the volume of blood collected for direct clinical use in transfusion, and for the manufacture of blood products, during the critical part of the reference period. It is impossible to say to what extent individual donors were aware of the many uses to which their donations were put, but it appears that to generate these increasing levels of donation, there must have been confidence generally in the benefits conferred on others by the effective use of donated blood. There was clearly, in Professor Titmuss's words 'some awareness of the need and of the purpose of the blood gift'.<sup>13</sup>

<sup>11</sup> The data have been derived from extant SNBTS and PFC records that were not maintained on a consistent basis over the whole period. The data reflected in Figure 18.1 were published in the Preliminary Report paragraph 5.52 and were not challenged in later evidence. As at 1990, the total for donations before deferrals was 332,236. Data on donations from 1991 to 2009 are summarised in SNBTS Infection Surveillance Report No. 11 [PEN.001.0053] at 0055 and 0056. Donations in 1991 totalled 358,359. Total annual volume remained over 300,000 until 1995 after which it fell progressively to about 250,000 donations per annum.

<sup>12</sup> Donations before rejections and deferrals for part of the period are presented in Chapter 26, *Donor Selection – Higher Risk Donors*, at Appendix 2.

<sup>13</sup> Titmuss, 'The Blood Donor' *Proceedings of The Royal Society of Edinburgh*, section B (Biology) 1972; vol 71 Supplement. s. 59 at s. 61 [PEN.002.0570] at 0571

**18.14** Regular donors always were, and remain of, considerable importance to the effectiveness of blood collection in Scotland. As illustrated in the Preliminary Report, data for the mid-1970s indicates some turnover in donors.<sup>14</sup> That seems to have been inevitable, and to be a continuing feature of voluntary donation, given the peripatetic nature of collection and basic human nature. Individually, donors' patterns of activity would have varied and still do vary. Apart from regular donors called up for a specific session, there must inevitably be an element of chance in matching the timing and place of a session to the availability and needs of prospective donors. Perhaps there is also a variability of response inherent in the voluntary principle, given the variability of donors' circumstances. Seasonal shortages occurred in some areas from time to time, while emergencies created exceptional demand. Viewed broadly, however, the data illustrate a reasonably steady state of commitment. The total figures imply a high percentage of return donors: Approximately 80% of the donors bled were not 'new'. At the present time, return donors contribute about 85% of all donations.<sup>15</sup> Consistency in total supply was achieved notwithstanding these levels of variation.

**18.15** Dependence on a high proportion of regular donation was a general phenomenon related to increasing demand for blood for transfusion and therapeutic application. Professor Titmuss commented in 1972 that it was becoming clearer to those responsible for organising recruitment programmes that:

[E]ffective transfusion services cannot be run on the basis of dramatic and 'crisis' appeals to transient or sporadic givers or suppliers of blood.<sup>16</sup>

**18.16** Professor Marc Turner emphasised that the importance of voluntary donors went beyond maintaining the volume of blood available to the service. Regular donors were registered and could be called upon to form a core for planned sessions, ensuring a structured approach to the collection of human blood and its components. In addition, because they were subject to regular screening, returning donors had a much lower deferral rate than new donors.<sup>17</sup> Donor selection practice and procedures would be expected to reflect the characteristics of the donor population, and in particular the high proportion of return donors comprised in it. The lower deferral rate among return donors supported confidence in the safety of most of the supply.

**18.17** The corollary of donor commitment was reflected in the transfusion service's recognition of an obligation of care for the health of donors, as well as the health of recipients of blood and blood components. Recognition of this obligation was a further factor that had a significant bearing on donor selection practice. In a discussion on recruiting methods, the WHO *Guide to the Formation and Operation of a Transfusion Service* stated:

The motto of the medical director should be: "Without the donor panel there would be no blood transfusion service; therefore the convenience, comfort, and wishes of the donors should be given every consideration." For the donor organizer the motto should be: "The blood must be available in the quantity needed, at the place and time required. All other considerations are subservient to this."<sup>18</sup>

<sup>14</sup> Preliminary Report, paragraphs 5.50 and 5.51, based on the SNBTS Annual Report for 1975–1976: [SNB.010.3921]

<sup>15</sup> Professor Turner – Day 7, Page 15

<sup>16</sup> Titmuss, 'The Blood Donor', *Proceedings of The Royal Society of Edinburgh*, section B (Biology) 1972; vol 71 Supplement. s.60. [PEN.002.0570] at 0571

<sup>17</sup> Professor Turner – Day 7, pages 15–23

<sup>18</sup> *Blood Transfusion: a Guide to the Formation and Operation of a Transfusion Service* [PEN.002.0462] at 0474

**18.18** Within the UK's blood transfusion services, and the SNBTS in particular, the implications of relying on a voluntary system were recognised:

Firstly, the goodwill of the donor population is essential and the utmost care is necessary to ensure that no individual nor collective causes for dissatisfaction arise. To a large extent this depends on a high state of morale and dedication on the part of all members of the SNBTS, including voluntary workers, and it is essential that this be kept to the forefront in any discussions on transfusion policy and its implementation.<sup>19</sup>

**18.19** In its submission to the Royal Commission on the National Health Service, dated February 1977, the SNBTS said:

16. A fact so obvious that it is often overlooked by clinicians and NHS management is that human blood and its constituents cannot be manufactured but must be obtained from members of the general public ....

17. The benefits of a voluntary donor system, in terms of purity of blood and reliability of the donor, were recognised in resolution No. WHA 28.72 passed at the 28<sup>th</sup> World Health Assembly in 1975 which fully endorsed the principle of voluntary donation and urged the governments of all nations to adopt the highest standards in providing a safe blood service to their citizens, formulating those standards on the concept of non-remunerated donors.

18. It is strongly felt in this service that the Central Departments in England and Scotland should be asked to pronounce publicly their support for voluntary blood donation and to consider its implications for the management and finance of the blood transfusion service. SNBTS feels that the indispensability of blood donors should be recognised by their being given an opportunity to participate once more in the management of the service as was the case before NHS reorganisation. Equally, the Central Departments should be taking active steps to counter the threat to voluntary blood donation posed by those multi-national pharmaceutical companies who are marketing in Scotland products, made from the blood of paid donors, which the blood transfusion service also manufactures from voluntary blood donations. This can be done by acknowledging the value of SNBTS products and investing in the service.<sup>20</sup>

**18.20** As indicated in Chapter 17, *Blood and Blood Products Management*, there was during this period a degree of concern among senior SNBTS officials related to structural changes in the Blood Transfusion Service at the time and the tone of the comment probably reflects that concern.<sup>21</sup> It is likely that the need for express political commitment to the voluntary principle indicated a lack of confidence on the part of SNBTS senior management that the principle was entirely secure at the material time. However, despite these observations, the voluntary principle remained intact, and universal support for it has been assured. Occasional threats of intrusion into the UK blood supply system by commercial pharmaceutical companies failed to materialise.<sup>22</sup> The collection of blood in Scotland remained, and remains, in the hands of the SNBTS, supported by the Scottish

---

<sup>19</sup> SNBTS Annual Report 1975–76 [SNB.010.3921] at 3922

<sup>20</sup> Royal Commission on the National Health Service: Evidence from the SNBTS, January 1977 [SNB.003.4592] at 4599

<sup>21</sup> See Chapter 17, *Blood and Blood Products Management*, at paragraphs 17.28 to 17.47

<sup>22</sup> Dr Wallace, regional director of the Glasgow and West of Scotland BTS, reflected his general concern in a letter dated 24 November 1976: [SNB.003.4539]. In September 1980, there was a proposal in England that Beechams should take over BPL: [DHF.003.0329]



National Blood Donors Association (the successor to the SNBTA) as a voluntary donation scheme.

### Collection procedures

**18.21** Despite the reassignment of the management of the SNBTS to the CSA in 1974, the Regional Transfusion Centres remained largely autonomous entities as far as many professional matters were concerned. The SNBTS said:

In respect of blood donor selection, the Regional Transfusion Director (RTD) and his/her consultant colleagues determined their own local policies and issued guidance to medical and nursing staff. Documents, for example information for donors, session records, publicity materials etc, were designed and printed locally, albeit with a national logo. Discussions between RTDs at national level were just that, and consensus was not always achieved.<sup>23</sup>

Dr John Gillon, searching through the SNBTS archive, could find no specifically Scottish documents containing details of donor selection procedures prior to about 1982. It appears that such documentation relating to donor selection criteria before 1982 had either been destroyed or lost with the passage of time.

**18.24** There was a progressive shift away from this position from the mid-1980s.<sup>24</sup> The SNBTS characterised this shift as a move from ‘more of a federation of collaborating centres than a national service’, towards general management and ultimately a national service with (generally) common systems, after re-organisation in 1999.<sup>25</sup>

**18.25** The position in respect of collection of donations can be contrasted with the approach adopted to transfusion and to manufacture of blood products. *Notes on Transfusion* were intended primarily for use by medical staff in hospitals.<sup>26</sup> They were not prescriptive. But they were issued by the DHSS, the SHHD and the Welsh Office jointly for the NBTS and the SNBTA, and carried the authority of the departments. The fifth edition was published in 1973. *Standards for the Collection and Processing of Blood and Blood Components and the Manufacture of Associated Sterile Fluids* was first published in 1979.<sup>27</sup> Revised editions were produced from time to time thereafter. The Standards were compiled by: the Department of Health and Social Security (DHSS) in England and Wales in consultation with the Regional Transfusion Directors (RTDs) of the NBTS and the SNBTS; the Directors of the fractionation laboratories – the Blood Products Laboratory (BPL) and Protein Fractionation Centre (PFC) – and the Scottish Home and Health Department (SHHD). The Standards were focused on aspects of collection and processing that might have a bearing on the safety and quality of blood products. Certain illnesses and conditions were identified as disqualifying a person from being a donor, including illicit drug taking, current jaundice or hepatitis or the presence in the blood of HBsAg. Deferment, or discretionary disqualification, applied where the person reported jaundice or hepatitis

<sup>23</sup> *Collection of Blood in Prisons*, SNBTS, 2011 [PEN.018.1521] at 1525. See similar comments by Dr McClelland in his statement [WIT.003.0072]

<sup>24</sup> See Chapter 17, *Blood and Blood Products Management*, at paragraph 17.77

<sup>25</sup> *Collection of Blood in Prisons*, SNBTS, 2011 [PEN.018.1521] at 1525

<sup>26</sup> *Notes on Transfusion*, DHSS etc, 1973 [DHF.001.2039] at 2041

<sup>27</sup> The 1979 edition of the *Standards etc* are [PEN.002.0249]. The Medicines Division, through the DHSS, also produced a *Guide to Good Pharmaceutical Practice* (known as ‘the Orange Book’), the first edition of which appeared in 1971. The second edition of the Orange Book was published in 1977 [DHF.001.2933] and the third edition in July 1983 [DHF.001.4990]. The current edition is *Rules and Guidance for Pharmaceutical Manufacturers and Distributors*, published in 2007 by the Medicines and Healthcare Regulatory Agency (MHRA). The guide still has an orange cover.

in the preceding year or contact with ‘a case’ within six months. Temporary deferment applied to an individual who had tattooing, acupuncture or ear-piercing within six months or who had a transfusion within that period. It was stated that the Standards should not be construed as comprehensive guidance on donor selection. Though not prescriptive or comprehensive, the Standards also had the authority of the health departments involved.

**18.26** In England and Wales, the National Blood Transfusion Service (NBTS) produced a *Memorandum on the Selection, Medical Examination and Care of Blood Donors*. The SNBTS Directors ‘noted’ the final version of the original document on 8 May 1978 when they expected that the document would be incorporated into the *Standards*.<sup>28</sup> However, it remained an independent document. The Inquiry has found versions of the *Memorandum* produced in 1977,<sup>29</sup> 1983,<sup>30</sup> 1985<sup>31</sup> and 1987.<sup>32</sup> Scottish Regional Directors used the 1977 *Memorandum* as guidance, and participated in its revision. Professor Stan Urbaniak indicated that his predecessor, Dr Brodie Lewis, used it and that he used it during his own tenure as Regional Director from 1983 onwards. Dr Ewa Brookes found it in use when she became the Regional Director at Dundee in 1981 and continued its use. Dr McClelland stated that his understanding was that ‘all the SNBTS regions had based their procedures on the 1977 guidance document’. Dr Ruthven Mitchell indicated that he also used the *Memorandum*. The extent to which the guidance was adapted for local use was not explored.

**18.27** Specific questions relating to the health of the donor were included in the *Memorandum* from 1977 onwards. It was stated that the donor’s medical history should be coupled with a careful assessment of the donor’s appearance:

‘The experienced doctor can detect at a glance the potentially unsuitable donor. Those of poor physique or who are underweight, the debilitated, the undernourished, the mentally unstable, and those bearing the obvious stigmata of disease should not be bled’.<sup>33</sup>

However, dependence on the donor was emphasised. The 1977 iteration stated:

A donor is the best judge of whether he is in normal health and truthful answers to simple questions concerning his medical history and general health form the main part of the examination.<sup>34</sup>

This was said against the background of recognition that a complete medical examination was impractical and that superficial medical examination, by auscultation (examination by stethoscope) and percussion of the chest, and measuring pulse and blood pressure, was in most cases of no great value. In some respects, the *Memorandum* repeated the *Standards*. Directions relating to tattooing, acupuncture or ear-piercing or those donors who had had a transfusion were the same in both publications.

<sup>28</sup> Minutes of SNBTS Directors’ meeting held on 8 May 1978 [SNB.002.5319] at 5320

<sup>29</sup> 1977 *Memorandum* [SNB.002.5348]

<sup>30</sup> 1983 *Memorandum* [SGF.001.0377]

<sup>31</sup> 1985 *Memorandum* [DHF.001.8931]

<sup>32</sup> 1987 *Memorandum* [SNB.006.6410]. The *Memorandum* was superseded in 1990 by the guidance published by the Department of Health on behalf of the UK Blood Transfusion Services and the NIBSC, *Guidelines for the Blood Transfusion Services in the UK*. These guidelines are more fully discussed in *Note on the various guidance documentation* produced by the Inquiry team [PEN.012.0347].

<sup>33</sup> 1977 *Memorandum* [SNB.002.5348] at 5351

<sup>34</sup> *Ibid* [SNB.002.5348]

**18.28** In relation to jaundice or hepatitis (then treated for many purposes as the same condition), the 1977 *Memorandum* provided:

Individuals who give a history of jaundice or hepatitis or in whose blood anti-HBsAg is present may be accepted as donors providing that they have not suffered from jaundice or hepatitis in the previous twelve months, have not been in house contact with hepatitis or received a transfusion of blood or blood products in the previous six months, and providing their blood gives a negative reaction for the presence of HBsAg when tested by a sensitive method (R.P.H<sup>35</sup> or R.I.A<sup>36</sup>). An accepted test for hepatitis B surface antigen shall be performed each time a donor is bled; donors whose blood reacts positively shall be excluded permanently from the donor panel.<sup>37</sup>

It was also repeated that illicit drug taking, if admitted or suspected, should debar a person from donating.

**18.29** A move away from use of the NBTS *Memorandum* began in about 1982. A revised guide to donor selection was prepared by Edinburgh and South East Scotland Blood Transfusion Service (ESES BTS) in 1982, in response to a comment by the Medicines Inspectorate on the consistency of decision-making regarding which donors to accept or reject.<sup>38</sup> In their response to the Medicines Inspectorate dated 12 January 1983, the ESES BTS noted that a new comprehensive guide to donor selection had been prepared and was in routine use by donor selection staff.<sup>39</sup>

**18.30** The ESES BTS guide comprised three documents: a *Guide to selection of blood donors*,<sup>40</sup> an *Alphabetical Guide to Medical Assessment*,<sup>41</sup> and a health check for new donors.<sup>42</sup> The first of these set out the general conditions to be met before a donation could be accepted. These dealt with the donor's age and weight, distinguishing new first-time donors and return donors, and prescribing the required haemoglobin level. It also restricted frequency of donation. In relation to hepatitis it provided that detection of HBsAg at any time excluded all donations except with the approval of the Transfusion Director. There were general directions related to medical conditions which might exclude donation, permanently or temporarily.

**18.31** The *Alphabetical Guide* contained an extensive list of specific conditions which might affect the acceptability of a donation, with guidance on the response of the session team and in particular the circumstances requiring reference to the doctor in charge. Under 'Hepatitis', the *Alphabetical Guide* provided generally that the doctor should be consulted. Further guidance was:

Defer for one full year after recovery. Check if donor knows he/she is a carrier for serum hepatitis, and if so, put off service. Otherwise, at their first donation 1 year after their recovery record 'Hepatitis' on donor's name slip and inform Hepatitis lab.<sup>43</sup>

<sup>35</sup> Reversed passive haemagglutination

<sup>36</sup> Radioimmunoassay. The use of these tests is discussed in Chapter 25, *Screening of Donated Blood for Hepatitis B*

<sup>37</sup> 1977 *Memorandum* [SNB.002.5348] at 5350

<sup>38</sup> Report by the Medicines Inspectorate following their visit to the Edinburgh and SE Scotland BTS on 10–11 March and 10–12 May 1982 [SGF.001.0351], at 0352, para 11(a). In that paragraph the Inspectors also asked 'whether donors really read the questionnaire' and 'Just how comprehensive is the questionnaire?'

<sup>39</sup> Response to Medicines Inspectors Report [SGH.003.5059] at 5063

<sup>40</sup> *Ibid* [SGH.003.5059] at 5089

<sup>41</sup> *Ibid* [SGH.003.5059] at 5093

<sup>42</sup> *Ibid* [SGH.003.5059] at 5123

<sup>43</sup> *Ibid* [SGH.003.5059] at 5105

In the case of ‘Hepatitis contact’ donors, where the donor and contact lived together, used the same towels, crockery, etc, the donor was to be deferred for six months after close contact. Recipients of blood transfusion were acceptable as donors six months after transfusion. The directions required staff to check the reason for the transfusion and to consult the doctor or nursing Sister if in doubt.

**18.32** The health check questionnaire was designed to elicit information relating to these and other issues.<sup>44</sup> There was a question on whether the donor had ever had a serious illness or operation, and questions related to piercing, acupuncture and tattoos. There was not a specific question relating to transfusion. But the information required by these guides required discussion and follow-up where the prospective donor gave a positive answer to any of the questions asked. These guidance documents were prepared in response to the Inspectorate’s concerns which the ESESBTS said it shared. It seems reasonable to infer that until 1982 there was no similar, well-structured interview routine in place in that region.

**18.33** In 1985 the SNBTS considered that *The Guidelines on the Care and Selection of Blood Donors*, issued by NBTS (the updated version of the *Memorandum*), required adaptation. Accordingly, the National Medical Director and the Regional Directors requested Dr Gillon, of ESESBTS, to prepare a report comparing donor selection practice in the five regional centres in an attempt to assess the significance of the existing differences between the SNBTS centres and the NBTS guidelines. In his report, dated 11 November 1985, he advised that there was general agreement that the NBTS *Guidelines* were unsatisfactory in format, and that, in addition, each centre criticised particular (and different) items, which he listed. His conclusion was that, having looked at donor selection criteria in the five regions, ‘major differences of opinion are few’, and that differences related to local factors could be accommodated. He had formed the impression that all centres were willing to attempt to reach a consensus and he commented that the ‘evidence suggests that this would be relatively easy to achieve’.<sup>45</sup>

**18.34** In his oral evidence Dr Gillon explained the position as at 1985:

There was a core of consistency .... So really we were working at the margins, largely on issues of donor safety rather than patient safety. By and large I think as far as recipient safety was concerned, there was greater commonality. But for the central core significant issues of patient safety, I don’t think there was any significant difference.<sup>46</sup>

**18.35** The report was considered at a co-ordinating group meeting of the SNBTS Directors on 30 April 1986. It was agreed that there was a need for an SNBTS set of criteria to serve as a framework for use by medical officers and team staff, with specific agreement that it was for each centre to decide who should take clinical decisions on donor acceptance. The Directors present agreed to recommend to the full co-ordinating group that a ‘standard guide’ should be produced, and that the ESESBTS donor selection document provided the basis for that.<sup>47</sup> In November 1988, *Guidance for the Selection of Blood Donors* was eventually agreed and issued.<sup>48</sup> In a note on the front page it was said to ‘represent the collective opinion of SNBTS’.

<sup>44</sup> Ibid [SGH.003.5059] at 5123

<sup>45</sup> Report on Donor Selection Criteria by Dr Gillon dated 11 November 1985 [SNB.003.9864] at 9867

<sup>46</sup> Dr Gillon – Day 11, page 48

<sup>47</sup> Minutes of SNBTS Co-ordinating Group meeting on 30 April 1986 [SNB.003.9905] at para 2

<sup>48</sup> *Guidance for the Selection of Blood Donors*, November 1988 [PEN.016.0479]. The document was re-issued in August 1990 [SNB.006.6484] and revised in early 1991 [SNB.011.7435]

**18.36** Use of the 1977 *Memorandum on the Selection, Medical Examination and Care of Blood Donors*, and its revised versions, by the Regional Directors of the SNBTS provided RTDs in Scotland with a common base for developing their own donor selection procedures. A former Regional Transfusion Director has provided the Inquiry with a description of a typical donor session. Session Medical Officers received training and a copy of the 'Guidance' at the start of their work with the Blood Transfusion Service. The donor team included a clerical officer, donor assistants and a team leader together with assistants to carry out the haemoglobin check. The prospective donor was welcomed and asked to read the donor questionnaire. It included the phrase 'Please tell us if you have ever suffered from Hepatitis (jaundice) or been in contact with a case in the past six months'. The donor was then interviewed by the clerk who went through a health check with the donor, the donor signing to confirm that they had read and understood. The haemoglobinist then carried out a finger stick test to exclude anaemia. When a medical query arose, if the Medical Officer could resolve it a note was made on the donor's record card and the donation accepted or temporary deferral advised, as appropriate. If the Medical Officer could not resolve it, the donation was temporarily deferred, GP details were obtained and the query referred to the Regional Centre medical staff. If the reply to the hepatitis/jaundice question was positive the donor was referred to the session Medical Officer, donation was deferred, GP details obtained and the report referred back to the Regional Centre staff. After a satisfactory history and blood check, the donor was made comfortable on the donation bed and the donation was taken. Accordingly, the donor's memory was prompted at three points and sometimes donors then mentioned something, for example, during the donation procedure or during the bed rest period afterwards. The team leader continuously scanned all donors in the premises, principally for signs of nausea or fainting but also for other things, sometimes sufficient to refer to the Medical Officer for another check. Consequently, the assessment of donors did not end until they were fully recovered and left the premises.

**18.37** In the ESESBTS, the conduct of donor sessions followed a similar pattern whatever the location, subject to necessary adaptation in institutions which will be discussed later. Routine donor sessions were arranged well in advance, usually between 12 and 15 months ahead, to allow for all necessary planning.<sup>49</sup> Dr McClelland described the approach in the late 1970s and early 1980s.<sup>50</sup> Donor sessions were conducted by a team. A doctor was always present at the session. There was a senior nurse or team leader and a group of what were then called 'donor attendants'. The donors would be welcomed to the session. In this period they would have been given an information card, which was fairly standard across the UK, which set out a series of exclusion criteria. A donor who had any of the listed features was asked not to donate. Those who were proceeding were seen by a clerical member of staff, who would take them through that card again and ask them questions to confirm that they had read it, record some of the information about the donor and then pass the donor on to another person who, using a finger prick technique, would take a sample of blood which was tested for haemoglobin. Provided the donor passed that test, they would be moved to another waiting area from which they would be taken to lie on the couch and have their blood taken.

<sup>49</sup> Dr McClelland – Day 9, page 18

<sup>50</sup> Ibid pages 19–20 The description related to prisons sessions specifically, but was said to operate identically at any other session.

**18.38** The interview routine was supplemented by observation. Dr McClelland commented that the donor would be seen, talked to and observed by SNBTS staff throughout the whole process of donation. If something struck a member of staff, perhaps even when the donor was giving blood, which caused them to be uncomfortable about the donor's suitability, that issue would be noted and acted on.<sup>51</sup>

**18.39** Matters of interest to staff would include whether a donor was heavily tattooed, which for some reason might not have been noticed at an earlier stage. Further, when the donor's arm was exposed to take a sample, evidence of needle injection tracks might be disclosed. It was not unheard of for a donor to appear to be inebriated. However, Dr McClelland emphasised that there was almost certainly a fair amount of individual variation in the way that individual members of staff assessed donors. He said that it was, and remains, extremely difficult to control practice with a very large team of people operating peripatetically. While the ESESBS had always striven for consistency in the application of donor session standards, he said that that was very difficult to achieve.<sup>52</sup>

**18.40** Dr Mitchell thought that factors related to donor care and maintenance militated against questions that placed the donor in a position in which they would have to self-exclude on grounds of health.<sup>53</sup> He thought it impossible to challenge a donor who asserted that they were healthy, when it appeared that was not true or reliable. In this, and in other aspects of his approach to practice, Dr Mitchell reflected most fully the dedication to the interests of the donor noted in paragraphs 18.15 to 18.17 above.

**18.41** The best evidence of the initial stages in donor procedure in the west of Scotland at the beginning of the reference period was provided by Mrs Rosalind Prior, who was employed by the SNBTS as a Mobile Team Assistant in the region between 1969 and March 1974. She described normal practice in the early 1970s as follows:

The normal practice was that after the donor had passed the haemoglobin test they would move on to another team assistant who would go through a series of questions with them. We didn't have a sheet concerning the questions that we read to the donor and we didn't have a sheet containing the questions which we handed to the donor and asked them to read. We were taught the questions which we had to remember and go through them with the donors. The first question was, "Have you given blood before". If the donor said "Yes" then we would ask "Is it over three months since the last time you donated". If the donor said "Yes" then we would ask, "Is there any reason why you shouldn't donate blood? For example, do you have a cold, flu, boils, abscesses or ulcers?" If the answer was "No", we would ask if they had recently had any injections or vaccinations. If they answered "No" to that we would ask if they had had mumps, measles, chickenpox, shingles or jaundice or been in contact with anyone who had had jaundice or had they had any recent illnesses or operations in the last two years. If the person said yes to any of these questions we would have to go and advise the doctor of this. In the case of jaundice the doctor would tell us that we had to inform the donor that they could donate blood that day but that it would be used for research purposes only. They were also informed that they had to be clear of jaundice for five years before they would be able to donate blood again ....

<sup>51</sup> Ibid page 20

<sup>52</sup> Ibid pages 20–21

<sup>53</sup> Dr Mitchell – Day 9, page 167

The procedure never changed in the five years I worked for the Blood Transfusion Service. We were never told to ask any donors if they had ever used intravenous drugs or had tattoos or piercings. At that time HIV was not known and we were not instructed to ask any questions about hepatitis ....

Just before I finished working with the Blood Transfusion Service they produced the questions that donors had to be asked on a sheet that we used but as far as I can recall the questions weren't any different from what we had previously asked donors.<sup>54</sup>

Mrs Prior's employment ceased at the very start of the reference period, some three years prior to the issuing of the 1977 *Memorandum*. However, Dr Mitchell's evidence noted at paragraph 18.40 suggests that it is unlikely that there would have been any change in the instructions to session staff in the West of Scotland relating to questioning about health.

**18.42** Full compliance with the requirements set out in the *Standards* and the 1977 *Memorandum* would have changed the procedure described by Mrs Prior to some extent. However, the most detailed evidence about what happened in a donor session came from her. The descriptions given by the former Regional Transfusion Director and Dr McClelland of donor sessions in their regions were very similar. Dr Gillon found differences in practice, sometimes a higher standard being applied, sometimes a lower one. His ultimate conclusion was that as far as recipient/patient safety was concerned there was not any 'significant difference'. However, as noted in paragraph 18.35, the view of the members of the co-ordinating group who discussed Dr Gillon's report was that there was a need for a Scottish framework for use by medical officers and team staff, in relation to decisions on donor acceptance, and that a 'standard guide' should be produced based on the ESESBTS donor selection document.

**18.43** At the start of the reference period there was confidence in the ability of medical staff to identify donors presenting risk. The authors of the 1971 WHO *Guide* reflected that confidence, commenting that 'the medical officer should be able to pick out those prospective donors who may be, for example, undernourished, crippled, mentally unstable, alcoholics, or drug addicts'.<sup>55</sup> As grounds for distinguishing acceptable from unacceptable potential donors, the comments use the language of the times but apart from that they reflect, in retrospect, an unsophisticated approach to the assessment of risk. It has to be noted, however, that in 1971 general medical knowledge of the risks that later came to be identified and understood, was equally unsophisticated.

**18.44** It is unlikely that there was questioning on sensitive personal matters. Obtrusive questioning, or questioning not felt to be appropriate, could have proved unacceptable to return donors and might have threatened the core supply on which the service depended.

**18.45** Dr Mitchell's relatively extreme attitude to these matters may have emphasised the risk of upsetting donors over the risk to recipients of potentially infected blood or blood products. The lack of systematic questioning of prospective donors about hepatitis, for example, might have led to the failure to identify donors whose donations would have been rejected if true and reliable answers had been given to questions about matters indicating or suggesting high risk of transmission of infection. A focus on the

<sup>54</sup> Mrs Prior's written statement [PEN.019.0107] at 0108

<sup>55</sup> *Blood Transfusion: a Guide to the Formation and Operation of a Transfusion Service* [PEN.002.0462] at 0488

best interests of the donor panel appears to have reflected the emphasis placed by the WHO on the convenience, comfort and wishes of the donor (paragraph 18.17 above). That is understandable, at least so long as the risk to the recipient of blood reflected the view that hepatitis was generally a low-risk infection. His was one of the range of views acceptable in a context that gave high priority to the practitioner's autonomy at a period when knowledge of risk was relatively undeveloped.

**18.46** Relevant risk factors were more focused following the acceptance that AIDS probably presented a transfusion risk.<sup>56</sup> This brought a step change in the rigour of the donor selection procedures, beginning in the spring of 1983,<sup>57</sup> and in the desire to have national consistency in proper documentation of the procedures as they evolved.<sup>58</sup> However, direct oral questioning on sexual matters was not introduced even then,<sup>59</sup> although whether the incidence of transmission of hepatitis would have been reduced by more active questioning, remains speculative. It has to be borne in mind that there was no screening test for Hepatitis C until after the discovery of the virus in 1988, and until 1985 non-A, non-B Hepatitis (NANB Hepatitis) was considered to be generally benign, largely because in most cases there were few clinical signs of infection that could be identified. It is not clear that there were questions that could have been formulated that would have elicited relevant information from donors. And up-to-date methods of screening for HBV were adopted, using the technology available at the time.

### Grounds of exclusion: medical history

**18.47** As is clear from the preceding discussion, from time to time particular groups of potential donors have been perceived to present a high risk of transmitting disease. These have included people with a record of parenteral (injecting) drug abuse. In addition, people detained in penal institutions were thought to present relatively high risks. It has been suggested to the Inquiry that US servicemen were relatively high risk donors. These groups are discussed separately in Chapter 26, *Donor Selection – Higher Risk Donors*. More generally, individuals with a history of hepatitis and individuals who had at some stage received blood transfusion, whatever their status otherwise, were perceived to present an unacceptable risk. This part of the discussion deals with these general issues.

### *Exclusion on grounds of jaundice or hepatitis*

**18.48** As discussed in Chapter 25, *Screening of Donated Blood for Hepatitis B*, practice relating to exclusion on grounds of hepatitis was closely related to technological changes in screening for hepatitis in blood donations. In the absence of contemporaneous documents setting out practice guidance it is difficult to relate changes in practice to changes in technology with any degree of precision. This section seeks to identify some stages in the evolving scene and to comment particularly on blood collection practice.

**18.49** As noted already, in the period up to the early 1970s the terms 'hepatitis' and 'jaundice' were often used indiscriminately: in general understanding, infection with hepatitis was typically evidenced by the clinical symptoms and signs of jaundice. It was known that there was a risk of transmission, but there was little understanding of that

<sup>56</sup> Dr McClelland – Day 9, page 24

<sup>57</sup> See Chapter 28, *Donor Selection – AIDS*, paragraph 28.2

<sup>58</sup> Dr McClelland – Day 9, page 23

<sup>59</sup> See Chapter 28, *Donor Selection – AIDS*. In some areas leaflets, of varying specificity, were used to inform donors of potential risks.



risk or of the clinical course and effects of infection. Initially, a conservative approach was taken to donor exclusion where there was evidence of exposure to hepatitis. By the mid-1960s, prospective donors giving a history of ever having had infective hepatitis, which almost always equated with a history of having had transient jaundice, were excluded from donor panels.<sup>60</sup> At this stage, before the Hepatitis A and B viruses were identified, the practice in the UK of excluding from donation any prospective donor with a history of jaundice, appears to have been common in Western countries.

**18.50** For many prospective donors, giving an accurate history of previous jaundice would have been challenging. Jaundice in infancy, jaundice many years previously at a time of other more serious illness, anicteric hepatitis and other conditions not noted at the time would have militated against disclosure, except perhaps on detailed investigation of medical records. The interview procedures discussed above were in many cases unlikely to succeed in eliciting a relevant history. It appears very unlikely that reporting would have been significantly distorted by purported disclosure of jaundice that had not been experienced. The consequence of relying on donor recollection is more likely to have been under-reporting of jaundice and, for that reason, a flawed understanding of the risks presented. The prevalence of anicteric forms of hepatitis, and in particular of NANB Hepatitis, further hampered understanding of the risks presented by hepatitis in the widest sense.

**18.51** The 1971 WHO *Guide to the Formation and Operation of a Transfusion Service* reflected a changed understanding of risk. It pointed to the risks of transmission of a number of diseases including hepatitis. The clinical signs and symptoms of infectious and serum hepatitis as then understood were described, and it was observed that:

Patients with clinical jaundice are not the main source of the disease; far more significant sources are the mild anicteric case [that is, mild cases without overt jaundice], the convalescent carrier, those incubating the disease, and the healthy contact carrier, all of whom at one time or another may be viraemic [carry the virus in their blood].<sup>61</sup>

**18.52** At that stage, NANB Hepatitis was unknown and inferences were drawn as to the nature of risk that subsequently proved to be seriously flawed. While there began to be references to other forms of hepatitis, attention was focused on Hepatitis B and the relationship, if any, between HBV antigen or antibody positivity and a past history of jaundice. A positive test for HBsAg indicated current viraemia. However, the relevance of a history of jaundice was undermined. A WHO expert group report of 1973 observed:

Limited surveys have also shown that the prevalence of hepatitis B antigen is no higher amongst donors with a past history of jaundice than in those without such a history.<sup>62</sup>

**18.53** The 1973 report also noted that it was generally agreed that not all cases of post-transfusion hepatitis were caused by Hepatitis B infection and that 'as more hepatitis B carriers are eliminated from serving as blood donors, the proportion of cases due to other

<sup>60</sup> *The Practitioner*: No 1166 (August 1965) pp 184–5 [LIT.001.4394]

<sup>61</sup> *Blood Transfusion – A Guide to the Formation and Operation of a Transfusion Service* [PEN.002.0462] at 0481

<sup>62</sup> 'Viral Hepatitis: Report of a WHO Scientific Group', *World Health Organization Technical Report Series*, 1973, No. 512 [SGH.002.9746] at 9761

types of hepatitis will increase'.<sup>63</sup> In relation to the exclusion of donors on grounds related to hepatitis, however, it was Hepatitis B that was discussed and the report marked the beginning of a change of attitude. The 1973 report developed the discussion of risk from the position set out in the 1971 report.<sup>64</sup> Firstly, it was observed that the exclusion from blood donation of individuals with a clinical history of Hepatitis B infection, but who did not have detectable antigen, might not materially reduce the frequency of hepatitis among the recipients of blood. Secondly, it was observed that the exclusion from blood donation of those with serological evidence of previous infection with Hepatitis B, indicated by the presence of antibody, might not be justified.

**18.54** In international guidance, this was the start of a move away from excluding all donors with a history of hepatitis, towards excluding more limited groups with a relevant recent history.<sup>65</sup> Only Hepatitis B was relevant in the context of contemporaneous knowledge. The 1973 WHO report noted that the existence of a chronic carrier state following Hepatitis A (HAV) infection had not been proved.<sup>66</sup> That turned out to be correct: there is no chronic carrier state for HAV. It is now clear that most of the individuals with a history of hepatitis were carriers of NANB Hepatitis virus and could not have been identified by the tests for HBV then becoming available.

**18.55** Leaving aside HBV screening results, the restriction of exclusion criteria related to a donor's history of jaundice or hepatitis appears questionable on logical grounds. The 1973 report recognised that post-transfusion hepatitis was not solely associated with HBV: there were thought to be a variety of causes of hepatitis. It was to become known that NANB Hepatitis was not generally associated with a history of jaundice. But that was not known in 1973, and there was no exhaustive analysis of the historical antecedents of any other transmissible agent of hepatic disease. The explanation appears to be that there was a strand of belief that was prevalent up to the early 1970s that once Hepatitis B had been dealt with, the problem of Post-Transfusion Hepatitis (PTH) would be solved.

**18.56** The same approach to donor exclusion, as expressed in the WHO report, appeared in a letter from Dr John Wallace of the Glasgow and West of Scotland BTS published in the *British Medical Journal* of 11 August 1973. Dr Wallace reported the findings of a study in his region that 'volunteers with a history of jaundice or of recent contact with a case of jaundice do not have a higher incidence of positivity for [Hepatitis B antigen and antibody] than in donors lacking this history'.<sup>67</sup>

**18.57** The Advisory Group on Testing for the Presence of Australia (Hepatitis Associated) Antigen and its Antibody (the Maycock Group),<sup>68</sup> originally set up in September 1970, was re-convened on 6 December 1973.<sup>69</sup> In its second report, published in September 1975, it recommended that the practice of excluding donors with a history of jaundice should be discontinued, provided that HBsAg was not detected using a sensitive test and the donor had not suffered from hepatitis or jaundice during the previous 12 months.<sup>70</sup>

<sup>63</sup> Ibid [SGH.002.9746] at 9754 and see also at 9762

<sup>64</sup> Ibid [SGH.002.9746] at 9761

<sup>65</sup> Dr McClelland – Day 9, page 106

<sup>66</sup> 'Viral Hepatitis: Report of a WHO Scientific Group', *World Health Organization Technical Report Series*, 1973, No. 512 [SGH.002.9746] at 9761

<sup>67</sup> Wallace, 'Hepatitis B antigen VD clinic patients', *British Medical Journal*, 1973; 347 [PEN.002.0821]

<sup>68</sup> See Chapter 25, *Screening of Donated Blood for Hepatitis B*, paragraphs 25.21 and 25.22

<sup>69</sup> Second Report of the Advisory Group on Testing for the Presence of Hepatitis B Surface Antigen and its Antibody [SGH.003.0079] at 0081

<sup>70</sup> Ibid [SGH.003.0079] at 0084

**18.58** Increased understanding of Hepatitis B had driven the change. But there was still no means of limiting the risk of transmission of other viruses causing post-transfusion hepatitis. The existence of long-incubation post-transfusion hepatitis unrelated to Hepatitis B, postulated by Dr Alfred Prince and colleagues in *The Lancet* published on 3 August 1974, was not noted in the Maycock Group's discussion of the topic of exclusion on grounds of jaundice or hepatitis history.<sup>71</sup>

**18.59** An internal DHSS memorandum dated 16 March 1976 noted that some RTDs in England and Wales 'express[ed] reservations about discontinuing (within prescribed safeguards) the practice of excluding from the panel donors with a history of jaundice but the majority favour admitting such donors from a given date'.<sup>72</sup> That became established advice.<sup>73</sup>

**18.60** Consistent advice was published by the WHO in 1975. Recommendations included:

6 At present blood donors should not be excluded on the evidence of previous hepatitis alone, whether it is based on a past history of infection or on the findings of hepatitis B surface antibody, provided that they have had no attack of hepatitis during the previous year and their blood has been found negative for hepatitis B surface antigen by a very sensitive test.

7 There can be no categorical designation of high risk blood donor groups; the situation is likely to vary from country to country from time to time and within countries. Any subpopulation with specific characteristics shown to have a continuing carrier rate of HBsAg at least three times that of the total potential blood donor population may be considered for exclusion. However, such decisions should be made on a local basis with due regard to the needs and availability of blood.<sup>74</sup>

**18.61** Dr McClelland said that paragraph 7 of the WHO report was relevant to the question of taking blood from donors in Scotland.<sup>75</sup> The advice was probably a reflection of the growing awareness at the time of the variability of the prevalence of Hepatitis B surface antigen carriage in the populations of different countries. But it was relevant to the assessment of the suitability of any population.

**18.62** The three WHO papers referred to reflected developments in opinion that coincided, in time, with growing knowledge of the hepatitis viruses and with the development of HBsAg assays. It would be unrealistic, however, to think that this increased knowledge would lead to the rapid production of new assays, or to the instant adoption of tests as they became available. In 1972, Dr Wallace commented:

The phenomenon of a long latent period between significant experimental observations and their application in clinical practice is not confined to blood transfusion. Part of the delay is caused by the need to develop new technical

<sup>71</sup> Prince et al, 'Long-incubation post-transfusion hepatitis without serological evidence of exposure to hepatitis-B virus', *The Lancet*, 1974; 241 [LIT.001.0363]. Professor Cash explained that 'I saw Alfred Prince in my 1969 visit to the States, he gave me a small vial of Australia antigen in New York and I brought it back, and that was the first beginnings of testing for Australia antigen, certainly in Scotland. This was an outstanding group'. Day 10, page 101

<sup>72</sup> Memorandum from TE Dutton to Dr Waiter dated 16 March 1976 at para 4, item 104A [SGF.001.2841] at 2842. South West Thames Regional Health Authority were also noted to have 'Reservations about including or readmitting donors with a history of jaundice' (para 4, item 102A).

<sup>73</sup> See Chapter 25, *Screening of Donated Blood for Hepatitis B*, paragraphs 25.38–25.39

<sup>74</sup> World Health Organisation – Technical Report Series – Report of a WHO Meeting [LIT.001.3272] at 3298

<sup>75</sup> Dr McClelland – Day 9, page 111

capabilities, and by having to await adequate financial support. Even more important is a human reluctance to depart from the familiarity of old habits and a natural suspicion of things new. In some respects progress in blood transfusion is being retarded because new ideas are not easy to sell to old heads.<sup>76</sup>

**18.63** General advice was developed in 1976 with the publication of the International Society of Blood Transfusion (ISBT) Guide *Criteria for the Selection of Blood Donors*.<sup>77</sup> Some of the guidance is relevant to later topics, but it is helpful to note the full range at this point, since it emphasised the need for general precautions notwithstanding developments in screening. In this respect the Guide marked a significant development in re-assessing general exclusion policy and practice. The Guide stated:

In spite of recently developed tests for the detection of HBsAg, only a relatively small proportion of carriers can presently be detected. No routine screening test is presently available for the detection of hepatitis A virus, or of other viral agents that cause transfusion-associated hepatitis. It follows, therefore, that some general precautions should be taken in an attempt to reduce the risk of such viral agents being transmitted from donor to recipient.

Prospective donors should be excluded if it is known that they:

1. Give a history of viral hepatitis at any time, except during the first months of life ...
2. Have received a transfusion of blood or blood products within the last six months.
3. Have been in close, household contact with a case of “infectious hepatitis” in the last six months.
4. Have donated blood which was strongly suspected of having been responsible for a case of post-transfusion hepatitis.
5. Are suspected to be parenteral drug addicts.
6. Have been tattooed, had their ears pierced, or experienced acupuncture within the past six months.
7. Are inmates of a correctional institution.
8. Are HBsAg positive.
9. Are working in high-risk areas such as haemodialysis centres.<sup>78</sup>

**18.64** The 1977 NBTS *Memorandum on the Selection of Donors* provided for exclusion in the same terms as items 2 and 3 of the ISBT Guide. Item 1 was not followed. The *Memorandum* reflected the advice of the Maycock Group and stated that those with a history of jaundice or hepatitis could be accepted as donors provided they had not suffered from jaundice or hepatitis in the previous 12 months and provided they tested negative for Hepatitis B surface antigen using a sensitive test (RPHA or RIA). Item 8 was reflected in a positive stipulation that an accepted test for HBsAg be performed each time

<sup>76</sup> Wallace, ‘New approaches to the supply of blood and plasma’, *Proceedings of the Royal Society of Edinburgh*, Section B (Biology) 1972; vol 71: Supplement: S.13 [PEN.018.1026] at 1032

<sup>77</sup> *Criteria for the Selection of Blood Donors* [DHF.001.2672]

<sup>78</sup> *Ibid* [DHF.001.2672] at 2683

a donor was bled, and that donors whose blood reacted positively should be excluded permanently from the donor panel.<sup>79</sup>

**18.65** In his evidence to the Inquiry, Dr McClelland stated that he believed that the SNBTS adopted a similar approach to the acceptance of donors with a history of jaundice as that set out in the 1977 NBTS *Memorandum*, albeit that some regions may have restricted acceptance to cases where the donor had only experienced jaundice before the age of 12 years.<sup>80</sup>

**18.66** The pattern of infection in Scotland was a factor underlying changes introduced to the 1977 guidance.<sup>81</sup> The restriction on accepting donors with a history of jaundice was relaxed in the case of donors infected under the age of 12 years because, where there was evidence of infection, it was almost always found to be an antibody to HAV. Dr McClelland thought that this was based on work done by Dr Brian Dow in Glasgow, who reported that many patients who had jaundice in childhood had been infected with Hepatitis A, a transient infection which was for all practical purposes considered not to be transmissible by transfusion. He suspected that the decision to restrict the acceptance of a donor with a jaundice history in later life was related to concern that jaundice occurring later might not be due to Hepatitis A, but due to NANB Hepatitis.<sup>82</sup>

**18.67** Dr Wallace's book, *Blood Transfusion for Clinicians*, was published in 1977. It noted, without criticism, the 1975 WHO recommendation that volunteers with a history of clinical hepatitis could be accepted as donors provided the clinical illness occurred more than 12 months previously, and the serum of the donor was shown not to contain HBsAg when tested by a sensitive method.<sup>83</sup>

**18.68** The topic continued to generate study and correspondence in professional publications. In October 1978, Renton and others, of the Manchester BTS, reported their findings on whether the inclusion of donors with a history of jaundice had led to an increased incidence of HBsAg positive tests.<sup>84</sup> Donors with a history of jaundice were 3.5 times as likely to be HBsAg positive as donors without such a history. The sensitivity of the test influenced their conclusion:

[T]he rate of HBsAg positives amongst these people is still small, and with the sensitive tests at present in use we do not believe that these figures mean that such donors ought to be excluded from the panels.

**18.69** Despite that, it was a challenge to the accepted understanding. Contrary views were also expressed. On 21 July 1979, *The Lancet* published a letter from Dr Robert Crawford and colleagues at the Glasgow and West of Scotland BTS reporting on their study into blood donors with a history of jaundice. The authors found that a history of jaundice was not materially higher in donors who tested positive for HBsAg than in those who did not. They stated:

<sup>79</sup> 1977 *Memorandum* [SNB.002.5348] at 5350. A similar provision was contained in the 1983 *Memorandum* ([SGF.001.0377] at 0388), the 1985 *Memorandum* ([DHF.001.8931] at 8943) and the 1987 *Memorandum* ([SNB.006.6410] at 6418)]. For completeness, it is noted that the *Standards for the Collection and Processing of Blood and Blood Components and the Manufacture of Associated Sterile Fluids*, published by the DHSS in 1979, stated that, 'The following diseases may lead to acceptance, deferment or disqualification as donors ... jaundice or hepatitis in the last year' [PEN.002.0249] at 0253.

<sup>80</sup> Dr McClelland – Day 9, pages 90–91

<sup>81</sup> *Ibid* pages 91–92

<sup>82</sup> *Ibid* pages 90–92

<sup>83</sup> Wallace, *Blood Transfusion for Clinicians*, 1977 [LIT.001.3058] at 3107

<sup>84</sup> Renton et al, 'Blood donors with a history of jaundice', *The Lancet*, 1978:833 [PEN.002.0851]

We conclude from these results that a history of jaundice does not materially increase the prevalence of HBsAg among blood-donors and is likely to imply previous infection with [Hepatitis A virus] rather than with [Hepatitis B virus].<sup>85</sup>

**18.70** The findings of the Glasgow BTS study were reported more fully in *The Lancet* on 2 February 1980. The authors stated:

The findings suggest that in a country with a low incidence of hepatitis-B carriage a history of jaundice is much more likely to equate with prior hepatitis-A infection than B infection. There is no evidence to support the practice of regarding blood donors or patients with a history of jaundice as a special group with more prior exposure to hepatitis B virus and thus more likelihood of being long-term carriers of hepatitis-B virus.<sup>86</sup>

**18.71** On 15 March 1980, *The Lancet* published a letter from Dr Robert Hopkins and colleagues at the ESESBTS on the topic of blood donors with a history of jaundice. The letter stated:

The former policy of the Scottish Blood Transfusion Service was to reject as donors all persons admitting a history of jaundice. Lately this policy has been modified to exclude only would-be donors with a history of jaundice within the previous twelve months: donations are now accepted from most persons with a history of jaundice, provided they are HBsAg negative upon routine testing.<sup>87</sup>

**18.72** After reporting the findings of their study the authors stated:

We conclude that in the donor population of South-East Scotland a history of jaundice is not associated with an increased risk of HBsAg carriage. This is in agreement with findings in the West of Scotland reported by Dr Follett and colleagues. The prevalence of antibody to hepatitis A in our region is similar in donors with and without a history of jaundice (84% and 78%). This suggests that the viruses of "non-A, non-B hepatitis" may be a significant cause of jaundice in this population.<sup>88</sup>

**18.73** This too was controversial. In his evidence to the Inquiry, Dr Dow stated that the finding in the Edinburgh study of a similar incidence of Hepatitis A in donors with a history of jaundice and in donors without such a history, was at variance with the findings in the west of Scotland where the incidence of Hepatitis A was much higher in donors with a history of jaundice. Dr Dow considered that one would need to know how many donors were tested in the Edinburgh study and considered that the suggestion in the last sentence about NANB Hepatitis was 'pure speculation'.<sup>89</sup>

**18.74** On 23 October 1982, the *British Medical Journal* published a letter by Mr Archie Barr and colleagues at the Glasgow BTS on the topic of blood donors with a history of jaundice. They reported:

We have now studied a group of donors according to the age at which the jaundice occurred. Almost all the episodes of jaundice occurring before the age of 13 years were due to hepatitis A infection, but about 20% of those

<sup>85</sup> Crawford et al, 'Blood donors with a history of jaundice', *The Lancet*, 1979:155 [LIT.001.2155]

<sup>86</sup> Follett et al, 'Viral hepatitis markers in blood donors and patients with a history of jaundice', *The Lancet*, 1980:246 [LIT.001.0430]

<sup>87</sup> Hopkins et al, 'Blood donors with a history of jaundice', *The Lancet*, 1980:596 [LIT.001.0429]

<sup>88</sup> Ibid [LIT.001.0429]

<sup>89</sup> Day 24, page 149

with jaundice in adolescence or later had no markers for hepatitis A or B. Other viruses can cause jaundice – for example, Epstein-Barr virus, cytomegalovirus, Coxsackie virus, adenovirus – and many other agents can cause liver problems. We cannot, therefore, equate unexplained jaundice with infection by the elusive non-A, non-B viruses. Indeed, it is uncertain whether sporadic non-A, non-B hepatitis is caused by the same agent as the form of the disease transmitted by transfusion, and it is not known how often a carrier state follows sporadic infection. Furthermore, it is possible that, as with hepatitis B, clinical jaundice may be an indicator of elimination of virus rather than carriage ....

In the last three years this region has transfused nearly 400,000 donations of blood and their derivatives. Only 12 cases of overt post-transfusion hepatitis possibly attributable to non-A, non-B agents have been notified .... None of the donors involved in the eight cases associated with red-cell transfusion had given a history of jaundice ....

The present British policy appears to be correct, and any change could cause a serious loss of blood products when some regions are still struggling to make 80% of the blood plasma they collect available for factor VIII production ....<sup>90</sup>

**18.75** In May 1986, Dr Dow presented a Special Report to the SNBTS Directors on Surrogate Tests for Non-A, Non-B Hepatitis. The report noted that:

In the USA individuals with a history of prior jaundice are excluded because of the possibility of their jaundice episode being due to NANB and subsequently becoming chronic carriers of NANB agent(s). Exclusion of such individuals in the West of Scotland population would incur a loss of around 2 to 3% of donors.<sup>91</sup>

**18.76** After commenting on the three NANB Hepatitis surrogate screening tests then under consideration, namely, excluding donors who had a history of jaundice, who were positive for antibodies to the Hepatitis B core antigen or who had an elevation of the liver enzyme ALT, the report stated:

The effect of these strategies in identifying implicated donors involved in NANB PTH cases.

The “acid” test for either of these three means of identifying potential NANB carrier donors is to examine the effect, if any, they would have in identifying such donors amongst those implicated in reported cases of NANB PTH.

Of the 65 donors implicated in 18 NANB PTH cases, only 2 had histories of jaundice and both were involved in the cases in which jaundice may have been caused by the effects of drugs rather than transfused blood.<sup>92</sup>

**18.77** The report concluded:

The present UK policy of accepting donors with raised ALT levels .... anti-HBc or histories of jaundice would appear to be correct. It would appear from the study that the introduction of such surrogate screening procedures would have

<sup>90</sup> Barr et al, ‘Blood donors with a history of jaundice’, *British Medical Journal*, 1952:285 [PEN.014.0067]

<sup>91</sup> Surrogate Tests for Non-A – Non-B Hepatitis – Special Report to Regional Transfusion Directors [SNF.001.1109]

<sup>92</sup> Ibid [SNF.001.1109] at 1110.

little impact on reducing the already low level of NANB PTH cases at present reported within the West of Scotland region.<sup>93</sup>

**18.78** Continuing controversy over these matters clouds the issue as to whether interview practices in the 1970s and early 1980s were likely to provide relevant and reliable information about the risk that an individual prospective donor's blood might be infective for Hepatitis B, or any other transmissible infection. As some of the evidence shows, the debate tended to move from Hepatitis B to NANB Hepatitis over this period. There was no test for any NANB Hepatitis virus before 1988. The use of surrogate testing in that context is discussed in Chapter 27, *Surrogate testing of Donated Blood for Non-A, Non-B Hepatitis*.

**18.79** In November 1987 the NBTS advice was modified.<sup>94</sup> Donors reporting jaundice or hepatitis in childhood followed by full recovery were to be accepted. Item 1 of the ISBT guidance was now reflected in the NBTS advice. Donors reporting adult jaundice or hepatitis were to be deferred pending additional information from their general practitioners. If it proved not to be Hepatitis B, they were to be accepted one year after full recovery. Donors known to have had Hepatitis B and who wished to donate were to be referred to their NBTS Centre for individual consideration. Hepatitis contacts were to be deferred for six months after close contact. It was recognised that defining high risk donor populations by means of fixed HBsAG prevalence rates could cause problems, and that it was necessary to have regard to the impact of guidance on the availability of blood supplies.<sup>95</sup> This was consistent with the Maycock report,<sup>96</sup> and in turn with the 1977 guidance.<sup>97</sup> That version of the NBTS *Memorandum on the Selection, Medical Examination and Care of Blood Donors* (1977) embodied the Maycock recommendation on exclusion. There was a change towards accepting donors with a history of jaundice or hepatitis, as long as the attack had been more than 12 months previously and the donor was proven negative for Hepatitis B surface antigen using a sensitive test.

**18.80** The progressive reduction in the range of individuals excluded would probably have improved to some extent the prospects of obtaining relevant information on interviewing potential blood donors. More recent episodes of hepatitis, particularly involving jaundice, would have been likely to have been recalled by donors. A person who had had no overt signs or symptoms of infection might be wholly unaware of his or her infection but, where there was a known infection, disclosure still depended on the ability and willingness of the individual presenting as a donor to provide a history. Some donor sessions, in factories or other work places and in public places such as shopping centres, were less than private, and a donor might prefer to conceal a relevant fact rather than explain to colleagues why no donation had been taken.

### ***Exclusion on the ground's of NANB Hepatitis and jaundice***

**18.81** Developing knowledge of NANB Hepatitis and the development of tests indicative of infection with that disease are dealt with in detail elsewhere. For the purposes of this discussion, the question is whether the interview techniques, focussed as they were

<sup>93</sup> Ibid [SNF.001.1109] at 1111. Dr Dow's research and the error inherent in the approach of relying on reported cases of post-transfusion jaundice to estimate the prevalence of post-transfusion NANB Hepatitis are more fully discussed in this Report in the chapter on surrogate testing.

<sup>94</sup> *Guidance for the Selection, Medical Examination and Care of Blood Donors* 1987 [SNB.006.6410] at 6418

<sup>95</sup> Dr McClelland – Day 9, page 111

<sup>96</sup> Second Report of the Advisory Group on Testing for the Presence of Hepatitis B Surface Antigen and its Antibody [SGH.003.0079]

<sup>97</sup> Dr McClelland – Day 9, page 110; *Memorandum on the Selection, Medical Examination and Care of Blood Donors* – Section 1 – Selection of Donors [SNB.002.5348]



on prior hepatitis and in particular on the signs of jaundice, were effective means of identifying potential donors infected with the NANB Hepatitis virus, as an incidental result of exploring the potential donor's exposure to HBV.

**18.82** The letter by Dr Hopkins and colleagues, referred to at paragraph 18.71 above, suggested an association of jaundice and the NANB Hepatitis/Hepatitis C (HCV) viruses. Dr Dow thought that was speculative. Mr Barr and colleagues considered that one could not associate unexplained jaundice with 'the elusive non-A, non-B viruses'. Dr Dow and colleagues thought that using histories of jaundice would have little impact on reducing NANB PTH cases. Two sources of evidence deal conclusively with the issue.

**18.83** In his written evidence to the Inquiry, Dr McClelland stated:

With respect to antibody to hepatitis C virus, Crawford et al 1994,<sup>98</sup> found that only 5.9% of the donors who had been found to be HCV positive gave a history of jaundice, suggesting that the result of this questioning would not be an effective screening test. This is consistent with observations that the natural history of hepatitis C infection does not typically include early episodes of jaundice. The infection can be asymptomatic for a long period after exposure, so it cannot be assumed that donors carrying the virus would recall any episode of jaundice or hepatitis ....

I am unable to estimate the size of any possible impact of an exclusion of donors with a history of jaundice on the incidence of post transfusion hepatitis, but I think it is unlikely that any effect would have been large.<sup>99</sup>

**18.84** Professor Juhani Leikola gave the following evidence:

On the basis of what was known at the time, in my opinion it was a reasonable policy to accept otherwise healthy individuals (after a quarantine time) but who gave a history of jaundice. In the past it was natural to think that the cause of jaundice would have been hepatitis A (after recovery blood is not infectious) since hepatitis B would have been detected in the laboratory. However, once it became clear by mid-1970s ... that after clinical hepatitis B the patient may become chronic carrier of the virus with HBsAg levels below detection limits and that there could be another hepatitis virus causing first jaundice and chronic carrier state without clinical symptoms, the policy could have been reconsidered. However, I think that precluding all donors giving a history of jaundice would not have had a major effect on the blood transfusion safety.<sup>100</sup>

**18.85** Professor Leikola was asked why the exclusion of donors with a history of jaundice was unlikely to have had a major effect on blood transfusion safety. He replied:

What we know about these diseases right now is that the vast majority of the carriers of either Hepatitis B or Hepatitis C virus, they have not had any jaundiced phase in their disease. The vast majority is really subclinical and maybe not causing any symptoms at all. On the other hand, some people with acute infectious hepatitis, especially Hepatitis A, they recover completely from

<sup>98</sup> Crawford et al, 'Prevalence and epidemiological characteristics of hepatitis C in Scottish blood donors', *Transfusion Medicine*, 1994; 4:121–124 [PEN.002.0582]

<sup>99</sup> Dr McClelland's written statement, [WIT.003.0072] at 0089

<sup>100</sup> Professor Leikola's written statement, [WIT.003.0027] at 0030

that jaundice and they are not hazardous to the blood transfusion matter. So in light of what we know now, I don't think that precluding people giving a history of jaundice would have very much influenced the final blood safety.<sup>101</sup>

**18.86** From what is now known, it seems unlikely that the practice of accepting donors with a history of jaundice did materially increase the risk of recipients developing post-transfusion NANB Hepatitis/HCV. Firstly, the vast majority of donors with a history of jaundice were likely to have been jaundiced as a result of causes other than Hepatitis C, for example:

- Hepatitis A (from which donors will have long since recovered and which is generally not transmissible by blood).
- Hepatitis B (in respect of which any donors carrying the antigen at the time of donation are likely to have been detected by the Hepatitis B screening tests and excluded).
- Non-hepatitis viruses (such as cytomegalovirus or Epstein Barr virus).
- Non-viral causes (including alcoholic liver disease, gallstones, and adverse reaction to medication).<sup>102</sup>

Secondly, only a small proportion of individuals who contract Hepatitis C develop jaundice, with the result that most donors with Hepatitis C would not have been excluded by a policy that excluded donors with a history of jaundice.<sup>103</sup> Thirdly, it appears that individuals who contract Hepatitis C and who have an acute episode of jaundice, are more likely to clear the virus, and no longer be infective, than individuals who contract Hepatitis C and who do not experience an acute episode of jaundice.<sup>104</sup>

**18.87** On the basis of what was known at the time, and in light of the recommendations contained in the 1975 WHO report and the second report of the Maycock Advisory Group, it seems reasonable for the Scottish Blood Transfusion Service, from around the mid-1970s, to have accepted donors with a history of jaundice and who were negative for HBsAg. Indeed, no suggestion to the contrary was made to or by any of the witnesses at the Inquiry. The policy of the SNBTS from around the middle of the 1970s to accept donors with a history of jaundice (and who tested negative for HBsAg) appears unlikely to have materially increased the risk of transfusion-transmitted Hepatitis C.

**18.88** Shortcomings in collection procedures, and in particular interview techniques, cannot be said to have had any material bearing on the outcome for recipients of blood products so far as NANB Hepatitis is concerned. There were no known signs and symptoms of infection that could have been elicited by interview of the potential donor, and the information that may have been elicited pointing to a history of Hepatitis B infection would not have alerted the transfusion service to the possibility of infection with NANB Hepatitis.

<sup>101</sup> Professor Leikola – Day 13, page 87

<sup>102</sup> Dr Dow – Day 24, Pages 161–162

<sup>103</sup> In his evidence to the Inquiry, for example, Dr Gillon stated that he had looked at the literature and, while it is very difficult to get a figure, 'It is a very small figure and I think most authorities accept that jaundice is an occasional but rare feature in non-A non-B hepatitis': Day 11, pages 15–16

<sup>104</sup> Professor Thomas – Day 52, page 69

### *Previous transfusion*

**18.89** A prospective donor who had previously had a transfusion of blood or blood components, or who had been treated with blood products, might have acquired disease on that occasion, transmitted by the blood from the original donor, and that was considered to be a risk leading to exclusion, at least within certain time limits.<sup>105</sup> The risk of that person transmitting infection was the same, however the donor of the source blood came to be infected.

**18.90** Item 2 in the section of the 1976 ISBT *Criteria for the Selection of Blood Donors* quoted in paragraph 18.63 above had provided for exclusion where the transfusion had been received within the previous six months.<sup>106</sup>

**18.91** In 1978 the WHO Expert Committee on Biological Standardization published a report.<sup>107</sup> The report noted that it had been agreed that it would be useful to have a single set of requirements applicable to all organisations and laboratories involved in the collection or fractionation of blood and blood products. The report included an Annex on Requirements for the Collection, Processing and Quality Control of Human Blood and Blood Products.<sup>108</sup> In respect of the medical history of donors and, in particular, infectious diseases, the report contained a similar recommendation to the ISBT *Guide*:

Donors shall have a negative history ... of receipt within six months of human blood or any blood component or fraction that might be a source of transmission of viral hepatitis.<sup>109</sup>

**18.92** The Memorandum on the Selection, Medical Examination and Care of Blood Donors, produced by the Transfusion Directors in England and Wales stated, since at least 1977, that donors should be temporarily deferred who, within the last six months, had either undergone a transfusion with blood or plasma or had undergone acupuncture or ear piercing.<sup>110</sup>

**18.93** As noted at paragraph 18.25 above, the 1979 edition of the *Standards for the Collection and Processing of Blood etc* stated that transfusion within the last six months should result in temporary deferment.<sup>111</sup>

**18.94** Two factors changed the context for exclusion on the grounds of prior transfusion. The first was an appreciation of the risks associated with AIDS, which brought about material changes in procedures in about 1983. These changes are dealt with in Chapter 28, *Donor Selection – AIDS*.

<sup>105</sup> *Memorandum on the Selection, Medical Examination and Care of Blood Donors – Section 1 – Selection of Donors 1977* [SNB.002.5348] at 5349

<sup>106</sup> *Criteria for the Selection of Blood Donors* [DHF.001.2672] at 2681

<sup>107</sup> WHO Expert Committee on Biological Standardization – Twenty-ninth Report [LIT.001.3627]

<sup>108</sup> *Ibid* [LIT.001.3627] at 3640

<sup>109</sup> *Ibid* [LIT.001.3627] at 3651. As regards the last recommendation quoted, relating to the avoidance of donor population showing a higher prevalence of acute or chronic hepatitis than in the general population, Professor Leikola explained in his evidence to the Inquiry that he would not place much weight on that recommendation because direct markers of disease (eg the presence of antigen) should be used when identifying a group with a higher prevalence of disease rather than indirect markers such as ‘acute or chronic hepatitis’; the recommendation does not say how much higher the prevalence of disease should be in a donor group for that group to be excluded and the committee who produced the recommendation comprised biologists, virologists and fractionators rather than those with practical experience of blood collection or transfusion: Day 13, pages 57-58

<sup>110</sup> *Memorandum on the Selection, Medical Examination and Care of Blood Donors – Section 1 – Selection of Donors 1977* [SNB.002.5348] at 5349. Similar guidance appeared in the 1983 Guidance [SGF.001.0377] at 0381, the 1985 Guidance [DHF.001.8931] at 8936 and the 1987 Guidance [SNB.006.6410] at 6411, 6413 and 6427

<sup>111</sup> *Standards for the Collection and Processing of Blood and Blood Components and the Manufacture of Associated Sterile Fluids – Section 1 – Selection of Donors 1979* [PEN.002.0249] at 0253 and 0254

**18.95** The second was the risk posed by variant CJD. In current practice, individuals who might have received a blood transfusion since 1980 are not accepted as donors.<sup>112</sup> That decision was taken in 2004 when the first documented clinical case of transmission of variant CJD by a red cell component was described.<sup>113</sup> The intention was to avoid the risk that individuals who themselves had variant CJD through a blood transfusion, might carry on donating and continue recycling the infection in the community. The decision excluded about 3.5% of the donor population at that time (2004), and a higher percentage of the blood donated because people who themselves had received blood transfusions in the past, or whose relatives had benefited from transfusion, were often very keen to contribute something to the community, so that they were often amongst the most dedicated donors. The Services may defer about 1% of donors on this ground on an ongoing basis.<sup>114</sup> As some people do not know whether they have been transfused, if it is inferred from other history that they probably have been transfused they will then be excluded on a precautionary basis.

### Comment

**18.96** The general policy of voluntary donation at the beginning of the period put emphasis on the exclusion of particular groups of potential donors, permanently or temporarily, from donating blood for clinical or therapeutic application as a means of limiting risk. The five regions of the SNBTS drew on the *Standards* and the 1977 *Memorandum on the Selection, Medical Examination and Care of Blood Donors*, as updated, and were involved in the development of the 1989 *UK Professional Guidelines for the Care and Selection of Blood Donors*. Until the advent of AIDS the questioning of donors was less rigorous, being both less direct and less personal. There were also differences of approach apparent between the Regional Centres in relation to donor selection as reported by Dr Gillon in 1985. As late as the early 1980s, a form in use in Glasgow and the West of Scotland identified certain infectious diseases and asked whether the individual had had contact with or had recently recovered from any of them; identified other serious illnesses and asked whether the individual had had such an illness. It also asked whether the individual had had inoculations, surgery or had worked or taken part in sports involving unusual hazards. It did not refer to drug abuse or any aspect of sexual orientation or behaviour.<sup>115</sup>

**18.97** Inhibitions on discussion of the previous medical history of the prospective donor affected the group of individuals that had received previous transfusions, as it did those with a history of jaundice. There were similar problems of recollection. Perinatal transfusion (that is, transfusion in the period immediately after birth, generally up to four weeks) is unlikely to have been known to the recipient. Some patients would never have known that they had been transfused in later life, or understood that the procedures they observed and recollected were transfusions of blood components, for example. If there was jaundice, all of the previous factors would have applied. If the hepatitis was NANB Hepatitis and there was no jaundice, there may have been no other sign or symptom to alert the individual to the need to disclose the event. By comparison, in current practice, questioning is more rigorous, and testing procedures reinforce the safety of the supply.

<sup>112</sup> Professor Turner – Day 7, page 17

<sup>113</sup> Ibid page 18. Professor Turner's evidence included a detailed explanation of modes of transmission. The 'infective agent' of vCJD, a prion protein, is not removed from blood by the conventional methods used to remove viruses, including HCV and HIV.

<sup>114</sup> Professor Turner – Day 7, Pages 19–20

<sup>115</sup> Glasgow & West of Scotland Blood Transfusion Service Questionnaire (1983) [PEN.013.1395]

**18.98** In reality, there were few if any known clinical signs and symptoms of infection with NANB Hepatitis/Hepatitis C that could have been elicited on interview of a prospective donor. Indeed, until a late stage in the development of disease there were a few clinical signs that could have been found by a competent physician on discussion with the individual. Developments in knowledge to the mid-1980s are discussed in Chapter 15, *Knowledge of Viral Hepatitis 2 – 1975 to 1985*. Until the end of that period there were substantial deficits in knowledge of the disease and its natural history.<sup>116</sup> Few of the patients studied in the period had any specific symptoms.<sup>117</sup> In the event, whatever deficits may have existed in the interview procedure, it is unlikely that they had any material impact on the transmission of the infections with which this Inquiry is concerned.

**18.99** Infected blood entered the system up to the mid-1980s primarily because screening of blood for virus infection was ineffective and not because of poor interviewing practices, or donor routines. Screening was recognised as essential to the safety of transfusion, but methods developed up to that time could not identify the main causes of post-transfusion hepatitis efficiently (in the case of Hepatitis B until the late 1970s) or at all (in the case of Hepatitis C).

**18.100** In summary, and having regard to earlier discussion of developing knowledge of NANB Hepatitis/HCV, considerations that had a bearing on the development and application of policies and practices relating to the collection of blood included the following:

- The voluntary principle acknowledged a long-held view that freely donated blood presented a lower level of risk of transmitting infection than blood collected commercially from paid donors.
- Voluntary donors performed a valuable service to society.
- Mutual trust was implicit in the voluntary principle, imposing on the transfusion services obligations of care towards donors, for their safety, and more particularly for present purposes for their general well-being in the course of management of donation procedures; and imposing on donors obligations of care for the ultimate recipients of donated blood.
- The emphasis on jaundice in determining the suitability of a donor to give blood for clinical use was generally irrelevant to the risk of transmission of NANB Hepatitis/Hepatitis C, but that was not understood until the prevalence of anicteric HCV infection began to be appreciated after the introduction of anti-HCV screening in the early 1990s.
- So far as a risk of transmission of NANB Hepatitis was understood to exist, until the second half of the 1980s the disease was generally understood to be benign in its progression.
- A donor's infection with NANB Hepatitis could not have been discovered by interview: medical knowledge did not provide a basis for relevant questioning.

---

<sup>116</sup> Chapter 15, *Knowledge of Viral Hepatitis 2 – 1975 to 1985*, paragraph 15.166

<sup>117</sup> *Ibid* paragraph 15.164

## Conclusions

- By the spring of 1983 it was accepted that AIDS presented a transfusion risk. This resulted in a step change in the rigour of donor selection procedures. Until then it is unlikely that generally recognised interview procedures at donation collections in Scotland were fully effective to elicit information about social or medical histories of donors in general which was relevant to risks of transmission of viral hepatitis.
- The emphasis on Hepatitis B reflected generally accepted views among medical experts until the end of the 1970s that HBV infection presented the most significant risk of transfusion-related transmission of viral hepatitis.
- Even after Regional Transfusion Directors introduced more rigorous interview practices in and after 1983, there were no procedures that could have elicited information indicative of asymptomatic NANB Hepatitis infection.
- Until the second half of the 1980s, NANB Hepatitis was generally understood to pose a lower risk to the recipient of an infected donation, than the underlying cause of medical or surgical treatment giving rise to the transfusion.
- Ignoring later scientific developments, so far as general members of the public offering blood donation were concerned, there was no method of identifying with interview those potential donors who were infected with NANB Hepatitis, but who remained asymptomatic at the donor session. No such interview could have been conceived at the time.

## CHAPTER 19

### PRODUCTION OF BLOOD PRODUCTS – FACILITIES

#### Introduction

**19.1** This chapter deals with the provision of facilities for the production of blood components and blood products, and in particular with the assumptions made as to process capacity in the development of plans for capital projects in the 1970s.

#### Origins

**19.2** As noted in Chapter 17, *Blood and Blood Products Management*, large-scale production of blood products in Scotland started with government-led initiatives in the 1940s leading to the establishment of facilities, first, for the preparation and storage of plasma to secure supplies to hospitals and the military, and then for the preparation of freeze-dried human plasma. The most significant developments were:

- The establishment of blood banks in the principal centres of population.
- The setting up of regional centres in Dundee, Edinburgh, Glasgow, Aberdeen and Inverness.
- The organisation of plasma filtration units in Edinburgh and Glasgow to process raw material collected locally and from other regions of Scotland.
- The installation of a Blood Products Unit (BPU) for the production of dried plasma in Edinburgh at the beginning of 1943, to meet all Scottish needs.
- The provision of a 'saline infusion fluids centre' for the preparation of saline glucose and other solutions used for intravenous injection at Glasgow, later relocated to Law Hospital, Carluke.

**19.3** The wartime facilities at the Royal Infirmary of Edinburgh (RIE) rapidly became overcrowded and unsuitable, and the centre was developed and expanded throughout the late 1940s and early 1950s, with new premises located at the RIE being opened in 1950. The BPU there began to produce a range of fractionated plasma products, beginning in 1952 with immunoglobulin and an early version of Factor VIII (Cohn Fraction I).<sup>1</sup> Despite a major reconstruction and extension of the centre in 1961 the facilities soon proved to be insufficient for the expanding operation. By early 1965, planning for a new centre (to become the new Protein Fractionation Centre (PFC) at Liberton, Edinburgh) was under discussion at government level.

**19.4** By the beginning of the reference period, the scope of the operations planned for the new PFC had changed considerably from anything that could have been envisaged in 1941, largely in response to changing demand for blood products. Cryoprecipitate had become a mainstay of haemophilia therapy, and factor concentrates were beginning to have an impact on the market. Two facilities were established in England, the Blood Products Laboratory, Elstree, (BPL) and the Plasma Fractionation Laboratory, Oxford (PFL). Planning for the Scottish facility proved to be a tortuous process, most aspects of which are of little relevance to the Inquiry. There are, however, a few matters that were important

---

<sup>1</sup> Foster, 'Plasma fractionation in Scotland', *Blood Letter*, Spring 2008 [PEN.017.2468]

when planning was completed and the construction and commissioning of the plant began.

**19.5** Two of those matters were the planned territorial scope of the PFC's operations, and the production volume targets for which the facility was to be designed. From the beginning there appears to have been uncertainty about both. It appears that from the outset the premises at the PFC, as designed, were more than large enough to accommodate a production plant sufficient to service local Scottish demand well into the 1980s. How that came about is less than completely clear. But it was to have a major impact on the ability of Scotland to meet demand for factor concentrates in this country as compared with the capacity of the BPL and the PFL to service demand in England and Wales.

**19.6** By February 1965 planning for a new centre was being discussed at meetings between the Scottish Home and Health Department (SHHD) and the Blood Transfusion Services of England and Wales and of Scotland.<sup>2</sup> It was initially estimated that the new facility required in Scotland to manufacture plasma products should be capable of processing up to 1000 litres of plasma per week, including plasma from England.<sup>3</sup> It appears that demand from Northern Ireland was to be serviced from Scotland.<sup>4</sup> Processing of plasma from England reflected a decision that would have required continuing cooperation between the Blood Transfusion Service in England and Wales on the one hand and in Scotland on the other, while managed by separate administrative agencies and subject to policy direction by separate government departments. On a practical level, it implied that a manufacturing capacity of 1000 litres of plasma per week was specified so that it would be sufficient to service demand in Scotland, Northern Ireland and in a northern part of England that still had to be defined.

**19.7** The projected capacity of the Scottish facility was amended in discussion. In May 1968, at a meeting at the RIE between SHHD, the Department of Health and Social Security (DHSS) and the Blood Transfusion Services of England and Wales and of Scotland it was anticipated that the PFC would be commissioned in June 1972 with an initial capacity of 1500 litres of plasma per week but capable of being increased to 3000 litres per week.<sup>5</sup> It was agreed that the PFC should be prepared to cope with the requirements of a larger part of England than originally intended. It was agreed that requirements for labile coagulation products (concentrates) needed to be revised.

**19.8** At a meeting in November 1968, at the BPL, between the SHHD and the Blood Transfusion Services, it was noted that approval in principle had been given for the new PFC.<sup>6</sup> It was also noted that commissioning of the new BPL extension was expected to be completed by mid-1971. It was anticipated that commissioning of the PFC would be completed early in 1973. It was hoped to start building the extension at the BPL in September 1969 with commissioning expected early in 1972. Procurement of the new centre was eventually approved in November 1969. Meantime, a new pilot plant for fractionation was established at the BPU at the RIE in 1968.<sup>7</sup>

<sup>2</sup> *Planning of Plasma Fractionation in Scotland*, synopsis by SNBTS of meetings February 1965–March 1973 [SNF.001.2412]

<sup>3</sup> Ibid

<sup>4</sup> Girdwood, *Fifty Years of an Organized Blood Transfusion Service in Scotland*, (undated) [SNB.010.1836] at 1840

<sup>5</sup> Present: IS Macdonald (SHHD), Dr Thomson (DHSS), W d'A Maycock, L Vallett (BPL), RA Cumming, JG Watt (Edinburgh). See *Planning of Plasma Fractionation in Scotland*, synopsis by SNBTS of meetings February 1965–March 1973 [SNF.001.2412]

<sup>6</sup> Same parties as 'the May 1968 meeting' excluding Dr Thomson. '*Planning of Plasma Fractionation in Scotland*', synopsis by SNBTS of meetings February 1965–March 1973 [SNF.001.2412]

<sup>7</sup> Maj. Gen. Jeffrey's letter of 6 January 1975 to Chief Administrative Medical Officers [SGH.007.7009]



**19.9** At a meeting on 14 March 1969, attended by representatives of the SHHD, the BPL, and the Scottish National Blood Transfusion Service (SNBTS), the need for standing arrangements for coordinating policy matters at departmental level was discussed, and a committee structure was proposed.<sup>8</sup> It was agreed that the SHHD should contact the DHSS with proposals to form a coordinating committee. The Medical Research Council (MRC) had a reference laboratory at Elstree, and might be involved in any new standing arrangements. Cooperation on professional and technical matters was expected to continue throughout the service, but within a formal relationship with the proposed coordinating committee. At this stage, it was agreed that the BPL should process two thirds of the plasma collected from England and Wales with the remainder being processed in Scotland.

**19.10** On 27 June 1969, a meeting took place at the BPL between the SHHD and the Blood Transfusion Services of England and Wales and of Scotland.<sup>9</sup> The discussion was largely confined to technology. Total production targets were not resolved. On the basis of the information available, it would be difficult to form the view that the planning of production was firmly established, on a UK or on a Scottish basis at this stage.

**19.11** In April 1970 the BPU was renamed the Scottish Protein Fractionation Centre (PFC). Mr John Watt was appointed Director of the BPU in 1967, and became the first Scientific Director of the new purpose-built facility in 1971 when building operations commenced.<sup>10</sup> In 1974 the PFC relocated to Liberton in Edinburgh.

### **Demand for blood products for coagulation disorder patients**

**19.12** There was considerable, and growing, uncertainty about levels of demand for haemophilia therapy in the UK as a whole. At 5 April 1971, it was recognised that the total ideal requirement of material for treating patients with coagulation defects was not known.<sup>11</sup> In 1969, the material used for treatment of 1032 haemophilia and Christmas disease patients at the 30 centres from whom records were received by the UK Haemophilia Centre Directors' Organisation (UKHCDO) then located in Oxford, was derived from 84,906 donor units, an average of just over 82 donor units per patient. The products used were:<sup>12</sup>

Amounts used		
Material	No of Donor Units	% total
Plasma	11,435	13.46
Cryoprecipitate	59,715	70.34
Concentrates	13,756	16.20
TOTAL	84,906	100.00

<sup>8</sup> Minutes of meeting [SNB.010.2066]

<sup>9</sup> Note of meeting [SNB.010.2059] Present: DM Pendreigh (SHHD), W d'A Maycock, L Vallett, D Ellis (BPL), RA Cumming, JG Watt (Edinburgh).

<sup>10</sup> Foster, *Self-sufficiency and the supply of blood products in Scotland*, SNBTS, February 2011 [PEN.013.1125]; Girdwood, *Fifty Years of an Organized Blood Transfusion Service in Scotland*, (undated) [SNB.010.1836] at 1840

<sup>11</sup> *Report on progress of an MRC Cryoprecipitate Working Party Survey*, provided to a meeting of Haemophilia Centre Directors in Oxford on 5 April 1971 [DHF.001.1811] at 1820

<sup>12</sup> *Ibid* [DHF.001.1811] at 1824

**19.13** This was said certainly to provide an underestimate of requirements. By way of example, it was observed that there was a waiting list of haemophilia patients requiring non-urgent surgery at Oxford and that it would require material from 10,000 donors to carry out the operations.<sup>13</sup> And the introduction of home treatment was expected to increase the amount of material used. It was noted that a record of total use year by year would give an estimate which would level off to ideal requirements. The annual figure could form a basis for an estimate of the amount of concentrate that might be required.

**19.14** Dr Rosemary Biggs and colleagues reported numbers for 1969–71 in a report prepared for the MRC.<sup>14</sup> Over that period 1608 different patients attended haemophilia centres. On their calculations, taking account of other sources of information, the minimum total number treated was estimated at 2434. That was rounded up to 3000, as an estimate of the number of haemophilia patients in the UK, a rate of about five to six per 100,000 of the population, which was reasonably in line with other estimates. The report estimated the demand for Factor VIII concentrate at 35,779,800 to 50,000,000 international units for on-demand therapy.<sup>15</sup> Making allowance for major surgery and dental extractions, the total material required was likely to lie between 38,327,800 and 53,000,000 units of Factor VIII, requiring 547,540 to 750,000 blood donations per year. Home treatment would be in substitution for hospital treatment, and would not generate additional demand. Prophylactic treatment was thought to be impractical at that stage.

**19.15** Mr Watt, the Scientific Director of the PFC, proceeded on a different basis when calculating need at June 1973.<sup>16</sup> He calculated the need for Plasma Protein Solution (PPS – a product of the final stage of Cohn fractionation, Fraction V), and concluded that the volume of plasma required for the preparation of antihaemophilic globulin (AHG), at Cohn stage I, would be readily achieved if his PPS target was met. He assumed that the population of the UK was 60 million, and the population of Scotland 5 million. The number of haemophilia patients in the UK was assumed to be 3000 (5/100,000). He calculated that the Scottish need for fresh frozen plasma for processing to meet the needs of the haemophilia population was 15,000 donations per million of population (45,000 donations) to provide 4.8 million plasma units per million population, or 20,000 plasma units per haemophilia patient per year. Extrapolated first to England and then to the UK as a whole (on the basis that there should be little difference in community need and that therefore the Scottish figures of need could be applied), he concluded that English need for AHG would be 48,000,000 plasma units, and total UK need would be 53,000,000 plasma units.

**19.16** In Mr Watt's view, the English facilities could not achieve the necessary level of production and the PFC would require to process material for England. He argued that development of the site at Liberton would be the most economic and rapid means of achieving adequate fractionation capacity for the UK. He said:

B.P.L. and P.F.C. are each specified for 70,000 – 80,000 litres of plasma per year. It is my opinion that B.P.L. production could be increased to about 150,000 litres but further increase would appear impossible on the present site and could hardly be justified. The difference of more than 250,000 litres includes 35,000 to 40,000 which the P.F.C. must process for Scotland.

<sup>13</sup> Ibid [DHF.001.1811] at 1820

<sup>14</sup> Report by Dr Biggs *et al*, [SNB.001.4871]

<sup>15</sup> The international unit (IU) was a measure of Factor VIII activity. The assumed level of activity in a given quantity of blood provided the conversion factor adopted, and varied from time to time.

<sup>16</sup> Watt, *Plasma fractionation in the United Kingdom – a personal appraisal*, (Draft) 12 June 1973 [SNB.010.1991]

**19.17** He noted that there was a risk of a dual standard of clinical availability as between Scotland and England, an intolerable situation which, he thought, could not be maintained.

**19.18** At this stage, in the early 1970s, as Dr Biggs' report indicates, the Haemophilia Centre Directors recognised that the pattern of demand was changing, and that data for actual demand would be required to form a view of ideal requirements. In the event, data returned for 1970 and 1971 saw the volumes used increase, in terms of blood donations used, to 105,531, and then to 132,743 donations. In 1971, 1100 patients were treated at the 35 centres which reported, at a rate of 120.7 donations per patient per year, not including donations used in elective surgery or dental procedures. The comparative figure for 1969 was 84.9 donations per patient per year.<sup>17</sup> As indicated later, by early 1973 it was recognised generally that considerably more concentrate was required than the output of the UK facilities if the needs of haemophilia clinicians were to be met.

**19.19** These changes in perception of the likely levels of demand were taking place as construction of production facilities was at an advanced stage of planning or had already begun in England and Scotland. In November 1969, there was a meeting at the RIE between the SHHD and the Blood Transfusion Services of England and Scotland.<sup>18</sup> It was reported that it would be about one year before contractors could move onto the site of the new Scottish fractionation centre, and it was estimated that commissioning would be completed in the latter half of 1974. Tenders for the work had been received by July 1971. Building of the new extension at the BPL had begun in November 1969 and was expected to be completed in September 1971.<sup>19</sup> Having gone to tender, and on to concluded contract, flexibility to respond to changing demands was necessarily limited, in the short term at least.

**19.20** In this period of change, those planning developments appear to have depended on the Haemophilia Centre Directors for information about demand for Factor VIII and IX (cryoprecipitate or concentrates). The 1969 data referred to above were not available until 1973, still less the 1970 and 1971 figures. None of these data provided a reliable basis for forecasting growth, and they could not have provided a rational basis for projecting UK demand based on donor units. Furthermore, planning for the size and capacity of the new UK fractionation facilities coming on stream in the early 1970s had been carried out at a time when there had been no clear idea whatever of possible future demand for Factor VIII and Factor IX products.

**19.21** Later analysis of data would have further undermined the reliability of the 1969 figures as a basis for projecting demand. Between 1969 and 1973, new demands were placed on suppliers by clarification of the numbers of patients needing treatment, and developments in the forms of treatment, such as home treatment of coagulation disorder patients and, to a lesser extent, prophylactic treatment, increasing the difficulties inherent in projecting demand. Further research was required. But the facilities already planned proceeded and were duly commissioned against a background of insufficient production to meet UK requirements as a whole.

<sup>17</sup> Biggs, 'Jaundice and antibodies directed against Factors VIII and IX in patients treated for Haemophilia or Christmas disease in the United Kingdom', *British Journal of Haematology*, 1974, 26, 313 [LIT.001.0099] at 0102

<sup>18</sup> *Planning of Plasma Fractionation in Scotland*, synopsis by SNBTS of meetings February 1965–March 1973 [SNF.001.2412] at 2413

<sup>19</sup> *Ibid* [SNF.001.2412] at 2413–2414

## Changing demand and the development process

**19.22** In July 1971, there was a further meeting at the RIE between the SHHD and the Blood Transfusion Services of England and Scotland.<sup>20</sup> It was agreed that discussions on central processing of Factor VIII and Factor IX concentrates were imperative because of major effects on production planning. Work began at Edinburgh with a planned commissioning date for the new PFC in January 1974,<sup>21</sup> which coincided, in the event, with the start of the reference period for this Inquiry.

**19.23** However, the wider context for these discussions changed early in 1973. The first UK licences for the US commercially produced Factor VIII concentrates Hemofil and Kryobulin were granted on 19 February and 22 March 1973 respectively.<sup>22</sup> On 6 March 1973, the Chief Medical Officer (CMO) for England and Wales wrote to all Senior Administrative Medical Officers.<sup>23</sup> He said:

The production of the human concentrate in the UK is at present insufficient to meet the stated needs of clinicians who care for patients requiring surgical, including dental, treatment or who have episodes of severe bleeding. The indications are that considerably more of this preparation would be used if it were available.

**19.24** The DHSS assembled a group of experts to advise generally on the likely trends in treatment of haemophilia and, more specifically, to make proposals on which realistic planning for the future could be based. The group met on 20 March 1973.<sup>24</sup> It was recognised that the scale of the problem had been underestimated and that UK production was less than required to meet anticipated demand.

**19.25** An updated version of Dr Biggs' report was available, still based on data for the period 1969–71.<sup>25</sup> On broadly the same assumptions as before, Dr Biggs estimated total demand for all types of therapy, excluding prophylaxis, at between 400,000 and 750,000 donor units per year. It was agreed that 400,000 donations would be required to treat UK sufferers, and more if strenuous efforts were made to clear surgical waiting lists and if home treatment or, eventually, prophylactic treatment were to become acceptable forms of therapy. Those planning for demand now had information from the haemophilia directors of their expectations for future demand. But it was recognised that a broader membership was required, including Regional Haemophilia Director, and Transfusion Director, representatives, the National Medical Director of the SNBTA and Mr Watt of 'the Edinburgh BPL'.<sup>26</sup>

**19.26** The expert group's views on the development of domestic facilities at March 1973 were:

It is essential the production and distribution of the therapeutic agents concerned should be considered as a U.K. exercise.

....

<sup>20</sup> Ibid [SNF.001.2412] at 2413

<sup>21</sup> Ibid [SNF.001.2412] at 2413

<sup>22</sup> Chronology of events with relevance to 'self-sufficiency' etc [SGH.002.1313]. See Chapter 21, *Haemophilia Therapy – Use of Blood Products*

<sup>23</sup> CMO's letter [DHF.001.2122]

<sup>24</sup> Minutes of Expert Group on the Treatment of Haemophilia, 20 March 1973 [SNB.006.7631] at 7633

<sup>25</sup> *Factor VIII Concentrates and the Treatment of Haemophilia*, Report by Dr Biggs [SNB.006.7775]

<sup>26</sup> Minutes of Expert Group on the Treatment of Haemophilia, 20 March 1973 [SNB.006.7631] at 7634

Close co-operation between England (including Wales and N. Ireland) and Scotland will be required in order to co-ordinate and optimise blood collection and transport, the fractionation processes, distribution of the therapeutic agents, and utilisation of other blood fraction by-products.<sup>27</sup>

**19.27** Recommendations of the group included that the UK should aim to become self-sufficient as soon as possible by increasing home production of freeze-dried concentrate. It would have been anticipated at the time that production would take place at the new PFC facility in Liberton in Scotland, still to be commissioned, and at the BPL and at the PFL in England.

**19.28** On 27 March 1973, there was a meeting at the BPL between the SHHD and the Blood Transfusion Services of England and Scotland.<sup>28</sup> The BPL facility was by that stage taking in plasma at its planned capacity of 1500 litres per week.<sup>29</sup> Good progress was reported in the construction of the Edinburgh fractionation centre, with commissioning expected to start in April 1974. The work was in fact completed at the end of 1974.<sup>30</sup> The total cost was expected to be just over £1 million. But there was still a degree of uncertainty about the scope of the plant's operations. There was concern that planning for annual requirements was inadequate. The processing of time-expired plasma had been provided for. But the Scottish facility did not have the capacity to process English fresh plasma. That was still to be considered for the UK as a whole. At this stage, when the use of coagulation factors was increasingly seen as of central importance in the treatment of haemophilia patients, the final planning of processing of raw material and production was still incomplete.

**19.29** The policy context for development took a change of direction when, on 20 June 1973, the first meeting of a Joint Steering Committee on Blood Products Production was held, bringing together DHSS and SHHD officials, representatives of the production facilities and Regional Transfusion Directors.<sup>31</sup> The policy implications of the entry of commercial producers into the market were acknowledged:

The first meeting of the Steering Committee had been precipitated by the fact that product licences had been granted to two firms to import antihaemophilic globulin concentrate which might entail large sums being spent by NHS authorities on these products.<sup>32</sup>

**19.30** Full-scale production had been achieved at the BPL. Mr Watt provided information on the programme and timetable for commissioning the PFC. Production targets were explained, as were limitations on plasma supplies. The PFC's capacity could be expanded, but it was urgent for the facility to know what volume of plasma it would be asked to process for England. The views that emerged included: (a) adopting the lower of Dr Biggs' estimates of demand for plasma at 400,000 donations as a first target, with her upper estimate of 700,000 donations as the ultimate target; (b) an initial aim of processing 250,000 donations by 1975; (c) preparation of 90% of total output as intermediate potency concentrate, and 10% as high potency product; and (d) self-sufficiency for the UK by 1975. DHSS indicated that a system of call-off contracts for imported material was

<sup>27</sup> Ibid [SNB.006.7631] at 7634

<sup>28</sup> Note of meeting [SNB.010.2009]

<sup>29</sup> Approximately the capacity mentioned by Mr Watt in his personal assessment of 12 June 1973.

<sup>30</sup> Foster 'Plasma fractionation in Scotland', *Blood Letter*, Spring 2008 [PEN.017.2468]

<sup>31</sup> Note of meeting [SNB.006.7767]

<sup>32</sup> Ibid [SNB.006.7767] at 7768

under consideration. Other developments were set out as possibilities.<sup>33</sup> It was noted that Scotland had apparently nearly reached and might exceed its proportion of the target for donations for the treatment of haemophilia suggested by Dr Biggs.

**19.31** In an undated report prepared for the MRC's Transfusion Research Committee, and made available for a meeting of Haemophilia Centre Directors on 31 January 1974, Dr Biggs and her colleagues set out a comprehensive review of the position based on studies of the period 1969–72.<sup>34</sup> The report again included an attempt to estimate the total amount of therapeutic materials containing Factor VIII activity that was likely to be needed in the UK together with the amount of fresh whole blood required for processing to meet that target.<sup>35</sup>

**19.32** Making allowance for haemophilia patients attending general hospitals, and extrapolating from accurate data for the Oxford Haemophilia Centre, the report estimated that, while they had information on 1100 patients attending 35 haemophilia centres in 1971, the number of haemophilia patients treated in 1971 in the UK as a whole was between 2434 and 3000.<sup>36</sup> Using data for donations used for cryoprecipitate and freeze-dried concentrate production and taking account of yield, the report concluded that for all types of bleeding (spontaneous, during surgery and for dentistry) the total demand required was between 547,540 and 750,000 blood donations per year. Home treatment would require 250,000 donations, as an alternative, but not cumulative, form of therapy. Prophylaxis would add further demand, but that approach to therapy was not recommended. At the time, 1.7 million blood donations were collected annually by the Blood Transfusion Services for all uses, including transfusion in surgery and medical procedures.

**19.33** Subsequently, Dr Biggs published information relating to the period 1969–74,<sup>37</sup> and the Haemophilia Centre Directors supplemented that for 1975.<sup>38</sup> In her publication covering 1969–74, Dr Biggs summarised the effect of earlier data:

[I]t was concluded that: 'An assessment of the total amount of factor VIII likely to be required for all types of treatment puts the total in excess of 500,000 blood donations annually or about 40 million factor VIII units'.<sup>39</sup>

**19.34** It was still not known how many blood coagulation disorder patients were treated at hospitals not designated as haemophilia centres, but it was thought that the previous estimate of total demand was unlikely to be excessive. The balance had shifted towards concentrate use, however, and it was now thought that 60% of Factor VIII should be freeze-dried<sup>40</sup> in order that home therapy could be instituted on a reasonable scale.<sup>41</sup>

<sup>33</sup> Ibid [SNB.006.7767] at 7769–7771

<sup>34</sup> Minute of meeting [SNB.007.2190]. The report is [SNB.001.4871]. Information has been taken from pages 4874, 4890, 4891 and 4892.

<sup>35</sup> From its terms, it appears that in this report 'United Kingdom' was used accurately to include Scotland.

<sup>36</sup> Biggs, 'Jaundice and antibodies directed against Factors VIII and IX in patients treated for Haemophilia or Christmas disease in the United Kingdom', *British Journal of Haematology*, 1974, 26, 313 [LIT.001.0099] at 0102

<sup>37</sup> Biggs, 'Haemophilia treatment in the United Kingdom from 1969 to 1974', *British Journal of Haematology*, 1977, 35, 487 [LIT.001.0159]

<sup>38</sup> Haemophilia Centre Directors' Annual Statistics for 1975, *British Journal of Haematology*, 1977, 36, 447 [SNB.001.7011]

<sup>39</sup> A 'unit' is defined relative to the material involved. A 'unit' of Factor VIII is arbitrarily defined as the amount of AHF activity present in 1 ml of normal male plasma: Buchholz, 'Blood Transfusion: Merits of Component Therapy', *The Journal of Pediatrics*, February 1974, 84/2, Page 165 [LIT.001.0141] Col 142

<sup>40</sup> FVIII concentrate

<sup>41</sup> Biggs, 'Haemophilia treatment in the United Kingdom from 1969 to 1974', *British Journal of Haematology*, 1977, 35, 487 [LIT.001.0159] at 0174

**19.35** The estimate was at the lower level in the MRC report. This series of reports by Dr Biggs and her colleagues reflects a more or less consistent application of a methodology developed by her team at Oxford. Individually, and in total, the reports show a movement towards a data-based assessment of demand that was not available previously to those planning the BPL and the PFC. As noted above, Mr Watt had a different view of total demand: he thought that demand could be higher. But the differences were not great in the overall scheme of things at this time.

**19.36** The comparison with the 1969 assessment is stark: by 1974, estimated use was over four times the use reported for 1969. Later papers showed dramatic growth in demand, reported generally in terms of international units, though falling short of the estimate of 40 million units within the period in question. By 1974, total demand had increased to 20,548,060 units of Factor VIII and 4,866,380 units of Factor IX (roughly equivalent to 300,000 blood donor units), amounts still far in excess of the 1969 estimate.<sup>42</sup> For 1975, the amounts increased to 24,886,218 units of Factor VIII, and 4,914,643 units of Factor IX.<sup>43</sup>

**19.37** It seems likely that a number of considerations affected the 1969 data. One matter affecting its reliability was exposed in the report prepared by Dr Biggs for the MRC in 1974, and repeated with reference to a later period in a report on behalf of the Haemophilia Reference Centre Directors published by Dr Biggs and Dr Rosemary Spooner in May 1978.<sup>44</sup> The 1978 report noted that data from 1974 implied that patients with haemophilia were attending hospitals which were not recognised as haemophilia centres under the designation scheme that had been in place since the mid-1950s. A survey was carried out. It disclosed a significant number of cases of treatment in hospitals that were not designated. The report observed that all severely affected patients would require frequent anti-haemophilic treatment each year, most of the moderately affected patients would require treatment two or three times a year, and that many of the mildly affected patients would require treatment at least once a year. The directors were concerned that large numbers of patients with Haemophilia A or B were not seen at a haemophilia centre to establish a diagnosis. In their opinion any patient who had a coagulation defect should be seen at a haemophilia centre for that purpose. To ensure a suitable supply of therapeutic material and the highest standard of treatment available, the care of these patients should also be coordinated by a haemophilia centre.

**19.38** The authors' primary concern was for the welfare of the patients. But the information required to prepare a valid projection of overall need for therapeutic material was deficient. That deficiency continued to be as significant in 1974 as it had been when assessing demand several years earlier.

**19.39** Other workers commented on factors that were creating increasing demand at about this time. Home treatment increased demand for factor concentrates in 1975 and 1976.<sup>45</sup> Dr Peter Jones and his colleagues at Newcastle examined data from all UK haemophilia centres and provided a picture of growth, from very early cases in 1960, and from the introduction of cryoprecipitate in 1964, but more particularly in 1975 and 1976. Over those two years, the number of patients on home treatment, or in training for home

<sup>42</sup> Ibid [LIT.001.0159] at 0165 and 0167

<sup>43</sup> Haemophilia Centre Directors' Annual Statistics for 1975, *British Journal of Haematology*, 1977, 36, 447 [SNB.001.7011]

<sup>44</sup> Biggs and Spooner, 'National survey of Haemophilia and Christmas disease patients in the United Kingdom', *The Lancet*, 27 May 1978, 1143–4 [LIT.001.0352]

<sup>45</sup> Jones *et al*, 'Haemophilia A home therapy in the United Kingdom 1975–6', *British Medical Journal*, 3 June 1978 [LIT.001.0258]

treatment, rose from 267 to 488. In addition, the directors of the centres estimated that 280 additional patients were awaiting entry to the scheme in 1975 and 241 in 1976. The products used included cryoprecipitate and factor concentrates, and the latter included a wide range of commercial products. Dr Jones and colleagues reported a significant rise in demand due to the number of patients involved; the variables in assessment of effective dosage; the use of prophylaxis; and the adequacy of supply. They commented that the demand in the UK as a whole could not have been met without recourse to commercial Factor VIII concentrates. About 55% of the blood product used for home treatment was imported, and in England and Wales necessarily so, because of the continued shortfall in production of NHS concentrate from voluntary donations.

**19.40** Dr Jones continued to promote the benefits of home therapy well after this period. In 1980, he edited a handbook for those involved in treatment, and for patients, that was published by Pitman: *Haemophilia Home Therapy*.<sup>46</sup> Home treatment was to continue to be a major element in total demand.

### The position in 1974 – the beginning of the reference period

**19.41** By 1974, the PFC was manufacturing a wide range of products: fibrinogen, human albumin, anti-vaccinia immunoglobulin, anti-D immunoglobulin, prothrombin complex (Factors II, VII, IX and X) concentrate, anti-tetanus and anti-rubella immunoglobulin. In 1974, production began of a new-generation intermediate-purity Factor VIII concentrate ('NY' Factor VIII). Manufacture of this range of products was impaired in 1974 and 1975 by the move to Liberton. Dr Peter Foster, who specialised in biochemical engineering and who was to play a major part in scientific developments at the PFC, joined the service in 1973. The new plant was in routine operation from 1976.

**19.42** Production targets and the scope of operations continued to be open for discussion. There was no concluded policy as to the extent of the facility's use, especially in relation to the processing of material from England and Wales. However, the lack of a formal policy at that time became more or less irrelevant. The Annual Report of the SNBTS for the year ended 31 March 1976 noted that the plant had been designed to accommodate material from England and that staff had been recruited and trained on the basis of shift-working.<sup>47</sup> But opposition from the trade unions, allied with demands relating to terms and conditions of employment which the employers found unacceptable, had made shift-working impracticable. In the result, the PFC could cope with Scottish needs on a day-staff only basis, but the absence of the other shifts decreased cost-effectiveness and precluded acceptance of plasma from furth of Scotland. At the beginning of the reference period, therefore, there was considerable doubt about the levels of demand that ought properly to be anticipated, and this necessarily affected the efficiency of planning of the production facilities required. Since the PFC had been conceived as one element in the total UK production capacity, its planning was directly affected.

**19.43** Some English plasma was dispatched to Edinburgh. On 11 April 1977, Mr Watt reported to the SNBTS that he held 10,000 litres of plasma from England, but did not have any arrangement in place for processing it.<sup>48</sup> By July, the quantity had increased to 20,000 litres. The minutes of a meeting of the SNBTS Directors on 12 July 1977 noted that a

<sup>46</sup> Jones, P., *Haemophilia Home Therapy*, 1980, Pitman, London.

<sup>47</sup> SNBTS Annual Report 1 April 1975–31 March 1976 [SNB.010.3921]

<sup>48</sup> Letter from Mr Watt to Miss Corrie, 11 April 1977 [SNB.002.1777]



system for handling English material that was acceptable both to BTS England and Wales and to the SNBTS would have to be evolved.<sup>49</sup> That had not been achieved by mid-1977.

**19.44** The issues remained unresolved by 17 January 1978, when again Mr Watt reported to the SNBTS Directors that the English plasma was still in store.<sup>50</sup> It was thought that it would require a plan drafted by the Joint Committee on Blood Products Production and agreed by Transfusion Directors north and south of the border to resolve the impasse. In the meantime, it was generally agreed that Scotland should secure its own supply of fractions before undertaking work for NBTs. Pending an agreement on shift-working Mr Watt felt he could process a limited amount of the plasma from the BPL on the basis of an extended working day, to ascertain the yield and establish costs. Directors agreed that he should do so, possibly devoting two weeks to fractionating English plasma only.

**19.45** The Joint Committee on Blood Products Production involving the Scottish service and that of England and Wales did not resolve these issues. In the event, it was decided that the PFC could deal with Scottish needs only, but could not take plasma from furth of Scotland. For the time being at least, the PFC would process Scottish plasma, and service the Scottish market alone. Arrangements were made for supplying Northern Ireland later.

**19.46** In retrospect, the final stages in the planning, commissioning, and initial use of the new PFC facility at Edinburgh therefore took place against the background of an underestimate of the demand for coagulation products in the UK generally, at a time when demand was increasing for a number of reasons, and without firm arrangements for the optimum use of the facilities planned for Scotland. The failure to take account of emerging demands related to new regimes such as home therapy and prophylaxis is understandable. In the initial planning stages of the PFC these treatment regimes would not have been developed as aspects of haemophilia practice. As discussed in Chapter 21, *Haemophilia Therapy – Use of Blood Products*, there was an element of reaction to the availability and importation of US concentrates that changed the pattern of demand. This came after the plants at the BPL and the PFC were built or in construction. And much of the latent demand for treatment could only be known when therapeutic materials became available for use.

**19.47** The result, however, was that for a considerable time Scottish premises were adequate and, with the processing plant required, coagulation products could be provided to meet the demands of clinicians in Scotland, while in England and Wales there were persistent deficiencies that had to be made good by commercial purchases.

### Self-sufficiency

**19.48** There had already been a political commitment to self-sufficiency, however. In December 1974, Dr David Owen MP, the UK Minister of State for Health, had announced exceptional government funding of £500,000 with the primary aim of making the NHS self-sufficient in blood products within two to three years, following recommendations by the World Health Organization (WHO).<sup>51</sup> The WHO reinforced its position in 1975.<sup>52</sup> The funding was to be used to provide the BPL in London with additional equipment

<sup>49</sup> Minutes of SNBTS Directors meeting, 12 July 1977 [SNB.002.1814] at 1816

<sup>50</sup> Minutes of SNBTS Directors meeting, 17 January 1978 [SGF.001.0341] at 0341–2

<sup>51</sup> Letter to Regional Administrators in England and Wales, 24 December 1974 [DHF.002.9393]

<sup>52</sup> WHO, Twenty-Eighth World Health Assembly, Geneva, 13–30 May 1975 WHA28.72 Utilization and supply of human blood and blood products [DHF.003.0764]

to process the increased quantities of plasma necessary to meet the rapidly increasing demands for clotting factors for treating haemophiliacs.

**19.49** So far as Scotland was concerned, it could not have been concluded at the beginning of the reference period that the country was or would be self-sufficient in Factor VIII blood products until the PFC was fully operational. The Annual Report of the SNBTS for the year ended 31 March 1976 reflects the developing position.<sup>53</sup> The commissioning of the PFC was almost complete, and full production to meet Scottish needs was said to be in sight, provided that appropriate supplies of plasma were forthcoming from the regions. As events were to unfold, it would be several years before the supply of plasma from the Scottish regions took up the PFC's production capacity.

**19.50** Progress towards self-sufficiency depended on policy decisions, and on raw material supplies to meet processing targets that were yet to be set and implemented. However, at this time there was a lack of confidence about the future. On 8 May 1975, the SNBTS and Haemophilia Directors met with SHHD officials.<sup>54</sup> Officials were conscious that, in advice given on replies to parliamentary questions, ministers were constantly being informed that, when the PFC was fully commissioned, long-term supplies of Factor VIII concentrate would be assured. It was observed that it was still not clear what the timetable was for the replacement of cryoprecipitate by concentrate: so long as there was significant use of cryoprecipitate, the full demand for concentrates would not be known, and the necessary full supply of plasma might not necessarily be available. The minutes of the meeting disclose little hard information, and expose wide-ranging doubts. No firm conclusions were reached on future demands. At the following meeting on 14 November 1975, there was little progress on demand. A study group was set up, convened by Major-General H.C. Jeffrey (National Medical Director of the SNBTS), and a pro-forma prepared for the collection of data.<sup>55</sup>

**19.51** More generally, there was explicit acknowledgement that Scotland was in part dependent on imported products prior to the full commissioning of the PFC. In England and Wales, central contracts for the purchase of commercial Factor VIII were held by the Department of Health from 1972–79.<sup>56</sup> On 11 June 1975, at a meeting of the SNBTS Directors, the procurement of commercial blood products was raised. It was noted that:

In response to a query from Dr Cash, General Jeffrey explained that SHHD had under urgent consideration the issue of whether commercially produced blood fractions which might be required should be purchased by the SNBTS or by Health Boards.<sup>57</sup>

**19.52** On 30 September 1975, at a subsequent meeting of the SNBTS Directors:

It was explained that, because of the comparatively minor nature of the problem, it should be left to Directors to purchase and distribute human blood products should this prove necessary. This was an ad hoc arrangement pending full commissioning of the PFC.<sup>58</sup>

<sup>53</sup> SNBTS Annual Report, 1 April 1975–31 March 1976 [SNB.010.3921]

<sup>54</sup> Minutes of meeting [SNB.001.4903]

<sup>55</sup> Minutes of meeting [SNB.001.4906]

<sup>56</sup> See briefing papers for Scottish Parliament Health Committee Meeting on 31 January 2006 [SNF.001.2449] at 2462

<sup>57</sup> Minutes of meeting [SNF.001.0001] at 0006

<sup>58</sup> Minutes of meeting [SGH.001.6135] at 6137

**19.53** Commercial purchases were not centralised in Scotland, and it was left to local health boards and their officers to purchase and distribute commercially produced blood fractions as required. This became a factor in relation to the assessment of total demand, and in particular, to the assessment of the production requirements at the PFC. In one of two 'World in Action' television programmes broadcast in or around the end of 1975, Mr John Watt stated that, with sufficient plasma supplies, the PFC, Edinburgh, could supply Factor VIII concentrate for about half of the needs of those with haemophilia in Britain.<sup>59</sup> However, its capacity was not fully utilised: the intention to process plasma from England was never realised. Mr Watt's interview caused concern. In a letter to the *British Medical Journal* dated 24 January 1976, Professor John Cash commented that the programme had created a misleading impression. He wrote:

Perhaps the most important misleading feature of the second television programme was the impression given that the recent and specific injection of £500,000 into the blood transfusion services will have worked its way through by mid-1977, and by that time the necessity to purchase further supplies of factor VIII concentrates will be eliminated. Our own experience indicates that this will not occur, not least because the present NHS production target for factor VIII concentrates is too low. What seems more certain, however, is that by mid-1977 we shall begin to understand that the problems are multifactorial, a good deal more complex than hitherto appreciated, and only partly related to the haemophiliac.<sup>60</sup>

**19.54** The failure to provide for total demand and the implied acceptance that the UK was heavily dependent on imported products were factors clearly acknowledged within the service throughout the UK. In the event, however, Scottish use of imported Factor VIII would prove to be relatively modest until about 1980.

### Demand levels re-assessed

**19.55** Professor Cash and Dr Mary Spencely discussed the issue of demand for Factor VIII products in Scotland in September 1976.<sup>61</sup> They expressed concern about forecasts based on Dr Biggs' research in 1974,<sup>62</sup> because of the wide range of values brought out. In their study in the south east of Scotland region based on treatment between 1961 and 1975, they had found a substantial increase in the donations required for Factor VIII production over the period. They had observed abrupt increases in demand in 1964, with the introduction of major reconstructive surgery. Subsequently, there were increases due to the gradual introduction of on-demand treatment; available to all patients. Demand increased from about 1300 donations in the period 1961–63, and reached a new plateau of about 2750 donations by 1970.

**19.56** Cash and Spencely suggested that a saturation level might have been reached. Like other commentators, they had not anticipated further changes in the pattern of demand, nor, ultimately, in the number of haemophilia patients with unmet needs. Furthermore, some of their data were specific to Edinburgh and south east of Scotland. Possible

<sup>59</sup> Transcript of 1975 World in Action programmes [PEN.013.1400] at 1421

<sup>60</sup> Cash, 'Commercial and NHS factor VIII concentrates', *British Medical Journal*, 24 January 1976, 221 [LIT.001.0245]

<sup>61</sup> Cash and Spencely, 'Haemophilia A and the blood transfusion service; a Scottish study', *British Medical Journal*, 18 September 1976 682 [LIT.001.0255]

<sup>62</sup> Biggs *et al*, 'Factor VIII concentrates made in the United Kingdom and the treatment of Haemophilia based on studies made during 1969–72', *British Journal of Haematology*, 1974; 27: 391 [PEN.016.0341]. (This is the published version of the typescript paper made available to the UK Haemophilia Directors meeting on 31 January 1974 – See paragraph 19.31 above.)

concerns about the approach adopted were set out in paragraphs 5.109 and 5.110 of the Preliminary Report. The suggestion that a level of saturation might have been reached remains an odd feature of the analysis. The success of factor therapy had to be reflected in an increase in life expectancy of haemophilia patients, and the concomitant extension of the term of treatment of the average haemophilia patient. One would have expected a rising trajectory even if all other factors had remained constant: treatment years per patient had to increase. As will appear, there was also the start of home treatment, and availability of imported products had already by 1975 found a response in demand for treatment of patients who had not been catered for previously.

**19.57** A further difficulty was that the paper depended on data peculiar to the region. No commercial products were used in south east Scotland over the period of the study. But there was extensive use of commercial products in Glasgow.<sup>63</sup> In the Glasgow and south west of Scotland region there was also extensive use of cryoprecipitate as the therapeutic product of choice. Apart from distinguishing the two regions' use of therapeutic materials, these two factors underline a basic issue over the definition of demand for NHS products generally. So long as haemophilia clinicians were free, in the exercise of their very considerable clinical autonomy, to elect for commercial products or for products other than concentrates in treating their patients, actual demand for NHS concentrates could never be relied on as a measure of total demand for therapeutic products generally. The position in Edinburgh and south-east Scotland over the period of study reflected the firm and apparently unwavering commitment of the then Haemophilia Director, Dr Howard Davies, to NHS material, much of it cryoprecipitate. That was not the position in Glasgow and south west Scotland, the largest region of the country. Imported material was making a significant contribution (over 90%) to the demand for Factor VIII concentrate in the period 1971–74. In both regions at that period there was significant use of cryoprecipitate, again reflecting the choices of the Haemophilia Directors at the time.

**19.58** The use of cryoprecipitate for the treatment of adults in the west of Scotland was reflected in the well-established pattern of production of cryoprecipitate in that region during the periods when successively Dr John Wallace and Dr Ruthven Mitchell were the SNBTS consultants in charge. Dr Davies in Edinburgh was also an advocate of cryoprecipitate use. Professor Cash and Dr Spencely based their calculations on the assumption that 70% of the therapeutic material used would be cryoprecipitate, reflecting product choice in the east of Scotland at the time. A material shift in haemophilia practice towards use of concentrate would necessarily depend on production capacity and the supply of raw material in the form of frozen plasma.

**19.59** The views set out by Cash and Spencely in this paper were clearly not accepted universally. In the paper, they commented at some length on the choice of therapeutic materials, and the efficiency of production of cryoprecipitate as against concentrate. But it is in the authors' estimation of demand that the paper is interesting for present purposes. They concluded that the Blood Transfusion Services should consider a production target of an average of 15,000 units of Factor VIII per patient per year with a total UK annual requirement of around 50 million units. Converting that into donations per million of population per year threw up a range of values from 15,000 to 20,000, with the qualification that the higher figure would rise further if the volume of fresh plasma obtained from each donation was reduced.

---

<sup>63</sup> See Chapter 23, *Viral Inactivation of Blood Products for Haemophilia Therapy up to 1985*

**19.60** At the date of the Cash and Spencely paper in September 1976, the authors believed that, following the commissioning of the PFC, the south east of Scotland was already self-sufficient in therapeutic Factor VIII products. But there remained considerable issues about the rest of Scotland. It was recognised that supplies of antihæmophilic factor (AHF) (concentrate) were limited: 'What supplies of AHF there are, should be reserved for outpatient use, while cryoprecipitate is used for inpatients'. The conclusion of the paper was:

In the meantime the blood transfusion services ought to look towards improving the quality of cryoprecipitate production and procedures for the procuring of bulk fresh plasma. The plasma fractionators should look towards technical developments that will lead to improved yields, the general hospital medical staff towards a dramatic increase in the use of red cell concentrates and packed red cells in preference to whole blood, and the staff of regional hæmophilia centres to the more economical and critical use of factor VIII concentrates. There is no evidence to suggest that the voluntary blood donor will not respond; indeed those in the regional blood transfusion centres know that quite the reverse is true.

**19.61** It is implicit in the proposals for restricted use that there would be deficiencies in supply if there was a significant change towards concentrate use. The authors advocated the use of packed red cells as a way of releasing more plasma for production. Apart from increases in the volume of plasma for processing, any deficiencies in domestic supplies of Factor VIII concentrate could only have been made up by the purchase of commercial products, which was already happening in the west of Scotland. Of possibly greater significance, so far as developing a strategy for self-sufficiency is concerned, is the clear message that there was no settled practice governing the choice of product for well-recognised categories of application. In particular, the factors identified as relevant to the choice of product were related to the economics of manufacture, and yield, predisposing the authors to recommend cryoprecipitate in preference to Factor VIII concentrates.

**19.62** An attempt to assess the resources for the adequate treatment of Scottish hæmophilia patients was set out in a paper prepared for a meeting of the SNBTS and Haemophilia Directors on 4 October 1976.<sup>64</sup> There were 436 registered hæmophilia patients. Their distribution across Scotland was: Glasgow 285, Edinburgh 95, Aberdeen 25, Dundee 17 and Inverness 14. Twenty to 22 of these required treatment three or four times a year. Eighty seven to 92 required more frequent therapy. The rest hardly ever required treatment or required it not more than twice a year. The data were not entirely reliable because of the practice of some patients of attending general hospitals. Factor VIII usage in the first six months of 1976 presented the following picture of the current position:<sup>65</sup>

	Aberdeen	Dundee	Edinburgh	Glasgow	Inverness
Cryoprecipitate as donations	467	121	5965	8829	154
PFC Factor VIII: vials	288	111	(307,700 units) 1231	1381	358
Commercial Factor VIII	0	0	0	(90,740 units)	0

<sup>64</sup> *Resources required for adequate treatment of Scottish Haemophiliacs* [SNB.001.4943]

<sup>65</sup> *Ibid* [SNB.001.4943] at 4944]

**19.63** There are obvious problems with the data. The inconsistent use of units of measurement is very confusing. An apparent problem is the absence of recorded use of commercial product outside Glasgow coupled with low use of PFC Factor VIII. Availability of the PFC concentrate at this period was affected by the transfer of production from the RIE to the new PFC. The data are not sufficiently specific to factor this into the assessment of the validity of the exercise. The impression given, as far as haemophilia treatment is concerned, is that at this time, as was clearly the case in Glasgow, most plasma was being retained locally for cryoprecipitate production, but the extent to which the disruption of the PFC supplies affected practice is unknown, and there remains a question whether the reports of commercial usage can be treated as wholly reliable.<sup>66</sup>

**19.64** Nevertheless, there is a marked difference between the Glasgow data for the first six months of 1976, and for the full year 1975 (as the PFC began to come on stream). For 1975, total cryoprecipitate of 26,616 donations and PFC Factor VIII of 1023 vials were recorded as used.<sup>67</sup> Superficially, the rate of use of PFC Factor VIII had more than doubled. The paper listed a number of topics for discussion which highlight concerns at the time over the assessment of total demand. These included the numbers of patients with haemophilia, moderate and severe, in the community; the amount of Factor VIII (cryoprecipitate and concentrate) required for each patient; the best use of resources; patients' lifestyles; and the follow-up and evaluation required. It was suggested that a national register might be justified. Two points warrant specific reference: the effect of home therapy on total consumption and, related to that, the approach to decision-making on suitability for home therapy; and the introduction of new surgical techniques likely to make heavy demands on resources over relatively short periods.

**19.65** The assessment of demand had begun to take into account factors that were to become significant within a short period. The context for the discussion had to take account of government policy to use blood from voluntary donations, in keeping with the WHO recommendations.<sup>68</sup>

**19.66** The minutes of the meeting on 4 October 1976 note that estimating requirements for Factor VIII had been causing concern at UK level.<sup>69</sup> The cost of maintaining a UK-wide register was said to be a 'practical obstacle' to implementation of that proposal. Two points were noted as being of particular concern: the increasing needs for clotting factor products as a child grew older, and the increasing prospects of longevity. The wider context was reflected in two paragraphs, the first of which (paragraph 7) said:

The primary need was seen as the provision of information to help on balancing use and requirements. Use would obviously increase if patients took up and were encouraged to take part in eg skiing or other outdoor pursuits. It was becoming increasingly apparent that haemophiliacs should be advised to live within the limits of their disability and in the more severe cases this could lead to them living a more sedentary life. While it was acknowledged that this is a difficult area, impinging as it did on the question of clinical freedom, it was thought to be a realistic approach.<sup>70</sup>

<sup>66</sup> The disruption due to the relocation of the PFC is discussed in Chapter 21, *Haemophilia Therapy – Use of Blood Products*, at paragraph 21.47

<sup>67</sup> 'Resources required for adequate treatment of Scottish Haemophiliacs' [SNB.001.4943] at 4944

<sup>68</sup> Ibid [SNB.001.4943] at 4945–4946

<sup>69</sup> Minutes of meeting [SGH.001.1320]

<sup>70</sup> Ibid [SGH.001.1320] at 1321

**19.67** The following paragraph (paragraph 8) proposed a UK-wide meeting with the Haemophilia Society with a view to discussing the use of the scarce resources available and other topics on a UK basis that might lead to the production of a register among other things. The importance of an agreed policy for Scotland with the support of clinicians in England and Wales was stressed.

**19.68** An exploratory meeting of Blood Transfusion Directors and Haemophilia Reference Centre Directors was held in Sheffield on 22 October 1976.<sup>71</sup> Dr Biggs and colleagues presented the data on need, estimated at 40 million units of freeze-dried Factor VIII. International data suggested a need for England, Wales and Northern Ireland of 36,481,890 units, and for Scotland 3,741,917 units, giving 40,223,807 units in total. These figures presented a picture of spurious arithmetical accuracy, but they agreed fairly well with estimates based on UK data. They anticipated a shift from the use of cryoprecipitate to the use of concentrates, noting that five commercial companies were licensed to supply very satisfactory products which offered convenience in use.

**19.69** In discussion, Dr Biggs is reported to have commented that 40 million units was too low an estimate for the future because use was increasing. Professor Cash agreed. He was alarmed by the games and sporting risks now covered and the implications for demand: he thought it was morally wrong to commit such large amounts of material.<sup>72</sup> Dr Wallace pressed for a common policy, but he too reflected the view that haemophilia patients should live within the limits of their disabilities.<sup>73</sup> In contrast to the views of these suppliers of clotting factor products, a representative of the 'consumers', the Haemophilia Centre Director Dr Jones, was of a different view, encouraging normal sporting activities such as football: if patients sat around they would need more therapy.<sup>74</sup> He proposed a target of 42.4 million units. Following extensive discussion, the final proposal, from Professor Colin Prentice, was that the current target should be 40 million units, rising to 50 million units over the following three years.<sup>75</sup> There were doubts about the usefulness of the exercise.<sup>76</sup> The fractionators were not in agreement about the criteria to apply and about the practical implications of working to the targets proposed. At least some haemophilia directors were apparently not according priority to the goal of UK self-sufficiency in blood products, particularly Factor VIII concentrates, and appear to have been content to continue to use increasing amounts of imported products rather than their domestic counterparts.

**19.70** At a meeting of the SNBTS Directors on 26 October 1976, in discussing the supply of Factor VIII concentrates, it was noted that, in Scotland as in England and Wales, there was still a long way to go towards setting ultimate targets for the production and use of Factor VIII products, though Scotland's problem was smaller than in England and Wales.<sup>77</sup> It was agreed that a firm attempt should be made at the meeting of the Haemophilia Directors planned for 24 January 1977 to set interim Scottish targets.

<sup>71</sup> The full list of participants sets out the major players in the field (other than DHSS, SHHD and Northern Ireland government officials, who had not been invited) at this period. Minutes of meeting [SNB.001.4953]

<sup>72</sup> Minutes of meeting [SNB.001.4953] at 4954

<sup>73</sup> Ibid [SNB.001.4953] at 4954

<sup>74</sup> Ibid [SNB.001.4953] at 4954–55

<sup>75</sup> Ibid [SNB.001.4953] at 4956

<sup>76</sup> Dr Wallace's report to SHHD dated 25 October 1976 [SNB.001.4960]; and Mr Watt's letter to Dr McIntyre of SHHD dated 29 October 1976 [SNB.001.4958]

<sup>77</sup> Minutes of Meeting [SGH.001.6042]

**19.71** The practitioners, in England and Wales as well as Scotland, had not resolved targets. In their paper, Professor Cash and Dr Spencely had not resolved the issue of methodology to the satisfaction of UK colleagues. Estimates of demand remained uncertain. The paper's projection of total UK demand at 50 million units exceeded Dr Biggs' estimate of 40 million, but reflected the longer-term projection for the UK as a whole. But each projection exceeded by a considerable margin the production targets on which the two major facilities in England and Scotland were planned, and constructed or developed at this time. There was little obvious collaboration between the two groups – the blood transfusionists and fractionators interested in production on the one hand, and the haemophilia clinicians preoccupied with consumption on the other. Neither group was successful in estimating demand and regulating both production and consumption in the period between 1972 and 1981 with much accuracy. A casualty of this overall lack of collaboration was the idea, or at least the practicality, of UK self-sufficiency during this period. That would become a matter of regret.

**19.72** In the event, in the UK as a whole, there was an emerging shortfall in production of growing significance. The comparative positions in Scotland and England are set out in Chapter 21, *Haemophilia Therapy – Use of Blood Products*. In retrospect it is clear that there was a material failure, at the beginning of the reference period, in the planning of production capacity to anticipate the actual emerging levels of demand; and a correlative failure to provide production facilities in the UK as a whole with the capacity to service domestic requirements. The positions in the two parts of the UK differed. In England and Wales, there was a significant shortfall in production capacity which, in absolute terms, made it impossible in the 1970s and early 1980s to produce enough material to meet domestic demand. In Scotland, the facilities were sufficient in scale, or at least flexible enough to adapt to meet growing demand, until the end of the 1970s. However, plasma supplies, yield of concentrate, out-of-date data on use of Factor VIII, and failure to appreciate the impact on total demand of changing haemophilia clinical practice all contributed to the problem there, as in the UK as a whole.

**19.73** Dr Biggs wrote a letter to *The Lancet* of 29 June 1974. It is quoted in the Preliminary Report, but captures the atmosphere at the time, and is worth repeating:

Those who treat haemophilic patients in the UK have in the past of necessity tolerated the chronic undertreatment of their patients and have put much time and effort into spreading the inadequate amounts of therapeutic material thinly so that deprivation should be least damaging. Essential but non-urgent operations have been postponed and are still being postponed. Economy has also been achieved by calculating the dose for each lesion for every patient to give the absolute minimum dose. In addition patients have not been put onto home therapy who would greatly benefit by this treatment .... There is, in fact, evidence that 90% of haemophilic patients in the UK receive less (and in some cases much less) than optimum treatment for their complaint. The consequences of this undertreatment include subjecting the patients to unnecessary, painful and destructive bleeding into joints and muscles. Ancillary effects of undertreatment include loss of educational time and inability to hold continuous employment.<sup>78</sup>

<sup>78</sup> Biggs, 'Supply of blood-clotting-factor VIII for treatment of haemophilia', *The Lancet*, 29 June 1974 [PEN.016.0440]; Preliminary Report, paragraph 5.122



**19.74** Dr Biggs proceeded to make an emotional appeal for the purchase and use of stocks of 'good quality human Factor VIII' readily available from commercial companies that were by then licensed to make supplies in this country, and dismissed, rather contemptuously, all arguments based on financial constraints. She concluded:

Whatever solutions there may be for problems of this sort in general, some immediate solution should be found for the ridiculous impasse of large available stocks of therapeutic materials locked up in stores because no-one will buy them and, on the other hand, patients in dire need of this same material.<sup>79</sup>

**19.75** At least so far as England and Wales were concerned, her comments underline the deficiencies in domestic production. As will be seen in Chapter 21, *Haemophilia Therapy – Use of Blood Products*, the purse strings were loosened and imported materials were used in large quantities as time passed. The description of the commercial concentrates in stock as 'good quality human Factor VIII' would be challenged within the following decade as the likely impact of non-A, non-B Hepatitis (NANB Hepatitis) came to be appreciated.

**19.76** It appears to be clear that the problems that preoccupied the medical profession and the technologists associated with blood product production in the mid- to late-1970s related to production capacity, cost, and adequacy of supply of therapeutic materials for appropriate treatment of the patient population. Awareness of NANB Hepatitis (later identified as Hepatitis C) became an emerging issue: AIDS had not yet been reported. As the 1980s progressed, the emphasis was to change dramatically.

### The final chapter

**19.77** The evolving history of blood product development in Scotland will be traced elsewhere in this report. At this stage, however, it is appropriate to define the end stage of the production of concentrates in Scotland, since that, incidentally, put an end finally to the pursuit of self-sufficiency and removed the scope for controversy over production targets.

**19.78** In 1998 the fractionation of plasma from UK donors was banned as a precaution against the risk that variant Creutzfeldt-Jakob disease (vCJD) might be transmitted by blood products. At UK level, precautionary concerns around vCJD risk drove the decision. Historically, sporadic vCJD was not thought to be transmissible by blood components or plasma products. When vCJD was first described in about 1996, it was recognised that it was a different kind of disease and there was concern that it might prove transmissible. The risk that, because of the pooling effect, one infected individual donor might contaminate a whole batch of products influenced the UK government to take the view that it would be preferable to move away from UK plasma. There was speculation that potentially vast numbers of people might develop the disease. Though that never came to pass, it was thought to be possible at the time.<sup>80</sup>

**19.79** It was assumed, correctly, that the risk of transmission of vCJD from blood collected in Britain was greater than the risk in source countries from which substitute supplies might be found and in which bovine spongiform encephalopathy (BSE), and hence vCJD, had not occurred. BSE was predominantly a UK-centred outbreak, with some cases in Ireland and Western Europe. Of approximately 220 to 230 cases of clinical vCJD, probably

<sup>79</sup> Biggs, 'Supply of blood-clotting-factor VIII for treatment of haemophilia', *The Lancet*, 29 June 1974 [PEN.016.0440]

<sup>80</sup> Professor Turner – Day 7, page 35

about 180 to 190 were in the UK. There had been two or three cases in the USA of vCJD but they were mainly in individuals who spent time in other countries, including the UK.<sup>81</sup>

**19.80** In the aftermath of the ban on UK plasma, it was announced in October 1998 that the SNBTS was to undergo a major modernisation programme.<sup>82</sup> Processing and testing functions were terminated at all five Blood Transfusion Centres and concentrated on two sites, Edinburgh and Gartnavel (replacing the Carluke Centre). The two national laboratories were to be developed and equipped to deal with new blood tests and processing technologies for the whole of Scotland. There was to be national coordination of the collection of blood and of blood stocks. It was also indicated that additional funds were to be allocated, among other things, for 'sourcing of non-UK plasma', presumably an indirect allusion to the risks potentially associated with vCJD in the domestic blood supply.

**19.81** There were factors other than vCJD, however, that affected the PFC's ability to continue functioning as a manufacturing facility. European regulatory authorities had pressed for additional viral inactivation following transmission of hepatitis and HIV during 1984 in Germany. These required changes in manufacturing processes and fresh clinical trials to obtain regulatory approval. New equipment was required. There was a decision to fund recombinant coagulation factor concentrates. At the same time, demand for human albumin fell following reports of adverse consequences for recipients.<sup>83</sup> These factors pointed to a further move from the PFC's established range of activities.

**19.82** While red cell and platelet production continued in Scotland; domestic blood, collected in Scotland (and throughout the UK), was no longer used for the production of plasma fractions.<sup>84</sup> As a result, the SNBTS had to import plasma or obtain it from commercial (non-UK) sources. Plasma was sourced commercially after 1999. That allowed fractionation to continue for a time.

**19.83** The next significant change in the scope of the operations of the SNBTS was prompted by the implications of the first documented clinical case of transmission of vCJD early in 2004.<sup>85</sup> The vCJD threat, together with the move away from human blood clotting factors to synthetic alternatives, contributed to the decision in June 2006 to accept the recommendations of National Health Services Scotland that it was no longer viable to operate the PFC as part of the NHS.<sup>86</sup> At the time the decision was taken production at the PFC had already been suspended due to concerns about quality assurance.<sup>87</sup> The economics of continuing production in Edinburgh influenced the decision. The PFC closed in 2008 after attempts to find a private buyer failed.

**19.84** So far as the PFC was concerned, there was a practical risk of continually recalling batches of product. The risk of recalling product carried a threat of shortages. In general terms, the PFC had become one of the smallest fractionators in the world, and was particularly small compared to large corporate commercial fractionators. But there was the added consideration that, with the end of an era of effectively free supply of plasma, the

<sup>81</sup> Professor Turner – Day 7, pages 36–37

<sup>82</sup> Scottish Office press notice, *Improvements to blood transfusion service announced*, 28 October 1998 [SGH.003.8451]

<sup>83</sup> Foster, 'Plasma fractionation in Scotland', *Blood Letter*, Spring 2008 [PEN.017.2468] at 2471

<sup>84</sup> Professor Turner – Day 7, page 33

<sup>85</sup> Professor Turner – Day 7, pages 18–19

<sup>86</sup> Scottish Government press notice, *Changes in blood processing activities*, 26 June 2006, Available: <http://www.scotland.gov.uk/News/Releases/2006/06/26131748>. Last accessed 15 Oct 2012

<sup>87</sup> *Ibid*

balance of economics changed in favour of purchase of products from the international commercial community.<sup>88</sup>

**19.85** Fresh frozen plasma for clinical use is still imported for two groups of patients. One group comprises children up to the age of 16 years. For that group, plasma has hitherto been imported from the USA but in the future will be imported from Austria. That product receives methylene blue treatment, a pathogen reduction treatment which can be applied to plasma. The second group comprises patients undergoing plasma exchange, particularly for a condition called Thrombotic thrombocytopenic purpura (TTP or *Moschcowitz syndrome*). Methylene blue treated plasma is thought not to be the best treatment for them. So pharmaceutically cooled plasma, called 'octoplas', is used. It is again manufactured from European plasma. Albumin and immunoglobulins are also supplied commercially.<sup>89</sup> However, for all practical purposes, fractionation, as the definitive manufacturing process, had ceased before the decision to place the facility on the market had been taken.

**19.86** With the closure of the PFC, Scotland lost many of the skill sets associated with fractionation. The technological developments that have followed since the millennium are largely irrelevant to practice in Scotland. The BPL, the English fractionation centre, remains open, but uses imported plasma.<sup>90</sup> The English Service has a plasma collection facility in New England, USA, from which it obtains supplies for the NHS.<sup>91</sup>

## Discussion and conclusions

**19.87** The planning and construction of the extended facility at the BPL, and the new PFC, took place at a time when there was already increasing demand generated by some known factors, for example, use of clotting factor products in major reconstructive surgery and the gradual introduction of on-demand treatment, available to all patients, in the period 1961–64. In 1976, changing policy relating to patients' lifestyles, moving from maintaining a protective environment towards encouraging sport and other potentially dangerous activities, had an impact on demand. At the meeting of Blood Transfusion Directors and Haemophilia Reference Centre Directors held in Sheffield on 22 October 1976 the views of haemophilia clinicians were made explicit: normal sporting activities such as football should be encouraged. The increasing needs for clotting factor products as a child grew older, and the increasing prospects of longevity required to be taken into account. By the autumn of 1976, also, it was appreciated that home therapy would be likely to increase demand. And it was anticipated that the introduction of new surgical techniques was likely to make further heavy demands on resources over relatively short periods.

**19.88** Overall there was a changing environment in which haemophilia care would come to demand increasing quantities of therapeutic materials beyond those anticipated in the planning of production facilities. And there was the beginning of an inexorable shift towards concentrates as the product of choice in haemophilia therapy, which would become clear as the use of Factor VIII in particular grew throughout the 1970s and early 1980s.

---

<sup>88</sup> Professor Turner – Day 7, page 36

<sup>89</sup> Ibid pages 33–34

<sup>90</sup> Ibid pages 33–34

<sup>91</sup> Dr Norfolk – Day 7, page 79

**19.89** Haemophilia clinicians' treatment policies, and the encouragement of patients to live a 'normal' lifestyle, associated with clinical independence that extended to the selection of therapeutic products thought best to suit the requirements of the individual patient, were factors beginning to affect the demand for concentrates. The lack of a centralised purchasing system for commercial products meant that purchases could be made without central monitoring. As will appear from Chapter 21, *Haemophilia Therapy – Use of Blood Products*, returns were made to UKHCDO of the use of commercial products. But in the absence of a haemophilia register there was not a comprehensive record of all demand.

**19.90** Unless the Blood Transfusion Services and the fractionators had full knowledge of the total demand for the current groups of therapeutic products required for effective treatment of patients, and of the proportion of that demand likely to be met by commercial purchases, effective planning of the production targets and production plant and processes required by the fractionation centres was unlikely to be achieved.

**19.91** Since the commercial market to which Dr Biggs referred was largely serviced by foreign pharmaceutical companies, clinical independence and a policy of national self-sufficiency in blood products were bound to come into conflict.

**19.92** While that would have been the case in a static market environment, the added elements of technological change and changing patterns of demand would inevitably add to the complexity of the problem of servicing the market.

**19.93** Tensions between fractionators and clinicians were also inevitable unless there was a properly coordinated policy and management framework that was effective to resolve issues and implement solutions to problems as they emerged and were identified. After full commissioning of the PFC and until the 1980s; Scottish production of concentrates largely met the demands of haemophilia clinicians for NHS factor products. However, total demand for NHS products was always lower than total demand overall, since commercial purchases reflected clinicians' preferences that involved choices that were independent of the availability of the domestic product. In the longer term, if true self-sufficiency were to be achieved and maintained, additional capital investment would have been required.

**19.94** In the circumstances, it is somewhat surprising that Scottish needs were as well catered for as, in the event, they proved to be. The SNBTS's ability to meet actual demand for therapeutic products from domestic sources was sustained from 1975–76 to 1981–82, and, with the exception of the two years 1978–79 and 1979–80, when demand for clinical use exceeded the PFC's output, available supplies of PFC Factor VIII concentrate exceeded demand for concentrate estimated at average UK rates.<sup>92</sup> This outcome, however, was a reflection of the failure at UK level to realise the policy objectives formulated at the planning of the production facilities in England and Scotland. If the PFC at Liberton had been called on to meet the demands of a significant part of northern England, Scotland's domestic supplies of Factor VIII concentrate would have fallen short of demand.

---

<sup>92</sup> Chapter 21, *Haemophilia Therapy – Use of Blood Products*, at paragraphs 21.62 to 21.65

## CHAPTER 20

### HAEMOPHILIA THERAPY – THE PERIOD UP TO THE EARLY 1980s

**20.1** So far as is relevant to the Terms of Reference, the early history of the administrative and management structures set up for the provision of blood services in Scotland is discussed in Chapter 17, *Blood and Blood Products Management*. Collection procedures and the provision of manufacturing facilities are discussed in Chapter 18, *Collection of Blood – General*, and Chapter 19, *Production of Blood Products – Facilities*. The use of blood products in haemophilia therapy is discussed in Chapters 21, *Haemophilia Therapy – Use of Blood Products*, and 22, *Haemophilia Therapy – Use of Blood Products 1985–1987*. These are all inter-related aspects of the background against which products came to be in use that were associated with the transmission of hepatitis and HIV. This chapter deals with the development of the products in Scotland that were manufactured, prescribed and used in the material period when patients were at risk of infection.

**20.2** The arrival of commercial concentrates in 1973 changed market conditions, and had a significant impact on the approach of the public sector producers in the UK as a whole to the production and distribution of NHS products. Coincidentally, plasma fractionation in Scotland was about to undergo very significant change with the opening of the new Protein Fractionation Centre (PFC) in Edinburgh.

**20.3** This chapter deals with developments in technology up to 1982–83. Up to that point the risk of infection, so far as it was understood, was of transmission of hepatitis, first Hepatitis B and then non-A, non-B Hepatitis (NANB Hepatitis). After that point, the reports of AIDS in haemophilia patients treated with blood products, and with no other risk factors for AIDS, brought about a significant change in the approach to factor concentrate therapy in the treatment of haemophilia. It is appropriate to deal with the periods separately. The focus in this chapter is on the development of early blood products, and, so far as related to that, the steps taken to meet demand for products for clinical use. The historical context is of some importance.

#### Origins

**20.4** The process of separation of whole blood into components for use, or further processing, already had a long history by the start of the reference period, reflecting the interaction of developing medical knowledge and technological progress. Blood is a complex mixture, including red cells, white cells and platelets, together with plasma which contains proteins, sugars, fats and a number of other smaller components such as hormones. The primary stage procedure of separation of whole blood into red cells, buffy coat (which contains white cells and platelets), and plasma depends particularly on the density differences between the corpuscular components and plasma.<sup>1</sup> Centrifugation of blood results in layering of components according to their density.

**20.5** From an early period, centrifugation was routinely performed at transfusion centres.<sup>2</sup> Initially, storage, whether of whole blood or blood components, was hampered by the coagulation that inevitably follows collection of blood from the body. Once the collection procedure begins, the blood is removed from the body's natural metabolic sustaining

<sup>1</sup> Harris, JR. *Blood Separation and Plasma Fractionation*, 1991, Wiley, New York, page 49

<sup>2</sup> *Ibid* page 6

environment, cools from body temperature, and is exposed to foreign substances.<sup>3</sup> The effective and efficient collection and storage of blood became the focus of technological research and development. Early in the twentieth century, it was discovered that various salts, and in particular citrates, in an unphysiological preservative anticoagulant solution, could maintain the fluidity of blood stored in containers. Citrate-based anticoagulants, usually with the addition of sugar, and heparin anticoagulants were developed progressively thereafter.<sup>4</sup> The blood collection procedures had to be rapid to avoid coagulation in the collection line. And the addition of the anticoagulant solution had to be prompt to prevent the development of foci of coagulation in the collection pack. Sterile disposable plastic pack assemblies introduced in the 1950s to replace glass bottles in the collection of blood donations provided for the easy introduction of the appropriate anticoagulant solution.<sup>5</sup> Once bagged, the material had to be stored at the appropriate temperature, depending on the purpose for which the components were required.<sup>6</sup> Centrifugation of the blood in plastic bags later provided the starting materials for further processing.<sup>7</sup>

**20.6** Three constituents of plasma were to become material to the development of therapeutic products: (i) the clotting factors, including fibrinogen and Factors VIII and IX; (ii) albumin, a normal protein in the blood which has oncotic properties and acts as a carrier protein for other substances; and, importantly, (though not directly relevant to the Terms of Reference) (iii) immunoglobulins (Ig), needed to boost antibodies in the blood of hypogammaglobulinemia patients, or patients who have suffered a needle stick injury, for example, to help fight off viral infections.<sup>8</sup>

**20.7** Refrigerated plasma was used clinically at or near the point of collection. Scientific developments in cryobiology enabled the storage of components for periods far greater than the point at which degradation would have occurred naturally in refrigerated materials. Typically, and with limited exceptions, plasma donations that were not required for immediate local clinical application were cooled rapidly and frozen. Fresh frozen plasma was retained for therapeutic application. Later, outdated stock was used for further processing. But at this early stage, it was used in the form in which it was separated immediately after the point of collection.

**20.8** It is important to note that plasma, fresh or fresh frozen, was simply a component of the donor's blood as collected, untreated and unprocessed. It inevitably carried with it all of the proteins, including virus particles, circulating in the donor's blood. The risk of transmission of virus infection reflected the prevalence of infection in the donor population, unaffected by the processes by which it was extracted.

### Early developments in process technology

**20.9** Early technological developments did little to change that risk. Plasma filtration, introduced in August 1941, dealt with bacterial contamination.<sup>9</sup> Freeze-drying, introduced at the Royal Infirmary of Edinburgh (RIE) in 1943, made plasma available as a powdered product that could be re-constituted at the point of use.<sup>10</sup> The technology was to be

<sup>3</sup> Ibid pages 48–49

<sup>4</sup> Ibid pages 28 and 44

<sup>5</sup> Ibid page 49

<sup>6</sup> Ibid page 44

<sup>7</sup> Ibid page xi

<sup>8</sup> Dr Cuthbertson – Day 46, pages 2–3

<sup>9</sup> See Chapter 17, *Blood and Blood Products Management*, paragraph 17.9

<sup>10</sup> Ibid paragraph 17.10

important in the development of factor concentrates, but in isolation did not alter the risk of transmission of infection.

**20.10** Efforts to produce factor concentrates began in the 1950s and progressed during the 1960s.<sup>11</sup> Before the reference period two procedures were developed in relation to the processing of plasma that became significant: fractionation and the preparation of cryoprecipitate. Two scientists achieved prominence for developing the fractionation technology applied in isolating specific proteins from blood plasma for clinical application, Professor Edwin J Cohn, a professor of biological chemistry at Harvard University Medical School, and Professor RA Keckwick of London. Both before and during the reference period Scottish scientists followed the Cohn methodology as it was developed from time to time, and this chapter therefore describes that methodology and its derivatives.

**20.11** The processes adopted in fractionating plasma reflect in part the complexity of blood. The components of blood do not withstand heating, for example, to a common degree. Red cells are contained within a membrane that starts to disrupt at about 40°C, and the components then clot. Platelets and white cells are similarly susceptible to temperature increases. The fluid component of blood – the plasma proteins, fats and sugars – can be heated, but still if heated together are subject to denaturation: they fall apart. Clotting begins, but at different temperature ranges from the cellular components. It is not possible to treat whole blood with heat. The characteristics of each component require to be taken into account separately in developing a heat treatment strategy.<sup>12</sup>

**20.12** The manufacture of blood concentrates depends on the chemical and physical characteristics of proteins contained in blood plasma. Plasma proteins vary in solubility when exposed to differential conditions of pH, ethanol concentration, temperature, ionic strength, and protein concentration. Professor Cohn and his colleagues showed that plasma proteins could be separated and partially purified in a reaction medium in which hydrogen ion concentration, ionic strength, temperature, protein concentration, and the amount of added ethanol were all carefully controlled.<sup>13</sup> A series of fractionation steps was devised for the major biological categories of plasma proteins: these were partitioned as precipitates or supernatants after each manipulative stage.

**20.13** The method was known as cold ethanol fractionation. Cohn fractionation exploited the physical changes induced in the frozen plasma by thawing under controlled conditions. When frozen plasma was immersed in a water bath at 4–6°C, thawing produced a liquid component (the supernatant) which could be extracted, leaving an illiquid residue. The Cohn process resulted in five stages of precipitation, the plasma ‘fractions’, which produced a range of derivatives for clinical application. Fraction I contained fibrinogen and antihæmophilic globulin (AHG, later known as Factor VIII), which was used to treat hæmophilia, Fraction III contained most of the lipid bearing  $\beta$ -globulins, and Fraction V contained albumin, which was used as a plasma substitute.<sup>14</sup> The plasma fractions were then removed by filtration or centrifugation.<sup>15</sup>

<sup>11</sup> Kasper et al, ‘Recent evolution of clotting factor concentrates for hemophilia A and B’, *Transfusion*, 1993; 33:422–434 [SGH.002.1947] at 1947

<sup>12</sup> Professor van Aken – Day 47, pages 3–5

<sup>13</sup> Cohn et al, ‘Preparation and properties of serum and plasma proteins. IV. A system for the separation into fractions of the protein and lipoprotein components of biological tissues and fluids’, *Journal of the American Chemical Society*, March 1946; 68:459 [LIT.001.0984]

<sup>14</sup> See Dr Foster’s paper, ‘Self Sufficiency and the Supply of Blood Products in Scotland’ [PEN.013.1125] at 1134 and Dr Foster – Day 22, pages 15–16

<sup>15</sup> Professor Van Aken – Day 2, pages 24–25. For a flow diagram of the process see: Watt et al, ‘New Developments in Large-scale plasma fractionation’, *PROC. R.S.E. (B)*, 71, (Supplement), 3, 1971/72 [PEN.002.0538] at 0539

**20.14** With later discoveries concerning the various clinical states in which deficiency in one or other of the blood constituents was the causative pathological abnormality in patients, the possibilities of specific remedial therapy became evident. The development of the Cohn fractionation scheme, which demonstrated that plasma could be split into various different components (each of which had different clinical properties), provided the basis for manufacture of a wide range of human blood products.<sup>16</sup> Process technology developed to exploit these characteristics of plasma.

**20.15** In the period between 1940 and the reference period of this Inquiry, scientists pioneered the use of a range of chemical additives during the manufacturing process which modified the Cohn ethanol fractionation procedure, resulting in Factor VIII concentrates of varying purity, a function of the removal of other proteins such as fibrinogen and fibronectin from the original Fraction I. By 1970, depending on the chemical agent introduced, low purity, intermediate purity, high purity and very high purity concentrates of Factor VIII could be produced, although the composition and structure of Factor VIII were not then known.<sup>17</sup>

**20.16** By 1972, the Cohn fractionation process had undergone many modifications. So far as is material for the purposes of this Report, it had been discovered at a very early stage in Cohn's work that Fraction I contained fibrinogen and AHG. But alcohol precipitation alone did not provide the range, quantity and purity of concentrates of coagulation factors that scientific research was making available for clinical application.<sup>18</sup>

**20.17** Professor Alan Johnson of New York, with Dr Margaret Karpatkin and Dr Jack Newman published a method for large-scale production of concentrates in 1969.<sup>19</sup> A further paper on the method was published in 1971.<sup>20</sup> It came to be known as the 'Newman' method. The supernatant plasma from which precipitates had been prepared using this technology was a source of Factor IX.<sup>21</sup> The Newman method was to become the basis of the processes for the production of protein factor concentrates adopted in Edinburgh.<sup>22</sup>

**20.18** Professor Johnson's 1971 paper described methods for the production of Factor VIII concentrates of intermediate and high purity. The paper traced the developments in technology based on increasingly sophisticated precipitation methods using chemical additives. They had published, in 1966 and later years, papers describing methods of producing clinically effective intermediate purity Factor VIII concentrate by simultaneous ethanol- and cryo-precipitation of Factor VIII from melting fresh-frozen plasma and adsorption of Factors II, VII, IX and X from the precipitate. The step forward in the 1971 paper was the introduction of polyethylene glycol (PEG) in the precipitation of intermediate purity concentrate, resulting in a concentrate purified 125 to 350-fold which was effective in the treatment of haemophilia patients. The technology could be adapted to large-scale production. The paper gave wide circulation to the methodologies involved.<sup>23</sup>

<sup>16</sup> Harris, JR. *Blood Separation and Plasma Fractionation*, 1991, Wiley, New York, page 45

<sup>17</sup> Preliminary Report, paragraph 1.43

<sup>18</sup> Watt et al, 'New Developments in Large-scale plasma fractionation', *PROC. R.S.E. (B)*, 71, (Supplement), 3, 1971/72 [PEN.002.0538] at 0541

<sup>19</sup> Johnson, Karpatkin and Newman, 'Preparation of and clinical experiences with antihemophilic factor concentrates', 1969; *Thrombosis et diathesis haemorrhagica*, (Supplement), 35:49 [LIT.001.4432]

<sup>20</sup> Newman et al, 'Methods for the Production of Clinically Effective Intermediate- and High-Purity Factor VIII Concentrates', *British Journal of Haematology*, 1971; 21:1 [SGF.001.1913]

<sup>21</sup> Douglas AS, 'Plasma Coagulation Factors', *PROC. R.S.E. (B)*, 71, (Supplement), 7, 1972/73 [PEN.002.0575]

<sup>22</sup> Foster PR and McIntosh RV, *The development of hepatitis-safe Factor VIII Concentrate by the Scottish National Blood Transfusion Service*, SNBTS, 9 December 1999 [SNB.001.6647]

<sup>23</sup> Preliminary Report, paragraph 1.44



**20.19** The Cohn/Newman method was used throughout the USA and in parts of Europe.

**20.20** Viewed as a whole, the method produced progressively depleted plasma by extracting intermediate materials, in each case a solid, suitable for the specified final products, and a liquid supernatant.<sup>24</sup> At the end stage of the original Cohn process a residue was left from the progressive thawing of frozen plasma, and the adsorption of proteins from the supernatant. The residue was slow to re-dissolve, and was initially discarded.<sup>25</sup>

**20.21** In 1959, before the refinements to the Cohn methodology described above had been introduced, Dr Judith Pool and her US colleagues had discovered that the residue left by Cohn fractionation, which remained at low temperature after drawing off the liquid produced in the thawing process, contained a high concentration of fibrinogen and Factor VIII, antihæmophilic activity. The residue also contained von Willebrand's Factor and other proteins, including fibronectin.<sup>26</sup> In 1964, Dr Pool described a method of producing these concentrated factors from plasma by freezing which was quite independent of the need for Cohn fractionation.<sup>27</sup> This was followed in 1965 by the publication by Pool and Shannon of further developments in the technology.<sup>28</sup> The product was named cryoprecipitate.

**20.22** The process devised by Dr Pool and her colleagues separated plasma from the red cells in whole blood donations by centrifugation at 4°C as soon as possible after collection, in the normal way, using standard compartmented plastic bags. The tubing connecting the compartments of the bag was clamped. The satellite bag containing the plasma was fast frozen. The whole bag was then refrigerated for cold-thawing of the frozen plasma. When thawed to only a few degrees above zero, and typically to 4°C, fibrinogen precipitated as a 'sludge' containing much of the Factor VIII content of the plasma.<sup>29</sup> The temporary clamps were removed, and the supernatant plasma was allowed to return to the red cell bag. The bags were separated, and the cryoprecipitate frozen for storage pending use. The process did not produce mutually exclusive components. Red cells used in clinical practice contained very small amounts of plasma. Platelets were suspended in plasma. Each had the potential to transmit infection.<sup>30</sup> However, the Pool and Shannon method produced a cryoprecipitate that was high in Factor VIII content, and that was stable and soluble.<sup>31</sup> This provided a relatively purified form of Factor VIII for hæmophilia therapy. Attempts had been made to isolate Factor VIII for clinical use in the treatment of hæmophilia in the 1930s.<sup>32</sup> But only now was there a relatively straightforward and effective procedure.

**20.23** Cryoprecipitation of Factor VIII from single units of fresh-frozen plasma was viewed as a simple, practical procedure that could be carried out by any blood bank.<sup>33</sup> It was used by blood transfusion centres in many countries and throughout Scotland. The single

<sup>24</sup> Dr Foster – Day 41, page 24

<sup>25</sup> Watt et al, 'New developments in large-scale plasma fractionation', *PROC. R.S.E. (B)*, 71, (Supplement), 3, 1971/72 [PEN.002.0538] at 0539–40. Compare Professor Van Aken – Day 2, pages 34–36

<sup>26</sup> Pool et al, 'Observations on plasma banking and transfusion procedures for hæmophilic patients using quantitative assay for antihæmophilic globulin', *British Journal of Haematology*, 1959; 5: 24–30 [LIT.001.4412]

<sup>27</sup> Pool et al, 'High-Potency Antihæmophilic Factor Concentrate prepared from Cryoglobulin Precipitate', *Nature*, 203: 312 [LIT.001.0097]

<sup>28</sup> Pool and Shannon, 'Production of high-potency concentrates of antihæmophilic globulin in a closed-bag system', *New England Journal of Medicine*, 30 December 1965; 273:1433–1447 [LIT.001.0967]

<sup>29</sup> Douglas AS, 'Plasma Coagulation Factors', *PROC. R.S.E. (B)*, 71, (Supplement), 7, 1972/73 [PEN.002.0575] at 0577

<sup>30</sup> Dr Norfolk – Day 7, page 66

<sup>31</sup> Newman et al, 'Methods for the Production of Clinically Effective Intermediate- and High-Purity Factor VIII Concentrates', *British Journal of Haematology*, 1971; 21:1 [SGF.001.1913]

<sup>32</sup> *Ibid* [SGF.001.1913]

<sup>33</sup> *Ibid* [SGF.001.1913]

cryoprecipitate units might thereafter be pooled for further processing,<sup>34</sup> but typically were used in multiples to make up a dose for Haemophilia A therapy. The product had lower coagulant activity than the material produced by Cohn Fraction I. But it was inexpensive to produce and the deficiency in coagulant activity could be made up by processing extra plasma.<sup>35</sup> However, in this application, the method depended on prompt processing after collection, when coagulant activity was high, and new technology was required to process plasma on a large scale. This became the principal approach to the research and development of plasma processing in Glasgow in the early years of the reference period.

**20.24** When cryoprecipitate from 10–15 individual plasma donations was combined and given to the patient it was possible to raise the Factor VIII level sufficiently to stop haemorrhage. During the late 1960s this treatment became available to haemophilia patients at hospitals on an out-patient basis. This was a major therapeutic advance for the treatment of Haemophilia A. Because cryoprecipitate does not contain very much Factor IX it was unsuitable for the treatment of Haemophilia B.<sup>36</sup>

## Haemophilia B

**20.25** Treatment of patients with Haemophilia B was initially with fresh-frozen plasma. Until 1967 that was the only treatment available for correction of deficiencies in coagulation Factors II, VII, IX and X. In 1967, the PFC began making PPSB,<sup>37</sup> a plasma derivative first produced in 1959 by Jean-Pierre Soulier in Paris for treatment of Haemophilia B patients. The demand for PPSB, which proved to have wide-ranging application, prompted research in Edinburgh into new methods of recovering Factor IX from the normal citrated plasma used in Cohn fractionation. The research, by Middleton, Bennett and Smith of the PFC, led to development of a Factor IX product, based on ion exchange purification.<sup>38</sup>

**20.26** In a similar fashion to Factor VIII, it had as its aim the production of a finished product with a specified amount of Factor IX activity per vial which would be suitable for home therapy and which would comply with the specifications of the British Pharmacopoeia (the UK standards for medicinal products).<sup>39</sup> The product known as 'DEFIX' was produced at the PFC from 1972.

**20.27** In the fractionation process, Factor IX was extracted downstream of Factor VIII, and it is appropriate to postpone discussion of Factor IX at this stage.

## Blood product development and production in Scotland

**20.28** The general trends in use of blood donations were followed in Scotland. Red cell preparations, including concentrates, were isolated. Platelet and leukocyte concentrates were derived from processing the buffy coat isolated in the primary separation procedure. As the twentieth century progressed, these operations superseded the use of whole blood for therapeutic purposes. The further processing of plasma became the principal

<sup>34</sup> Dr Foster – Day 41, page 48

<sup>35</sup> Watt et al, 'New Developments in large-scale plasma fractionation', *PROC. R.S.E. (B)*, 71, (Supplement), 3, 1971/72 [PEN.002.0538] at 0550–51

<sup>36</sup> Draft Expert Report prepared by Professor Ludlam for litigation in England and Wales in 1990, *Human Immunodeficiency Virus Infection in Haemophiliacs* [PEN.015.0385]; and for a more detailed explanation of blood products see Professor Ludlam's paper *Edinburgh Haemophilia Treatment Policy* [PEN.015.0375]

<sup>37</sup> Prothrombin, proconvertin, Stuart Factor and antihemophilic B Factor.

<sup>38</sup> Middleton, Bennett, & Smith, 'A therapeutic concentrate of coagulation Factors II, IX and X from citrated, Factor VIII-depleted plasma', *Vox Sanguinis*, 1973; 24: 441–456 [PEN.012.1984]

<sup>39</sup> Dr Foster – Day 41, page 52

downstream procedure of interest for present purposes. Developments in the production and use of cryoprecipitate were pursued in Glasgow and the west of Scotland, latterly centred on laboratories at Law Hospital. In Edinburgh and the South East of Scotland Region of the Blood Transfusion Service the emphasis came to be on fractionation.

**20.29** The development of the first Factor VIII concentrate by the SNBTS was based on information obtained from Dr Cohn's laboratory in the early 1950s by Dr Drummond Ellis, then Head of the Regional Blood Transfusion Centre and Blood Products Unit (known until 1970 as the 'BPU'), at the RIE, where Edinburgh and South East Scotland Blood Transfusion Service was based.<sup>40</sup> Dr Ellis later moved to the Blood Products Laboratory (BPL), Elstree, and was succeeded by Mr John Watt.<sup>41</sup>

**20.30** The early history of development work in the east of Scotland was described in an article published in 1965: *Red Cell Banking and the Production of a Factor VIII Concentrate* by Dr Cumming, Dr Ellis and Mr Grant of the BPU.<sup>42</sup> Scotland's first fractionated plasma product was normal immunoglobulin for the prevention of measles, produced in 1952 at the RIE laboratory.<sup>43</sup> Production of fibrinogen followed in 1956. Experimental quantities of Cohn Fraction I were made between 1952 and 1956.<sup>44</sup> Routine production of an early version of Factor VIII known as antihæmophilic factor or AHF (from Cohn Fraction I) followed in 1956 and albumin in 1965.<sup>45</sup> At this early period, the production of immunoglobulins was a significant part of the BPU's operations. A new pilot plant for fractionation was established at the BPU at the RIE in 1968.<sup>46</sup> Cohn Fraction I, relatively rich in Factor VIII (antihæmophilic globulin) activity was produced there until production moved to the new facility built at the PFC, Liberton.

**20.31** The fractionation process developed at BPU was initially very small-scale, as was the equivalent NHS process in England, and Factor VIII concentrates manufactured by the public service providers were available in very limited quantities. In Edinburgh, each bottle of Cohn Fraction I product was derived from six bottles of fresh plasma, the number of bottles that could be accommodated in one centrifuge load. Only one batch could be processed in a week. Dr Cumming and his colleagues reported, however, that it appeared from their results that it was possible to prepare a safe and reasonably active Cohn Fraction I from plasma, provided that suitable precautions were taken during processing.<sup>47</sup> The similar Factor VIII preparation used in England and Wales during the 1960s was referred to as 'NHS freeze dried factor VIII concentrate' by Dr Rosemary Biggs.<sup>48</sup>

### Product range in 1973

**20.32** So far as plasma products are concerned, the discussion in this report necessarily focuses on the production of factor concentrates and their use in haemophilia therapy. But it is important to note that, especially up to the beginning of the reference period, this bias gives a false impression of the scope of operations of the Blood Transfusion Services

<sup>40</sup> For details of the history of the PFC and work carried out at the RIE see paragraphs 5.6– 5.20 of the Preliminary Report.

<sup>41</sup> Dr Foster's paper, *Self Sufficiency and the Supply of Blood Products in Scotland* [PEN.013.1125] at 1164

<sup>42</sup> Cumming et al, 'Red cell banking and the production of a Factor VIII concentrate', *Vox Sanguinis*, 1965; 10:687–699 [PEN.017.2472]

<sup>43</sup> Foster, 'Plasma Fractionation in Scotland', *Blood Letter*, Spring 2008 [PEN.017.2468] at 2468

<sup>44</sup> This work may have started in 1951 according to Watt et al, 'New Developments in Large-scale plasma fractionation', *PROC. R.S.E. (B)*, 71, (Supplement), 3, 1971/72 [PEN.002.0538] at 0540

<sup>45</sup> Foster, 'Plasma Fractionation in Scotland', *Blood Letter*, Spring 2008 [PEN.017.2468]; and Dr Smith–Day 60, page 9

<sup>46</sup> Maj. Gen. Jeffrey's letter of 6 January 1975 to Chief Administrative Medical Officers [SGH.007.7009]

<sup>47</sup> Cash and Spencely, 'Haemophilia A and the blood transfusion service: A Scottish Study', *British Medical Journal*, 1976; 2:682–684 [LIT.001.0255]

<sup>48</sup> Biggs, 'Haemophilia Treatment in the United Kingdom from 1969 to 1974', *British Journal of Haematology*, 1977; 35:487 [LIT.001.0159]

and of the manufacturing facilities. Dr James Smith said of the period before he moved to Oxford, in 1975:

This Inquiry focuses on haemophilia but at no time during these years were we able to neglect the many, many more patients who required immunoglobulins, albumin and other products, which we did not have the right to interfere with too much. These patients were more diffuse in their needs and the clinicians who used these products were scattered. So there was no, if I can call it, pressure group from patients with immunodeficiencies, for instance .... We all had to take account, equal account, of all the users of our products.<sup>49</sup>

**20.33** In a personal assessment of needs dated 12 June 1973, Mr Watt analysed the demand for plasma, drawing on a wide range of information. He wrote:

Discussion on the probable need for plasma for fractionation indicates that, of all fractions prepared, the main limiting consideration is the need for Plasma Protein Solution.<sup>50</sup> The need for specific immune globulin and salt poor albumin will create errors in calculation but, in a coherent policy of overall balanced use of blood and its fractions, these errors practically cancel each other out to make a net error factor of less than 1% in the total estimate.<sup>51</sup>

**20.34** In his view, at that time, if plasma requirements for plasma protein solution (PPS) or stable plasma protein solution (SPPS) could be met, the supply of plasma would be sufficient for other fraction production. In particular, the amount of plasma, 200,000 litres or 1 million donations, required for AHG (antihaemophilic globulin) preparation was 'of no account in consideration of overall need'.<sup>52</sup> The critical figure was the 400,000 litres required for PPS. At that stage the PFC had process potential to handle up to 300,000 litres of plasma per year, but could not finish PPS at equivalent rates.<sup>53</sup>

**20.35** Leaving aside questions of projected demand in numerical terms, the balance between AHG and PPS needs reflects Mr Watt's assessment that the principal driver of demand for plasma products in 1973 was the need for albumin, specifically PPS.

**20.36** It is possible that the paper may have been, in part, an attempt by Mr Watt to respond to controversy that had developed within the SNBTS relating to developing technologies. There were some significant differences of opinion over the development of plasma products. As already noted, two processes for the production of Factor VIII products had developed, resulting in different products each of which sought to compensate for low Factor VIII levels in the patient's blood. Each allowed reliable Factor VIII treatment, when applied appropriately. Some experts favoured the use of cryoprecipitate, as for example in Glasgow. From around 1968, refinements in Cohn fractionation led to a product of comparable potency in Factor VIII activity which was easier to use, but which involved increased demand on the scarce resource of plasma.

---

<sup>49</sup> Dr Smith – Day 59, page 8

<sup>50</sup> SPPS, Stable Plasma Protein Solution, is an albumin product of slightly lesser purity than the product competently described as Albumin in terms of the British Pharmacopeia.

<sup>51</sup> Watt JG, *Plasma fractionation in the United Kingdom – a personal appraisal* (Draft) 12 June 1973 [SNB.010.1991] at 1993

<sup>52</sup> *Ibid* at 1996

<sup>53</sup> *Ibid* at 1997

**20.37** The controversy was explicit at a joint symposium held on 4 February 1972 by the Royal Society of Edinburgh and the Royal College of Physicians. Professor Cash (then Deputy Director of the Edinburgh and South East Scotland BTS) reflected one view:<sup>54</sup>

One of the disquieting trends in the last few years has been the energetic activities of the protein chemists. On the basis of the clinical desirability for a small-volume high factor VIII content product, techniques have been developed which go a long way towards this end .... The serious drawback in this work is the high production losses. The shortage of raw material for the treatment of all haemophiliacs at the present time is such that until comparable yields are obtained the production of this type of product should be actively discouraged, or at least strictly controlled and its use limited to a small group of patients, such as those with acquired inhibitors.

**20.38** At that stage, in 1972, Mr Watt and colleagues from the PFC (as the BPU had now been re-named) had reservations about the stage technological development had reached. At the symposium they commented that the Newman method was promising, but that it lacked the clinical data necessary to support its effectiveness.

**20.39** However, opinion was to change rapidly. Mr Watt had met Dr Johnson in Australia in 1966, and as a result the PFC was provided with advice from Dr Johnson when Mr Watt joined the PFC the following year.<sup>55</sup> Dr Johnson's 1971 paper was not referred to in the symposium presentation by Mr Watt and his colleagues. It was to provide the methodology for Factor VIII preparation adopted in Scotland.<sup>56</sup> In the course of the reference period, close collaboration developed between the SNBTS and Dr Johnson's team.<sup>57</sup> For present purposes, the development of the new PFC at Liberton, Edinburgh, and the adoption of the Newman method there, marked the move towards commercial-scale production of factor concentrates in Scotland.

**20.40** The incentive to produce factor concentrates was described by Dr Peter Foster:

They were more potent, defined and purified than cryoprecipitate; they could be filtered to remove bacterial contaminants and had a lower incidence of allergic reactions than cryoprecipitate. In contrast to cryoprecipitate they were also amenable to large volume manufacture compliant with good pharmaceutical manufacturing practice (GMP). The fact that they were freeze dried also made them easier, quicker and more convenient to use than cryoprecipitate, which had to be stored frozen. Crucially, they enabled patients to treat themselves at home, giving people with haemophilia access to education and employment which had not previously been possible.<sup>58</sup>

**20.41** Mr Watt wrote a report (with the assistance of Dr Smith) on the 'Development of Factor VIII concentrates' in December 1973.<sup>59</sup> The paper focused on the transition from the production of Fraction I, antihaemolytic factor, into the start of the new era of production of more potent concentrates inspired by Johnson and Newman.<sup>60</sup> He described recent

<sup>54</sup> Cash JD, 'Principles of effective and safe transfusion', *PROC. R.S.E. (B)*, 71, (Supplement), 5, 1971/72 [PEN.002.0559] at 0560–61

<sup>55</sup> Dr Foster's paper, *Self Sufficiency and the Supply of Blood Products in Scotland* [PEN.013.1125] at 1164

<sup>56</sup> *Ibid* [PEN.013.1125] at 1164

<sup>57</sup> Foster PR and McIntosh RV, *The development of hepatitis-safe Factor VIII concentrate by the Scottish National Blood Transfusion Service*, SNBTS, 9 December 1999 [SNB.001.6647] at 6650

<sup>58</sup> Dr Foster's paper, *Self Sufficiency and the Supply of Blood Products in Scotland* [PEN.013.1125] at 1135

<sup>59</sup> Dr Smith – Day 59, page 11; Mr Watt's report, *Development of Factor VIII concentrates*, December 1973 [SNB.001.6903]

<sup>60</sup> Dr Smith – Day 59, page 14

developments. In the latter part of 1972, laboratory-scale batches of plasma, 2–10 litres, were fractionated by the method of Newman and Johnson to intermediate potency Factor VIII. In February 1973, they progressed to the 10–60 litre scale. By the date of his report, a product of intermediate type had been expanded to 100-litre scale and was obtaining 30–40% yield. The report stated:

Large scale crushing and thawing equipment was commissioned in early September 1973, and is functioning adequately on a load of 100 [litres] plasma. It is expected that with minor improvements the batch size may be increased to 180 [litres].

**20.42** Cohn Fraction I was produced until the quarter ended 27 September 1974. In the quarterly report for that period it was noted:

This is the last occasion on which A.H.F. (Cohn Fraction I) will appear in these reports. The ... old item (Cohn Fraction I) will not appear after this quarter.<sup>61</sup>

**20.43** By this time, the PFC employed a small volume computer-controlled continuous fractionation process invented by Mr Watt. This contributed to the increased throughput possible at the RIE in the last phase of operation of the facility there, and it was to promote considerably larger-scale production of concentrates after the move to Liberton. Until the move, however, factor concentrate production in Edinburgh remained a small-scale operation, and already exposed the market to imported products as discussed in Chapter 21 *Haemophilia Therapy – Use of Blood Products*.

**20.44** A report to Area Health Boards set out the position as at 6 January 1975:

It is not possible to overlap production at the Royal Infirmary and Ellen's Glen as the computer has been moved to the latter and hence there will be an interim period, as the new plant is tested and brought into production, when the supply of blood products will be reduced. The length of this interim period will depend on the rapidity with which the new plant can be brought into full production; there are many novel features in its design and all must be thoroughly tested.<sup>62</sup>

**20.45** In the Inquiry's Preliminary Report an attempt was made to reflect trends in production by reference to a selection of data from annual reports of the SNBTS which appeared to show that the production of anti-D immunoglobulin and SPPS was more significant than the production of AHF as the PFC at Liberton came on stream (consistent with Mr Watt's approach to calculating production targets for the new facility<sup>63</sup>). In response to the Preliminary Report, the SNBTS observed that it was unclear what the figures represented as no units had been given. That criticism is accepted. However, with limited exceptions, the source material, SNBTS data, did not specify the units applicable to the several products listed.<sup>64</sup> The disruptive effect of the move on concentrate production is illustrated in Chapter 21, *Haemophilia Therapy – Use of Blood Products*, Figure 21.5

<sup>61</sup> PFC Report on production of plasma fractions for quarter ended 27 September 1984 [SNB.010.3712]

<sup>62</sup> Maj. Gen. Jeffrey's letter of 6 January 1975 to Chief Administrative Medical Officers [SGH.007.7009]

<sup>63</sup> See Chapter 19, *Production of Blood Products – Facilities*, paragraph 19.15

<sup>64</sup> For example, the information recorded for 1975–76 in the SNBTS Annual Report, Appendix 2, provided comparative data for 1964–65 [SNB.010.3921] at 3957. No units were specified for Fibrinogen, Normal Immunoglobulin, or SPPS. Units were specified for Anti-D and Anti-Tetanus, and for II, VII, IX, X combination products only.

**20.46** The production of intermediate Factor VIII fell from its 1972–73 level as preparations were made to transfer to the PFC facility. Leaving aside comparisons between products, Anti-D and SPPS production fell to a more limited extent in 1973–75, the construction and commissioning phase. The rapid build-up of production of Factor VIII concentrate after commissioning of the PFC reflected a change of emphasis in production towards meeting the demand for products for haemophilia therapy.

### **Technology after the Protein Fractionation Centre moved to Liberton**

**20.47** There were major changes in the technology employed in the PFC at Liberton at or about the beginning of the reference period and continuing throughout the period dealt with in this chapter. They were generally related to increasing process capacity and efficiency, but included work aimed at the removal of virus from concentrates. Although the PFC's Factor VIII concentrate processes were based on Dr Johnson's work, scientists at the PFC contributed to the development of process technology over the period covered in this chapter, internally and in collaboration with Dr Johnson.

**20.48** As at April 1975, Dr Foster, then Head of Research and Development at the PFC, wrote a summary report on research and development work in progress.<sup>65</sup> A wide range of projects, begun on various dates from 1970, were described. The report indicated that there was about to be a step change in the volume of production of Cohn fraction products. A basic continuous fractionation unit, with semi-automatic computer control, would be commissioned at the new facility. It would give a processing capability of at least 2000 litres a week for SPPS. Extension of the system to other PFC products was being evaluated and was expected to allow process optimisation in terms of yield, purity and daily work schedules and an increase in throughput. The development of Factor IX products was in hand. The evaluation and re-design of the Factor VIII systems and processes were also in hand for the production of intermediate Factor VIII concentrate. The use of sonic vibration for precipitate conditioning was being studied with a view to improving centrifugal separation, particularly in continuous processing.

**20.49** Two significant aspects of this work were continuous processing, and precipitate conditioning. Dr Foster commented that precipitate conditioning had always formed an important part of fractionation, but that little information had been published on the subject, and the physico-chemical changes involved had not been identified. Significant advances in centrifugal separation in continuous processing were anticipated, along with gains in general knowledge of plasma fractionation and protein isolation.

**20.50** The SNBTS followed up the topics: by early 1976 it was becoming apparent that there might be an increase in demand for fractionation. A report was prepared in January 1976.<sup>66</sup> Dr Johnson had been involved in discussions in November of the previous year. Length of storage of frozen plasma for fractionation was considered. The use of polyethylene glycol to enhance Factor VIII recovery and of heparin to stabilise plasma were to be studied. The design of a continuous thawing system to produce more granular cryoprecipitate was in hand. The PFC's Factor VIII products were known as 'NY' between late 1979 and late 1984 to reflect the collaboration with New York University (and Dr Johnson in particular).<sup>67</sup>

---

<sup>65</sup> Dr Foster's summary report, April 1975 [SNB.010.4779]

<sup>66</sup> Project proposal – The isolation of FVIII, January 1976 [SNB.007.0783]

<sup>67</sup> Dr Foster – Day 41, page 26

**20.51** For the fractionator, yield of Factor VIII activity was important, and the balance between purity and yield was vital. When the Edinburgh scientist Dr Duncan Pepper<sup>68</sup> applied for a research grant on 15 June 1978,<sup>69</sup> the specified areas of interest were Factor VIII stability and yield. Edinburgh research had dealt with methods of maximising the rate of thaw of frozen plasma within the constraint imposed by Factor VIII solubility, and the use of sophisticated mixing and temperature control systems using a thaw-siphon technique. Blocks of frozen plasma were crushed to increase the surface area over which heat was applied. By continuously removing the thawed plasma, below the solubility temperature of the Factor VIII component, over a wide area of plasma 'snow' produced by crushing, dissolution of the Factor VIII was avoided and the degree of Factor VIII degradation was reduced. It was said that the surface area factor had been ignored by others. The design of processes for crushing and continuous thawing, using fluid removal for temperature control, became one of the defining features of research and development work at the PFC for a considerable time. Dr Foster published a poster presentation and abstract of their work at the Seventh International Congress of Thrombosis and Haemostasis, London, in July 1979. The emphasis within the PFC on techniques for large-scale plasma thawing for the recovery of cryoprecipitate Factor VIII continued.

**20.52** In the end, not all of the developments proposed by Dr Johnson were taken up universally. Dr Smith commented that the higher purity concentrate using polyethylene glycol and glycine never gained wide use, and was not continued beyond initial experiments in Edinburgh.<sup>70</sup>

**20.53** It is not necessary to trace all of the developments in technology in this period for the purposes of this report. The manufacturing process became complex and highly defined. The emphasis was on technological improvements in processing raw materials to increase efficiency in the production of an intermediate purity concentrate, while meeting demand for other blood products such as immunoglobulins and albumin products, particularly SPPS.

**20.54** A statement was provided by Dr Foster which includes a narrative of the various manufacturing steps along with simplified flow diagrams as at the end of 1983. (See Figures 20.1, 20.2 and 20.3 at the end of this chapter for the flow diagrams.) Dr Foster had also earlier supplied a floor plan of the ground floor of the PFC,<sup>71</sup> a series of photographs detailing elements of the fractionation process<sup>72</sup> and a film of the process made in 1995, which was viewed on day 41 of the public hearings.<sup>73</sup>

**20.55** A total of 17 steps were needed in order to achieve a finished product with a specified amount of Factor VIII activity per vial, starting from frozen plasma which the PFC received from the SNBTS. They were described in some detail by Dr Foster as at the end of 1983 in response to a request by the Inquiry<sup>74</sup> and were discussed at length during Day 41 of the Inquiry's hearings.<sup>75</sup> The aim was to create a product which would be suitable for home therapy and which would comply with the specifications of the British Pharmacopoeia.

<sup>68</sup> Dr Pepper was at that time Principal Scientific Officer, SE Scotland BTS.

<sup>69</sup> Dr Pepper's research grant application [SNB.007.1398]

<sup>70</sup> Dr Smith – Day 59, page 13

<sup>71</sup> PFC ground floor plan [PEN.012.1694]

<sup>72</sup> Photos of fractionation process [PEN.012.1695]

<sup>73</sup> Dr Foster – Day 41, page 56

<sup>74</sup> Dr Foster's statement on the PFC's manufacturing process for the production of Factor VIII and IX concentrates [PEN.012.1852]

<sup>75</sup> Dr Foster – Day 41, pages 22–55



**20.56** The process began with ‘plasma conditioning’ by bringing the frozen plasma delivered to the PFC from minus 40°C to a temperature of about minus 15 to minus 10°C. Batches of 4000 donations each were processed at the rate of about two per week.<sup>76</sup> The plasma was then stripped from its plastic containers, crushed in a hammer mill, and thawed as quickly as possible to recover cryoprecipitate particles for processing.<sup>77</sup> The plasma had to be thawed at a temperature that avoided the particles of cryoprecipitate from being dissolved.

**20.57** The crushed plasma ‘ice’ was discharged continuously into a cylindrical thawing vessel which heated the ice to just above its melting point, and released melted plasma, containing particles of cryoprecipitate, to drain by gravity into a holding vessel. From there, the material was pumped to a centrifuge where cryoprecipitate particles were accumulated on the walls of the vessel, and the clarified liquid supernatant drained into a collection vessel for further processing. The cryoprecipitate was used to make Factor VIII and the cryo-supernatant was used to make Factor IX.<sup>78</sup>

**20.58** Continuous thawing was a major advance on previous technology which had depended on thawing in small-volume batch tanks, and in changing temperature conditions. It enabled plasma throughput to be increased relatively easily.<sup>79</sup> In comparison with the superseded batch thawing method, the yield of Factor VIII activity was increased by about 50%.<sup>80</sup> Solubility was enhanced, and in due course this enabled the product (NY) to withstand dry heat treatment at 68°C for 2 hours without further process modification.

**20.59** The use of continuous thawing was devised by the SNBTS and published in 1978.<sup>81</sup> It was introduced for routine production in August 1979, and progressed to faster production with upgraded equipment in January 1981.<sup>82</sup> The improvements were reported in 1982.<sup>83</sup>

**20.60** After centrifugation, the cryoprecipitate was rinsed in a 2% solution of ethanol at 2°C to remove any residual plasma which might contain potentially damaging substances. The rinsed cryoprecipitate was suspended in a buffer solution which was designed to protect the material from chemical shock as processing continued to dissolve most of the cryoprecipitate whilst excluding material that was poorly soluble.<sup>84</sup> The pH of the solution was adjusted to pH 7.0, the optimum pH for the recovery of Factor VIII, by the slow addition of dilute hydrochloric acid.

**20.61** At this stage a residue of unwanted coagulation factor proteins remained in the cryoprecipitate, including other coagulation factors (Factors II, VII, IX and X) which had not been removed by the thawing process, as well as impurities which could otherwise cause the Factor VIII to become unstable. These were known to bind preferentially to aluminium hydroxide [Al(OH)<sub>3</sub>] and a stable gel of that material was introduced to remove them. This

<sup>76</sup> Ibid pages 38–39

<sup>77</sup> Ibid pages 29–31

<sup>78</sup> Ibid pages 23–25

<sup>79</sup> Dr Foster’s statement on the PFC’s manufacturing process for the production of Factor VIII and IX concentrates [PEN.012.1852] at 1860

<sup>80</sup> Dr Foster – Day 41, page 40; Dr Foster’s statement on the PFC’s manufacturing process for the production of Factor VIII and IX concentrates [PEN.012.1852] at 1861

<sup>81</sup> Foster & White, ‘Thaw-Siphon technique of Factor VIII cryoprecipitate’ *The Lancet*, 1978; 2, 574 [LIT.001.0351]

<sup>82</sup> Dr Foster – Day 41, pages 34–35

<sup>83</sup> Ibid page 76; Foster et al, ‘Control of large-scale plasma thawing for recovery of cryoprecipitate Factor VIII’, *Vox Sanguinis* 42, 180–189 (1982) [LIT.001.0790]

<sup>84</sup> A buffer is a chemical, or mixture of chemicals, which is designed to regulate the pH of a solution. For more information see Dr Foster – Day 41, pages 43–44

occurred by adsorption of the unwanted materials, leaving the Factor VIII in solution. The aluminium hydroxide gel and the adsorbed materials were then separated from the main solution by centrifugation in bottles, and the supernatant solution was decanted from the bottles into a sterile pressure vessel for filtration through a series of successively finer filters.

**20.62** An anticoagulant, tri-sodium citrate, was then added to prevent de-stabilisation of the Factor VIII by any residual activity from trace levels of coagulation factors other than Factor VIII. The pH was adjusted to pH 6.8 with dilute hydrochloric acid. Further filtration with even finer filters followed.

**20.63** The final Factor VIII solution was then dispensed into sterile glass vials using an automated aseptic dispensing system. The amount of Factor VIII dispensed was less than the capacity of the glass vial so that patients could add distilled water to the final freeze-dried product. Each vial was fitted with a raised stopper with small grooves in the side to allow moisture to escape from the vials during freeze-drying. The products were frozen solid, and then dehydrated by freeze-drying.

**20.64** Overall, the process to this stage took around one week. Three to four months were then needed for inspection, labelling and other procedures before the batch could be released for use.<sup>85</sup>

## Factor IX

**20.65** The manufacture of DEFIX was also described in depth in Dr Foster's statement on manufacturing.<sup>86</sup> The process was also discussed during Day 41 of the Inquiry's hearings.<sup>87</sup> A total of 17 additional steps were involved after the removal of the cryosupernatant from the cryoprecipitate. Ion exchange technology was used to separate Factor IX and related proteins from a supernatant containing immunoglobulin and SPPS/albumin. The cryosupernatant was prepared for ion exchange by use of sterile, pyrogen<sup>88</sup> free water at 4°C and adjustment of the pH to 6.9. Ion exchange gel was added and Factor IX and related proteins became attached to the gel. The separation was achieved by centrifugation. The ion exchange gel and adhering proteins were suspended in a buffer 'wash' solution for ease of pouring into a chromatography column.

**20.66** The wash solution was allowed to drain from the column, leaving the ion exchange gel and its bound proteins as a squat column. In a process known as elution, the chromatography column was flushed with a buffer solution containing sodium chloride and other sodium compounds until the coagulation factors were observed to begin emerging from the column, detected by a sharp rise in the conductivity of the solution at the column's out-flow. Various different 'eluates' or fractions were collected in containers. The fractions which met the requisite specifications for Factor IX activity and non-thrombogenicity were then thawed, in sealed containers, at room temperature. When thawed, the containers were opened, the selected fractions pooled and samples taken of Factor IX activity. After that, the solution was diluted, if necessary, to achieve a target Factor IX potency of 34 IU/ml. Filtration to 0.22 micrometres followed, as in the

<sup>85</sup> Dr Foster's statement on the PFC's manufacturing process for the production of Factor VIII and IX concentrates [PEN.012.1852] at 1867

<sup>86</sup> Ibid [PEN.012.1852]

<sup>87</sup> Dr Foster – Day 41, pages 28–50

<sup>88</sup> Pyrogens are substances produced by bacteria which cause a rise in human body temperature (ie fever).

case of Factor VIII, and the solution was dispensed aseptically into glass vials, which were then frozen in the same manner as outlined for Factor VIII above.

**20.67** Two of the steps common to the processes were to become significant at a later period: plasma conditioning and continuous thawing.

### **Virus research at the Protein Fractionation Centre in the 1970s**

**20.68** The processes for Factor VIII and Factor IX production so far described were the result of extensive research and development, much of it involving innovative science and technology. The removal of unwanted proteins at successive stages of the programme probably removed virus particles incidentally in the preparation of the concentrates prepared for clinical use. But they did not provide for the inactivation of any residual virus particles remaining in the final product. The products remained potentially infective in clinical use. Subject to any parallel developments in virus inactivation that were achieved, increases in the efficiency of process technology, leading to increased production capacity and output, necessarily increased the exposure of patients to risk. Until 1975 at the earliest, the known risk was of transmission of Hepatitis B. Blood donations were screened with increasing efficiency, so that the plasma received for fractionation became less likely to carry virus. For immediate purposes, the focus is on fractionation technology and the steps taken to reduce risk in processing. Virus inactivation by heat treatment is discussed in greater detail in Chapter 23, *Viral Inactivation of Blood Products for Haemophilia Therapy up to 1985*.

**20.69** In the 1970s, researchers at the PFC were active in exploring the physical removal of the Hepatitis B virus by precipitation of the virus using polyethylene glycol (PEG) as part of the Factor IX production process.<sup>89</sup> The research was part of the 'Supernine Project', a collaborative exercise with Dr Johnson and other scientists at New York University, which aimed to replace the PFC's standard DEFIX product for Haemophilia B with a concentrate that would be three to five times more potent, and have a reduced risk of transmitting Hepatitis B.<sup>90</sup> The US part of the project ultimately ran into funding difficulties when the USA National Institute of Health refused an application for further chimpanzee studies.<sup>91</sup> These funding difficulties meant that research could not be continued to assess whether the process was successful in removing Hepatitis B infectivity.

**20.70** Another part of the project involved an assessment of possible thrombogenic reactions connected to the new Supernine product, a known complication of the use of Factor IX therapy.<sup>92</sup> A team at the PFC led by Dr Foster demonstrated that the PEG processing used in an advanced form of the product reduced the amount of thrombogenic material present.<sup>93</sup> Supernine was ultimately never released for clinical use as the Medicines Control Agency were reluctant to issue a second Factor IX licence. But the work on thrombogenic reactions was of continuing benefit.

<sup>89</sup> Dr Foster's statement on viral inactivation to 1985 [PEN.012.1438] at 1439–44; and SNBTS Briefing Paper on development of heat treatment of coagulation factors [PEN.013.1309] at 1339–40; also Dr Foster – Day 41, pages 87–109

<sup>90</sup> Information on this project is available in a PFC Research and Development Department report from 1975 [SNB.010.4779]

<sup>91</sup> Ibid

<sup>92</sup> See Cash et al, 'Studies on the Thrombogenicity of Scottish Factor IX Concentrates in Dogs', *Thrombosis et diathesis haemorrhagica*, 1975; 33:632 [LIT.001.0959]; and Dr Foster – Day 41, page 99

<sup>93</sup> See Foster et al, 'Thrombogenicity of Factor IX Concentrates and Polyethylene Glycol Processing', *Thrombosis Research*, 1980; 17(1–2): 273–9 [LIT.001.0208]; Dr Foster's statement on viral inactivation to 1985 [PEN.012.1438] at 1441; and Dr Foster – Day 41, pages 100–101

**20.71** In February 1982, Dr Alex MacLeod, PFC, conducted a series of experiments in the pasteurisation of PFC's intermediate Factor VIII product with a view to inactivating NANB Hepatitis virus. It was found that if the standard product was diluted in its normal reconstituted volume, heating resulted in clotting. However, they found that if the product was diluted in the presence of certain stabilisers, the product could be heated at 60°C in a water bath and remain fluid, though becoming cloudy. It was concluded at that time that the ability to pasteurise Factor VIII concentrate was linked to purity, and that a high purity product would be required for effective treatment. The project did not progress further at that stage. But, once more, research had provided information that would prove to be of value later in the 1980s.

**20.72** The PEG precipitation method was not applicable to Factor VIII because the sizes of the Factor VIII complex and the virus molecule were not sufficiently different for effective separation by the process technology developed at the time.<sup>94</sup> In his report dated December 1973,<sup>95</sup> Mr Watt included in his narrative of candidates for investigation the use of specific solid-phase polyelectrolytes in a procedure for the purification of Factor VIII. The procedure had been developed by Dr Johnson. It exploited a characteristic of Factor VIII which resulted in the protein attaching preferentially to the polyelectrolyte, while other substances (including viruses) were not attached and could, in theory, be separated by washing.<sup>96</sup> The PFC's research had depended on proprietary polyelectrolytes supplied by Monsanto for research purposes only. The company had required that the project should be carried out under strict confidentiality and that all research reports should be destroyed or returned to them. Monsanto were unwilling to agree to license-out the reagent for production purposes, and the project was discontinued.<sup>97</sup>

**20.73** In view of the difficulties encountered, Dr Foster approached research groups, including groups already involved in research collaboration with the SNBTS, at a number of UK universities to encourage them to undertake fundamental research into ways of eliminating the risk of coagulation factor concentrates transmitting hepatitis.<sup>98</sup> However, his attempts to set up collaborations with UK universities were unsuccessful.

**20.74** Until 1981, and the publication of the work of Behring on the pasteurisation of Factor VIII,<sup>99</sup> knowledge of the possibility that Factor VIII might be treated with heat to inactivate virus contamination was limited to those who were aware of the first public disclosure of the work at a symposium in Bonn in October 1980. Professor Cash attended that symposium and reported the information to Dr Foster among others.<sup>100</sup> Dr Foster commented on his response to the information:

I was quite shocked when I heard this claim, as the notion that factor VIII might be able to be heat treated under conditions that would destroy hepatitis viruses was inconceivable to me.<sup>101</sup>

<sup>94</sup> Dr Foster's statement [PEN.012.1438] at 1442

<sup>95</sup> Dr Smith – Day 59, page 11; Mr Watt's report 'Development of Factor VIII concentrates', December 1973 [SNB.001.6903]; see paragraph 20.41 above

<sup>96</sup> Dr Foster's statement [PEN.012.1438] at 1442

<sup>97</sup> Dr Foster's statement [PEN.012.1438] at 1442–43

<sup>98</sup> *Ibid* at 1445–46

<sup>99</sup> Heimburger et al, 'A Factor VIII concentrate, highly purified and heated in solution', *Haemostasis*, 1981; 10 (Supp 1) 204 [SNB.007.3300]

<sup>100</sup> Dr Foster's statement [PEN.012.1438] at 1445–47

<sup>101</sup> *Ibid* [PEN.012.1438] at 1447–48

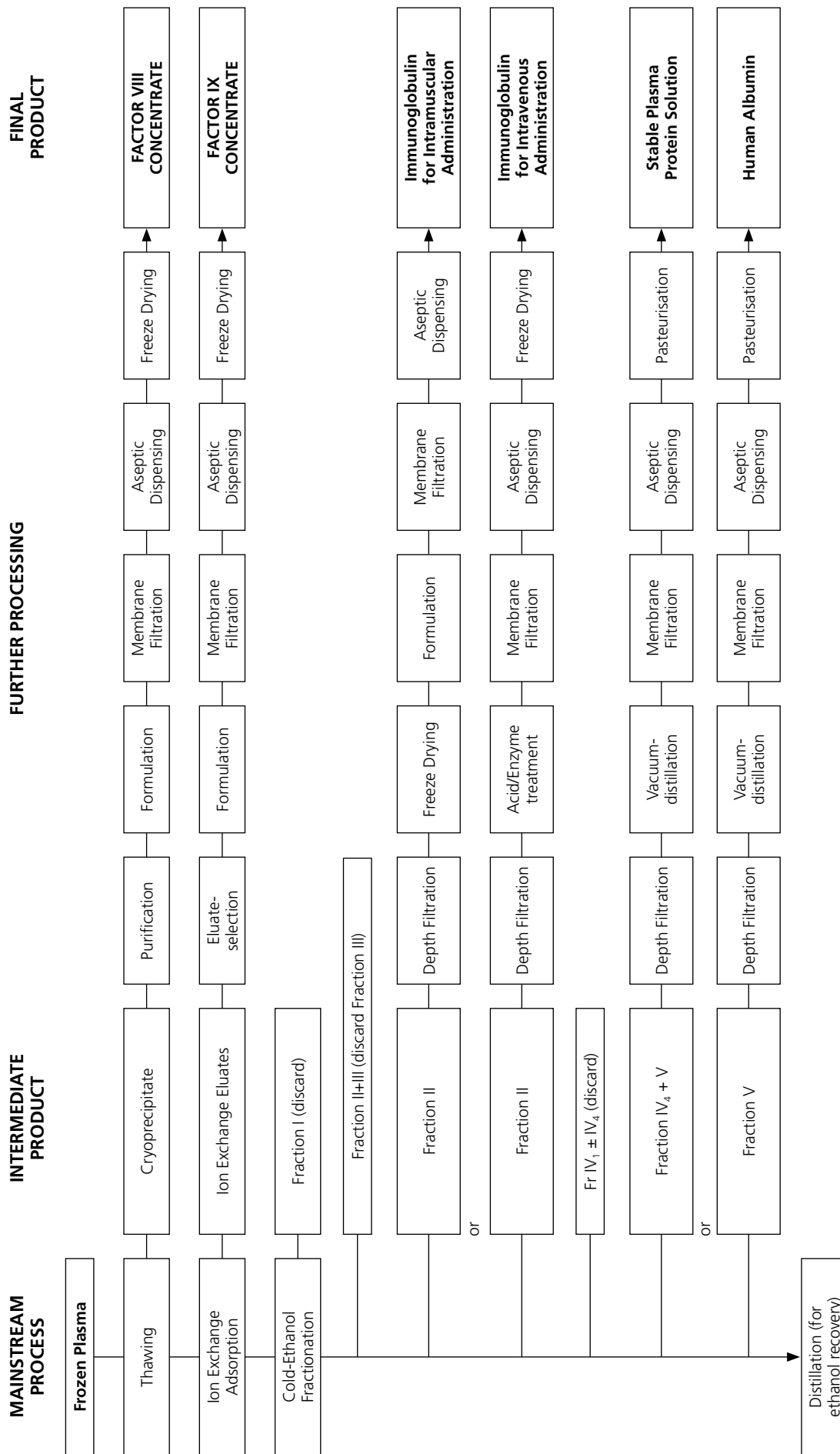
**20.75** Dr Foster had substantial reasons for his reaction. The view of Dr Webb, under whom he had studied at University College London, was that apart from albumin all fractions were heat labile. Dr Foster's own doctoral research made Factor VIII an implausible candidate for research on heat treatment; and experience of the PFC's experiments of filtration performed at 20°C and progressively higher temperatures had confirmed his view that Factor VIII was sensitive to an increase in temperature and that loss of Factor VIII activity was temperature-dependent. The view of others, including Dr Frank Boulton, was that Behring's claims could not possibly be true, and that eventually it would be discovered that it was a mistake.<sup>102</sup>

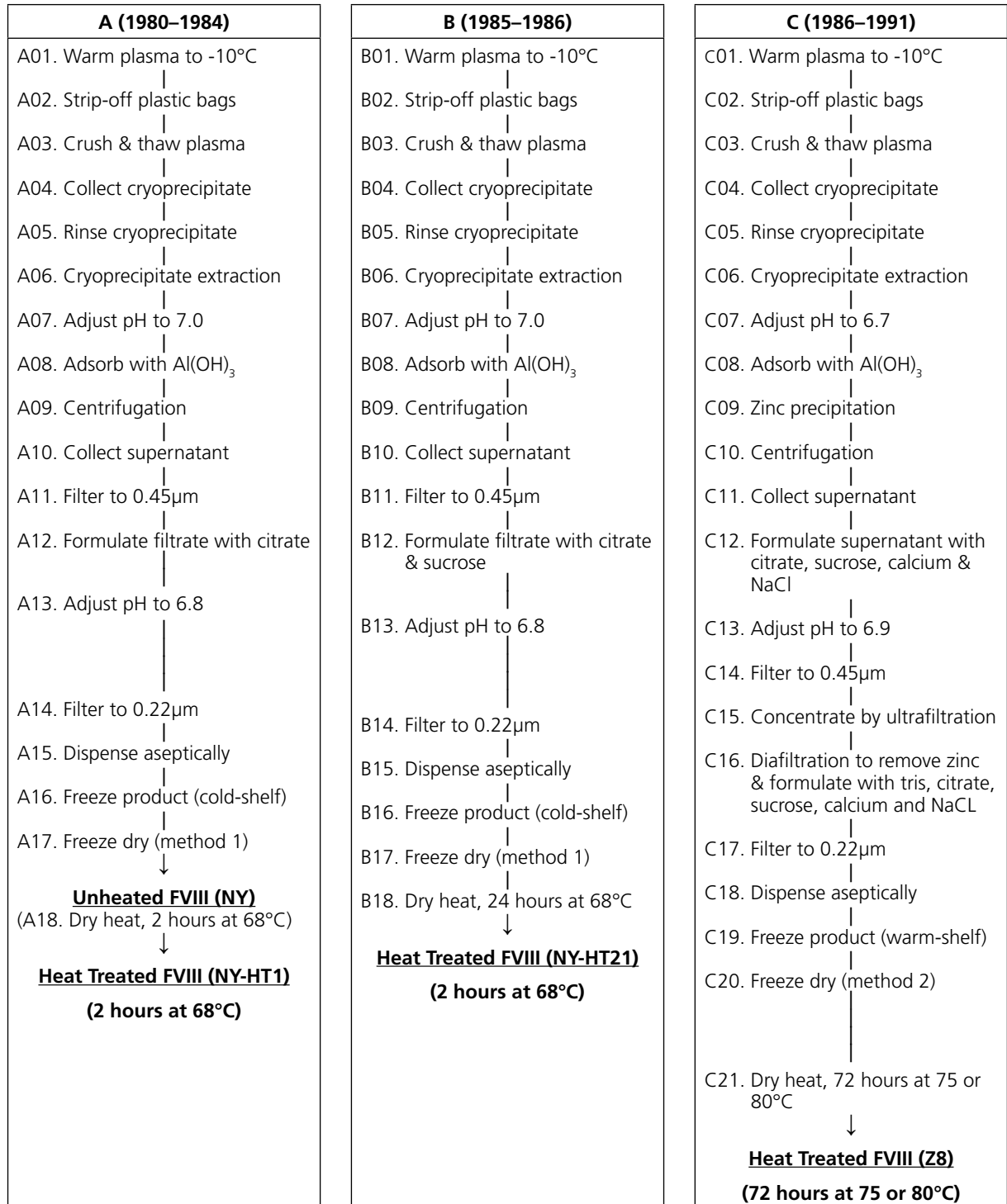
**20.76** On the eve of the outbreak of AIDS, therefore, there was a step change in perception of the possibilities of heat treatment to inactivate hepatitis viruses, but continuing scepticism among scientists. Meantime, research in England, led by Dr John Craske, was reaching the conclusion that all Factor VIII concentrates in production in the early 1980s, imported or NHS, were potentially infective for NANB Hepatitis. The scene was changing rapidly. Viral inactivation by heat treatment is discussed in the following chapters.

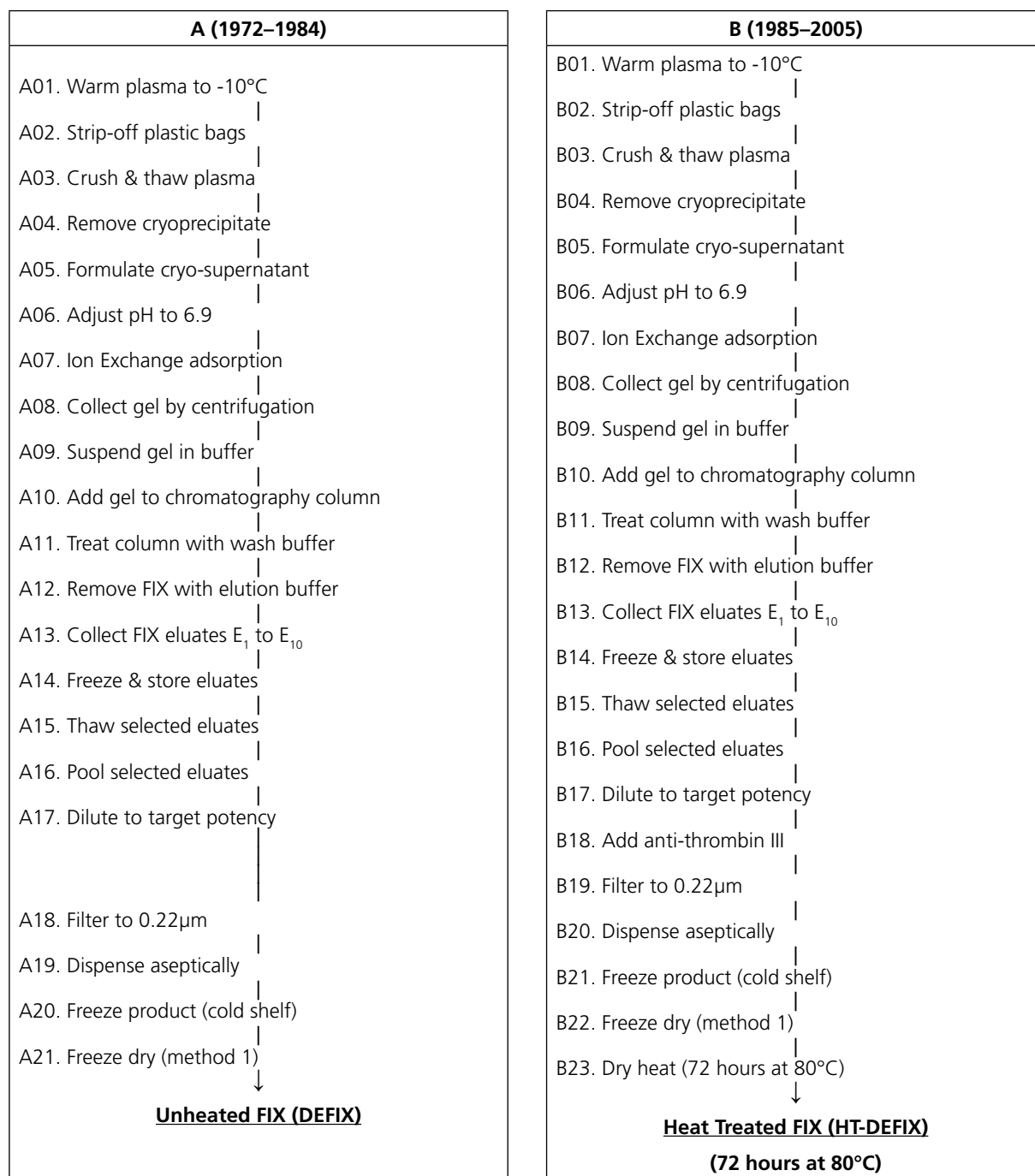
---

<sup>102</sup> Ibid [PEN.012.1438] at 1448–49

**Figure 20.1**  
**Simplified process flow-sheet for the fractionation of plasma at the pfc at the end of 1983**



**Figure 20.2 (A, B & C)****Outline Processes for the Preparation of Factor VIII Concentrate at PFC, 1980–1991**

**Figure 20.3 (A & B)****Outline Processes for the Preparation of Factor IX Concentrate (DEFIX) at PFC**



# CHAPTER 21

## HAEMOPHILIA THERAPY – USE OF BLOOD PRODUCTS

### Introduction

**21.1** Aspects of two of the Terms of Reference set the general context for discussion of the topics dealt with in this and the 10 chapters:

1. To investigate the systems in place in Scotland for the ... preparation for supply and supply for use by the NHS of blood and blood products with particular reference to the risks of transmission of the Hepatitis C virus ... to patients treated by the NHS in Scotland ....

and

8. To investigate the steps taken by those involved in, and those responsible for, the NHS in Scotland including NHS boards and SNBTS, their officers and employees and associated agencies, to prevent the provision of infected blood and blood products.

**21.2** Reports of AIDS in haemophilia patients treated with blood products, and with no other risk factors for AIDS, brought about a major change in the approach to factor concentrate therapy in the treatment of coagulation disorders in 1983–84. Up to that point, the focus was on the risk of transmission of hepatitis arising from the use of coagulation therapy and on the risk of other adverse effects of therapy such as the development of inhibitors. The history of developing knowledge of hepatitis is discussed in Chapter 14, *Knowledge of Viral Hepatitis 1*, and Chapter 15, *Knowledge of Viral Hepatitis 2 – 1975 to 1985*. It will be appropriate to rehearse some of that history in this chapter to provide context for the decisions taken by haemophilia clinicians in selecting products for therapy.

**21.3** It is necessary to disentangle a number of interrelated strands of history to provide a reasoned response to the Terms of Reference. It is clear, however, that in reality the developing position over this period was 'multifactorial', an expression used frequently in the course of the evidence.

**21.4** The arrival of commercial concentrates in 1973 changed market conditions, and had an impact on the public sector producers in the UK as a whole. Coincidentally, plasma fractionation facilities in Scotland and in England were in the course of or about to undergo major structural changes at the Protein Fractionation Centre (PFC) and the Blood Products Laboratory (BPL) respectively.<sup>1</sup>

**21.5** The first use of commercial concentrates from 1972 coincided with the identification of the Hepatitis B virus (HBV), an agent responsible for blood-borne hepatitis, and development of a test to indicate exposure to HBV by presence in the blood of its surface antigen, subsequently referred to as HBsAg. For a brief period it was hoped that using the HBsAg test to identify all blood donors previously exposed to, and possibly still infected by, HBV would eliminate post-transfusion hepatitis and hepatitis among people with haemophilia. By 1975, studies (mainly in the USA) were indicating that there were one or more other infective agents responsible for a significant proportion of post-transfusion

---

<sup>1</sup> See Chapter 19, *Production of Blood Products – Facilities*

hepatitis, the so-called non-A, non-B Hepatitis (NANBH) virus(es). Producers of Factor VIII products and haemophilia clinicians prescribing their use were faced with a dilemma: whether, on the one hand, to manufacture and use products to relieve real and known risks to the patient and accept the relatively unknown or partially understood risks associated with developing therapy, or, on the other hand, avoid treatment altogether. No form of therapy was without risk to the patient. As commented in Chapter 2, *Patients at Risk*, some risks are inherent in the use of human blood and its components and are always present. Whole blood, fresh and fresh frozen plasma and cryoprecipitate were all associated with risk of transmission of virus infections such as hepatitis.

**21.6** AIDS became the most significant consideration for patients and for medical and scientific staff in the period from about 1982 to about 1985. There are no precise dates that define the period more particularly. After about 1985, transmission of NANBH (later the Hepatitis C virus) and its natural history emerged as the main focal points affecting the management of patients. This chapter will deal with developments before the AIDS period. However, it will be convenient to deal with statistical data for the period to 1991 as a whole.

**21.7** It has been necessary to deal with some aspects of the relevant history separately. The evolution and manufacture of blood products before and during the period was dealt with in Chapter 20, *Haemophilia Therapy – The Period up to the Early 1980s*. This chapter deals with the availability and use of human blood products in haemophilia therapy.

### **Treatment of haemophilia: Overview**

**21.8** Until well into the twentieth century, treatment of haemophilia and other coagulation deficiencies and the complications associated with the diseases was rudimentary. Whole blood or fresh plasma might be transfused in an attempt to replace missing or deficient levels of clotting factors. A major risk associated with those forms of treatment was overload of the recipient's circulatory system which could result in heart failure. From about 1941, human plasma was freeze-dried (lyophilised).<sup>2</sup> The preparation of frozen plasma from whole blood was the first step towards developing therapeutic plasma products. In freeze-dried form, plasma had a substantial shelf-life. It could be stored for up to three months without perceptible change.<sup>3</sup> That removed the need for immediately available supplies of fresh plasma. But it did not solve the problem of circulatory overload.

**21.9** Professor Christopher Ludlam explained the treatments that were available before concentrates were developed.<sup>4</sup> If bleeding into a joint occurred, the patient was advised to take bed rest. He might spend up to several weeks resting until the painful swelling gradually subsided. Fresh frozen plasma was administered on occasion but, because of the risk of overloading the circulation, it was not given in quantities large enough to raise the patient's Factor VIII level sufficiently to stop the bleeding. A bleed was a significant event, often requiring a stay in hospital.

**21.10** A major advance in therapy came in the 1950s with the development of methods of plasma fractionation. This enabled the production of early forms of coagulation factor concentrates. From the 1960s, a simpler process of partitioning of whole blood led to

---

<sup>2</sup> Foster, 'Plasma Fractionation in Scotland', *Blood Letter*, Spring 2008; 21–25 [PEN.017.2468]

<sup>3</sup> Newman et al, 'Methods for the Production of Clinically Effective Intermediate- and High-Purity Factor VIII Concentrates', *British Journal of Haematology*, 1971; 21:1 [SGF.001.1913]

<sup>4</sup> Professor Ludlam's draft, *Expert Report Human Immunodeficiency Virus Infection in Haemophiliacs*, 1990 [PEN.015.0385]

the production of cryoprecipitate.<sup>5</sup> Subject to availability of supplies, by the very early 1970s, haemophilia clinicians had at their disposal, in addition to fresh frozen plasma, early concentrates of Factor VIII and Factor IX, and cryoprecipitate.

**21.11** As set out in Chapter 19, *Production of Blood Products – Facilities*, there was considerable uncertainty about the levels of demand for haemophilia therapy in the UK as a whole in the late 1960s and early 1970s. That affected the planning of production facilities in England and in Scotland. It also affected perceptions of developments in the market for blood products. When development of the NHS plasma fractionation facilities was planned, there was a poor understanding of the likely drivers of domestic demand for haemophilia therapy. The history of reactive, and often in-patient, treatment of bleeds, with a limited range of therapeutic materials, did not prepare policy-makers or the public sector manufacturers of blood products for changes in clinical practice that generated ever-increasing demand for concentrates, and for improvements in their effectiveness and ease of use.

**21.12** In general terms it was understood that demand would rise. In *Self-Sufficiency in Blood Products in England and Wales: a Chronology from 1973 to 1991*, the Department of Health (DoH) commented:

It became apparent in early 1973 that production of factor VIII concentrate in the UK was insufficient to meet the stated needs of clinicians. There was a body of evidence suggesting that considerably more concentrate would be used if it were available.<sup>6</sup>

However, the general understanding reflected in the statement did not inform planners of the enormous scope for use of coagulation products that was to emerge.

**21.13** As a result, there was a deficiency in planning. It is, however, relevant to note that by 1973 forms of concentrate had been produced in the UK for nearly 20 years, and cryoprecipitate had been readily available for about 15 years. Actual demand for therapeutic materials had been limited by the supplies available. Clinicians could not prescribe what they could not procure, and there was to prove to be very substantial unmet demand. But it had also taken a considerable time for the potential of coagulation products to be understood, and growing knowledge aggravated the problems of supply as clinicians explored treatment options. Furthermore, by no means all patients with haemophilia who might require treatment had been identified by 1973 in the UK.

**21.14** In 1973, Scotland was preparing to move production to a new PFC facility that would change the supply position in this country, but not because of a more accurate assessment of domestic Scottish needs in response to changing demand. In that respect the Scottish position was similar to that in England and Wales ('UK' in DoH terms): the potential demand was underestimated. Commercial pharmaceutical companies had already identified the market for increased supplies of concentrates. On 3 December 1972 Baxter applied for a UK licence for Hemofil, which was granted on 19 February 1973. On 8 December Immuno applied for a UK licence for Kryobulin, which was granted on 22 March 1973.<sup>7</sup> Early release of their products stimulated demand.

<sup>5</sup> See Chapter 20, *Haemophilia Therapy – The Period up to the Early 1980s*, paragraphs 20.21–20.24

<sup>6</sup> *Self-Sufficiency in Blood Products in England and Wales: a Chronology from 1973 to 1991*, Department of Health, 2006 [DHF.003.0931] at 0947

<sup>7</sup> Chronology of events with relevance to 'self-sufficiency', Hepatitis C transmission and the establishment of terminal dry heat treatment for UK coagulation factor concentrates, Department of Health [SGH.002.1313]

### Treatment policy in England and Wales: The early 1970s

**21.15** During 1972, the majority of Haemophilia Centre Directors in England and Wales had expressed a preference for freeze-dried concentrate therapy.<sup>8</sup> Dr Brian Colvin said that he and his colleagues at the London Hospital began to use them in 1970.<sup>9</sup> It seems likely that, at such an early date, the materials would have been used in clinical trials. Commercial products were more generally available and in use on a named patient basis in 1972.

**21.16** On 6 March 1973 a letter was sent by the Chief Medical Officer (CMO) for England and Wales to all senior administrative medical officers (SAMOs) advising them that two product licences referred to had recently been granted to Baxter and Immuno which enabled the licensees to supply foreign human Anti-haemophiliac Globulin (AHG) concentrate to hospitals and haemophilia centres in the UK. Hemofil and Kryobulin could now be prescribed as licensed products.<sup>10</sup> The CMO noted that AHG concentrate was in many instances the therapeutic agent of choice in the treatment of haemophilia patients, and that at the time production of concentrate in the UK was insufficient to meet the stated needs of clinicians who cared for patients requiring surgical, including dental, treatment or who had episodes of severe bleeding. The letter noted that one of the two firms had indicated that it could supply large quantities of AHG. The dynamics of the market place were obvious: if the UK (and more specifically England and Wales) had the demand, the pharmaceutical companies could supply it.

**21.17** But there were serious concerns about the very high cost of the foreign AHG. An expert group was set up by the Medical Division of the Department of Health to assess need and arrangements for the purchase of the product and also the possibility of producing sufficient material in the UK, and to advise the Department.<sup>11</sup> The expert group included representatives from Scotland, and policy recommendations reflected the view held at that time that it was essential that the production and distribution of the therapeutic agents for haemophilia care should be considered as a UK exercise. However, the data on demand and supply discussed by the group related mainly to England and Wales.

**21.18** So far as they related to planning of domestic production, the expert group's views are discussed in Chapter 19, *Production of Blood Products – Facilities*.<sup>12</sup> It was recognised by the group that the number of registered patients with haemophilia underestimated the scale of demand.<sup>13</sup> It was thought that 3000 was a reasonable estimate of the number of individuals affected with haemophilia. The discussion covered the grounds for preference of cryoprecipitate and freeze-dried concentrate over other products and their relative advantages and disadvantages.

**21.19** The reported discussion of the group provides insight into the view of risk associated with therapeutic products that was prevalent at the time. As a practical matter, transmission of Hepatitis B was the central issue.

The present policy of rejecting donations which give a positive test for hepatitis B antigen will reduce the incidence of virus in the blood used to make plasma pools. In practice, studies in several centres have shown that the incidence of

<sup>8</sup> Note of meeting of Expert Group on the Treatment of Haemophilia, 20 March 1973 [SNB.006.7631] at 7633

<sup>9</sup> Dr Colvin – Day 2, page 119

<sup>10</sup> CMO's letter of 6 March 1973 [DHF.001.2122]

<sup>11</sup> Ibid [DHF.001.2122] at 2124

<sup>12</sup> Paragraphs 19.26–19.30

<sup>13</sup> Note of meeting of Expert Group on the Treatment of Haemophilia, 20 March 1973 [SNB.006.7631]

hepatitis among severely affected patients who have been treated with the freeze-dried preparation is not very much higher than that at centres not using freeze-dried concentrate and this suggests that the development of hepatitis in these multitransfused patients may be dose-related. It was agreed that the theoretically increased risk of acquiring hepatitis (which does not seem to be borne out in practice) should not be a deterrent to using the freeze-dried preparation and in any case this complication will decrease with universal screening of donors for hepatitis antigen.<sup>14</sup>

It was agreed within the group that products from 400,000 donations would be required to treat UK sufferers from haemophilia of all degrees of severity. More would be required if strenuous efforts were made to clear surgical waiting lists and if home treatment, or eventually prophylactic treatment, became accepted ways of dealing with the needs of haemophilia patients. Demand exceeded NHS production capacity, but it was agreed that:

Since more freeze-dried AHG concentrate has become available from two foreign sources the prospects of improved management of day-to-day bleeding episodes using this therapeutic agent has become realistic.<sup>15</sup>

**21.20** It was accepted at that stage, as a reality, that the NHS production facilities in England could not cope with the anticipated demand and that commercial purchases would be necessary. NHS concentrate from 30,000 blood donations had been issued in England, Wales and Northern Ireland in 1972, as against the estimated future requirement of 400,000 donations.

**21.21** Recommendations of the group included:

- DHSS should give early consideration to central purchase of freeze-dried AHG concentrate from the firms who had recently been granted product licences.
- Distribution to haemophilia centres and hospitals in Scotland should be through the regional centres (either Edinburgh or Glasgow).
- Discussions were to take place between DHSS and the Regional Transfusion Directors about the problems of decreasing production of cryoprecipitate, increasing production of fresh-frozen plasma for fractionation and the possibility of increased collection of plasma by plasmapheresis.
- Home treatment and, in due course, prophylactic treatment were subjects that needed to be discussed further at future meetings.

**21.22** These recommendations, concentrating on practical implementation of policy, reflect the group's assessment of related risk. The general understanding of risk is discussed in Chapter 14, *Knowledge of Viral Hepatitis 1*. When the expert group met in 1973 the Maycock report for the MRC had not been published,<sup>16</sup> but when it did appear in 1974 the Maycock report would underestimate the true incidence of post-transfusion hepatitis, largely because of the requirements stipulated for a diagnosis of the disease.<sup>17</sup> Dr William

<sup>14</sup> Ibid [SNB.006.7631] at 7633

<sup>15</sup> Ibid

<sup>16</sup> Chapter 14, *Knowledge of Viral Hepatitis 1*, paragraph 14.20

<sup>17</sup> Ibid paragraph 14.22

Maycock was a member of the expert group, and knowledge of the report's findings can reasonably be assumed. At this stage it is sufficient to note that the expert group's discussions in 1973 did not reflect any perception that there was a relatively high risk of transmission of infection associated with commercial products, or that such increased risk as was recognised was significant.

### **Self-sufficiency**

**21.23** During the early and mid-1970s there was emphasis in UK Government policy on achieving self-sufficiency in blood and blood products, reflecting views expressed by the World Health Organization (WHO). The reasons advanced for self-sufficiency are again significant.

**21.24** In May 1975, a WHO resolution was passed by delegates conscious of the increasing use of blood and blood products. It urged Member States:

- To promote the development of national blood services based on voluntary non-remunerated donation of blood.
- To enact effective legislation governing the operation of blood services and to take other actions necessary to protect and promote the health of blood donors and of recipients of blood and blood products.

**21.25** In making its recommendations the WHO had considered:

[T]he extensive and increasing activities of private firms in trying to establish commercial blood collection and plasmapheresis projects in developing countries.

[C]oncern that such activities might interfere with efforts to establish efficient national blood transfusion services based on voluntary non remunerated donations.

[A]wareness of the higher risk of transmitting diseases when blood products have been obtained from paid rather than voluntary donors, and of the harmful consequences to the health of donors of too frequent blood donations (one of the causes being remuneration) ....<sup>18</sup>

Relative risk had been identified as an issue, focused on the dangers associated with paid donors.

**21.26** On 24 December 1974 the DHSS wrote to all regional administrators about the problems of blood product production and in particular the inability of the Blood Transfusion Service to meet the demands of clinicians for certain preparations of human blood. There was an immediate need to provide more AHG (Factor VIII) concentrate. The memorandum stated:

At present part of the demand ... is being met by expensive imported material which is now marketed in this country, and as the demand increases commercial firms may consider it worth their while to establish panels of paid donors in this country in order to obtain their supplies of human blood. Such

---

<sup>18</sup> WHO, World Health Assembly Resolution 28.72 of May 1975: *Utilization and Supply of Human Blood & Blood Products* [DHF.003.0764]

a development would constitute a most serious threat to the voluntary donor system upon which the NBTS is founded. The Department therefore regards it as of the greatest importance, quite apart from the question of cost, that the NHS should become self-sufficient as soon as practicable in the production of PPF [plasma protein fraction] and other blood products ....<sup>19</sup>

**21.27** There was a proposal to invite estimates of requirements in regional transfusion centres for the increased production of plasma, with the primary aim of making the NHS self-sufficient in AHG concentrate in two to three years.<sup>20</sup> The concern expressed in the circular letter reflected the second WHO point in paragraph 21.25: it did not express concern about relative infectivity.

**21.28** On one level that is hardly surprising. Following the CMO letters of March 1973, the DHSS had notified relevant parties in England and Wales in October 1973 that the supply division of DHSS had negotiated with Travenol Laboratories Ltd and Serological Products Ltd to enable haemophilia centres to purchase AHG concentrate.<sup>21</sup> This letter advised parties that the department was in close cooperation with the SHHD in considering ways of increasing NHS production. In November 1973 a circular letter was sent to Scottish administrative medical officers in very similar terms.<sup>22</sup> Adverse comment on commercial products generally would have been inconsistent with this approach to meeting need, and comment on specific products would have offered a hostage to fortune. But, perhaps more pertinent to this discussion, it reflected a common understanding in government that distinctions related to transmission of infection were not significant.

**21.29** In January and February 1975 Dr David Owen told the House of Commons that the amount of Factor VIII materials, including cryoprecipitate, produced within the NHS was not sufficient to meet demand at that time. In particular, there was an immediate need for AHG concentrate (acknowledged as the preferred treatment for haemophilia). Dr Owen stressed that it was of vital importance that the NHS should become self-sufficient as soon as practicable in the production of Factor VIII, including AHG concentrate. He announced that special finance of up to £500,000 had been allocated with the objective of the NHS becoming self-sufficient over the next few years, and expected that this would stop the dependence on commercial imports and make the best known treatment more readily available to people suffering from haemophilia.<sup>23</sup> There was no separate policy statement relating to self-sufficiency in Scotland at this time.<sup>24</sup> There was awareness in Scotland among all those working in the field that self-sufficiency was what was being sought: Dr Robert Perry referred to self-sufficiency as 'the only game in town'.<sup>25</sup>

**21.30** However, across the UK as a whole, the reality of burgeoning demand for Factor VIII replacement therapy posed a serious challenge to the government's commitment to self-sufficiency. Data are available for the amounts of Factor VIII concentrates used in the whole of the UK. Equivalent information is not available for the use of Factor IX or cryoprecipitate, both of which were largely produced locally and met local demand for NHS products. The discussion which follows does not present a comprehensive picture of

<sup>19</sup> DHSS letter of 24 December 1974 to Regional Administrators [DHF.002.9393]

<sup>20</sup> Ibid [DHF.002.9393] at 9394

<sup>21</sup> Letter from CMO to English Senior Administrative Medical Officers, 23 October 1973 [SGH.002.9308]

<sup>22</sup> Letter from CMO to Scottish Senior Administrative Medical Officers, 6 November 1973 [SGH.002.9306]

<sup>23</sup> HC Hansard, Vol 884, cols 392–3, 22 January 1975 [PEN.012.0185]; HC Hansard, Vol 887, cols 262–264, 25 February 1975 [PEN.012.0186]; HC Hansard, Vol 887, cols 144–146, 26 February 1975 [PEN.012.0183]

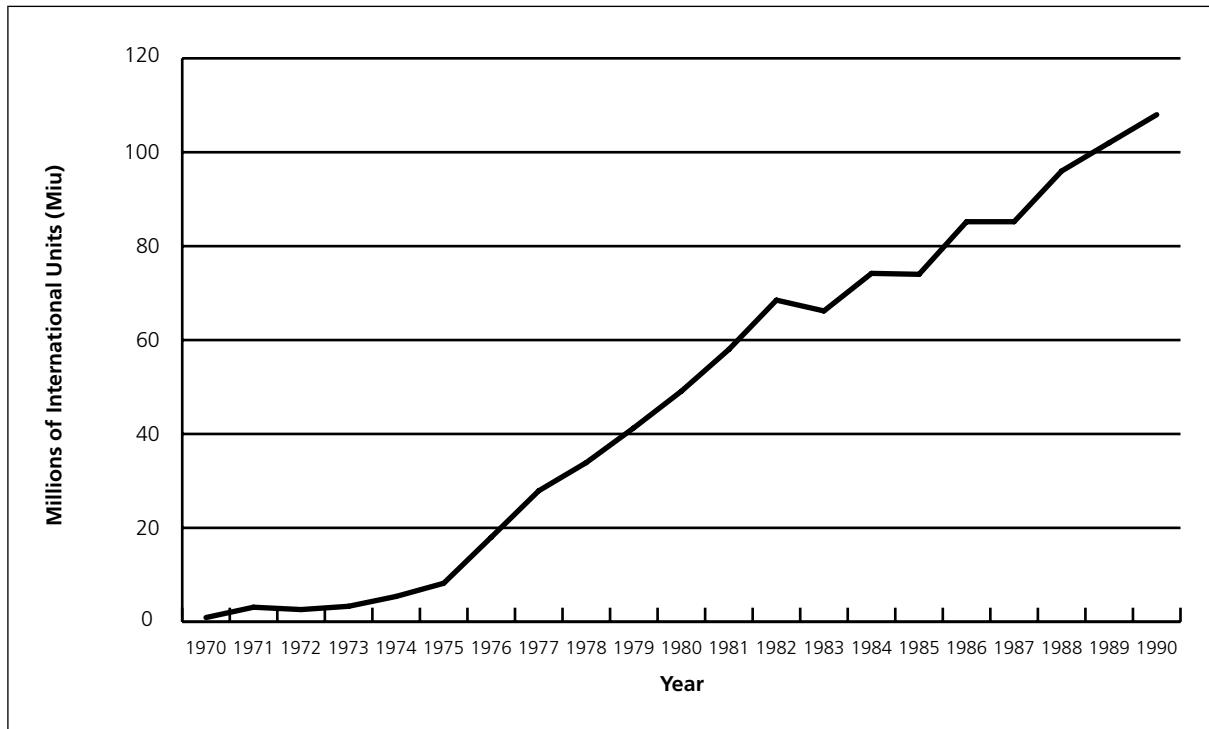
<sup>24</sup> Professor Cash – Day 25, pages 83–85

<sup>25</sup> Dr Perry – Day 25, page 5

total haemophilia, but it was the demand for Factor VIII that was the critical consideration in aiming at self-sufficiency.

**21.31** Total annual consumption of Factor VIII concentrates in the UK between 1970 and 1990 is shown in Figure 21.1. The data are set out in Table 21.1 in the Appendix to this chapter.

**Figure 21.1: Total annual consumption of Factor VIII concentrates in the UK, 1970–1990**



**21.32** These data for the UK as a whole show sustained growth in use of Factor VIII concentrates from 1975 onwards, with a dip in 1983 that was reversed thereafter. The dip in 1983 probably related to the switch to cryoprecipitate in response to the threat of AIDS.

**21.33** The trend shown in Figure 21.1 suggests planning for the provision of NHS Factor VIII based on experience up to the mid-1970s was unlikely to be remotely accurate. It would have required a high degree of imaginative foresight rather than statistical projection to forecast and provide for demand.

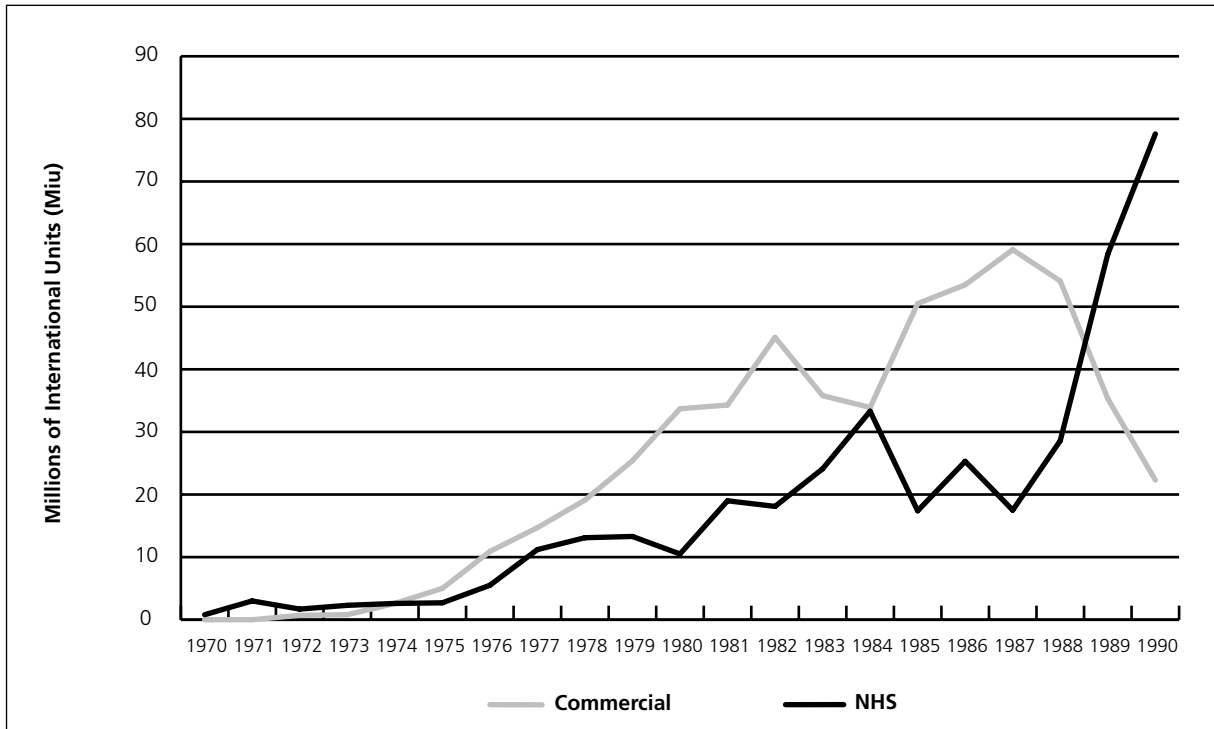
**21.34** Although all parts of the UK were subject to the same growing demand throughout this period, the circumstances in which the different parts of the UK found themselves towards the end of the 1970s led to the demand for Factor VIII concentrates being met in different ways.

**21.35** As events happened, and despite WHO encouragement, the target of self-sufficiency in England, Wales and Northern Ireland was most unlikely to have been achieved with the level of expenditure granted by Parliament while demand was left free to grow without restriction.



**21.36** Figure 21.2 shows, for England, Wales and Northern Ireland, the annual consumption of NHS and imported commercial Factor VIII concentrates between 1970 and 1990. The data are set out in Table 21.1 in the Appendix to this Chapter.

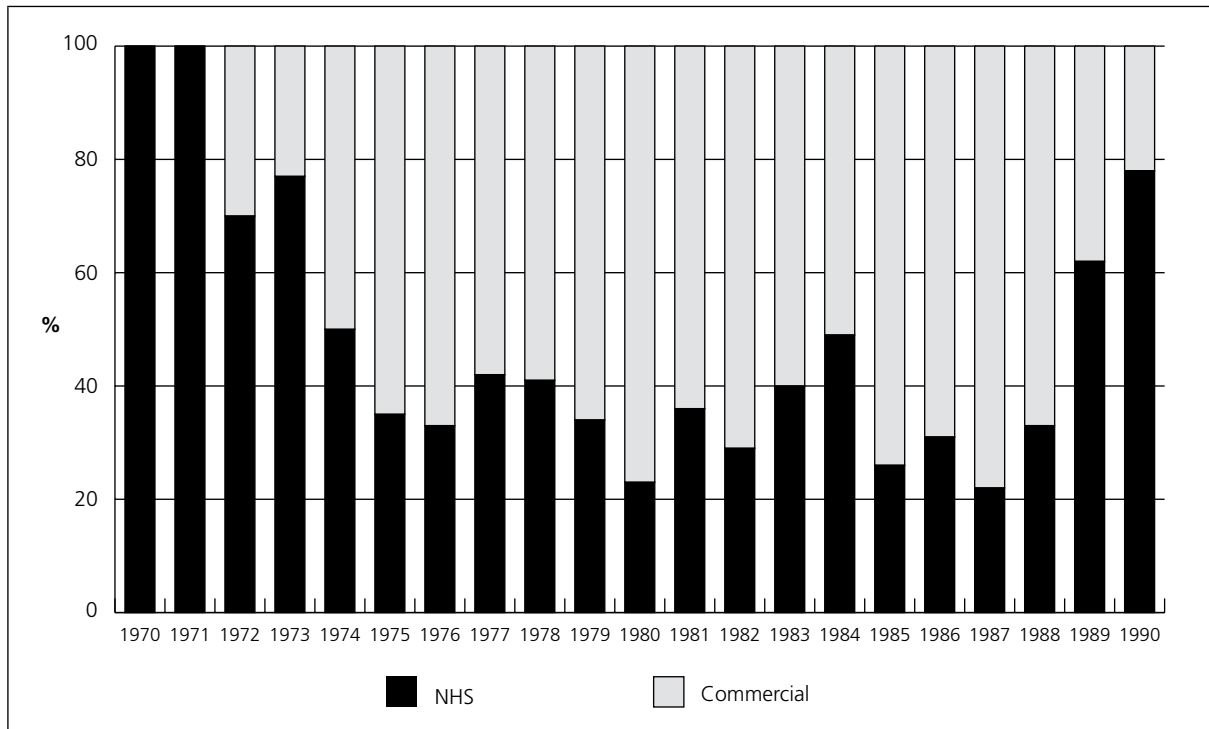
**Figure 21.2: Annual consumption of NHS and commercial Factor VIII concentrates in the UK, excluding Scotland, 1970–1990**



**21.37** Figure 21.2 illustrates the extent of the use by clinicians of imported commercial Factor VIII concentrate and, in respect of that product, shows the deficiencies in domestic supplies. The source data do not distinguish use related to clinical preference from use dictated by available supplies. Total use of commercial products cannot be explained exclusively on the basis of clinical choice in the circumstances, but it may have been a contributory factor. Subject to that, the overall impression is of rapidly increasing demand for Factor VIII concentrate, met substantially by imported product.

**21.38** Figure 21.3 shows, for the UK excluding Scotland, the percentage of total Factor VIII concentrate consumption from NHS and from commercial supplies in each year from 1970 to 1990. The data are contained in Table 21.1 in the Appendix to this chapter.

**Figure 21.3: Percentage of total Factor VIII concentrate consumption from NHS and commercial sources for the UK, excluding Scotland, 1970–1990**



**21.39** On the evidence before the Inquiry, there was some scepticism whether self-sufficiency was possible. In relation to England and Wales, Professor Cash said that he did not consider self-sufficiency was a realistic goal as there were insufficient resources. In his opinion, Scotland was already ahead of England and Wales in the mid-1970s in achieving this aim.<sup>26</sup>

**21.40** Professor Cash described the reaction to a talk he gave on the notion of self-sufficiency at a World Federation of Hemophilia congress in New York in 1977. His talk was interrupted by the then Chief Executive of Immuno, Dr Eibl, who, as Professor Cash recalled it, told the audience that he, John Cash, was talking nonsense and that the UK government did not accept that the WHO commitment to self-sufficiency was achievable. A member of the UK Haemophilia Society who was present, told Professor Cash that the Society agreed with Dr Eibl. Moreover, the Society did not think that the NHS would get anywhere near self-sufficiency in England and Wales.<sup>27</sup> Professor Cash thought that, despite the talk in England and Wales about self-sufficiency, 'they just weren't in the hunt' and had been told so.

**21.41** It is unnecessary, and would be inappropriate, to express any view on these observations. The steep increase in demand from 1975 would have challenged the ability of policy-makers to respond. Comparison with Scotland (so far as concerns the capacity to respond to increasing demand) is particularly inappropriate. It is necessary to bear in mind that, as discussed in Chapter 19, *Production of Blood Products – Facilities*, Scotland's favourable position in relation to meeting growing demand was due to the government providing resources to build a new centre – the PFC – at which it was originally aimed to process about a third of English plasma in addition to all Scottish plasma. Making use of

<sup>26</sup> Professor Cash – Day 25, pages 83–85

<sup>27</sup> Ibid pages 87–88

the Scottish facility for processing output of plasma produced in England and Wales was proposed in the Department of Health's letter to regional administrators on 24 December 1974, for example.<sup>28</sup> The failure to achieve a practical means of realising that policy objective made a significant contribution to Scotland's relative lack of dependence on imports, and aggravated the problem in the rest of the UK, in the 1980s.

### **Demand and supply in Scotland**

**21.42** In Scotland, as in the rest of the UK, there was interest in the impending arrival of commercial concentrates in the early 1970s. A Working Party was set up by the Central Consultative Committee on Blood Transfusion (CCC): 'To consider the production, laboratory and clinical evaluation of the various factor VIII and IX products in relation to the overall production capacity of the Blood Transfusion Service and to report.'<sup>29</sup> The group met on 21 September 1972 and the minutes of the meeting were circulated for discussion. It was estimated that 30,000 donations a year would be required for the production of Factor VIII concentrate.

**21.43** It was recorded that consideration must be given to how much Factor VIII should be provided in the form of cryoglobulin precipitate (cryoprecipitate) and how much in the form of an AHF (Factor VIII) concentrate prepared by the fractionation unit (then still a small-scale operation at the Royal Infirmary of Edinburgh (RIE)). The recent appearance of commercially prepared concentrate was also discussed, although licences had not been granted at that point. It was agreed that treatment in the form of cryoprecipitate would continue for most patients for the foreseeable future but the desire was to replace this treatment and Cohn Fraction I with a potent AHF concentrate. Such a concentrate was liable to be subjected to more rigorous quality control. However it was conceded that estimating demand for a new product was difficult and was on a 'guess at best' basis.

**21.44** Availability of a 'super-concentrate' (the commercial concentrate) was discussed in Scotland when the CCC itself met on 15 March 1973.<sup>30</sup> The general feeling was that Scotland should be able to manufacture enough of its own product from Scottish blood donations and would only require commercial material in very small quantities. By this time the estimated requirement of 30,000 donations a year for production of Factor VIII concentrate for Scottish patients was thought likely to be an underestimate, and the more realistic figure would be 50,000 donations.<sup>31</sup>

**21.45** On 28 March 1973, the SHHD issued a letter to the SAMOs (copied to the Directors of Haemophilia Centres, Regional Directors of the Blood Transfusion Service (BTS) and the Scientific Director of PFC) on 'Trends in the Treatment of Haemophilia', in terms almost identical to the English CMO letter of 6 March 1973.<sup>32</sup>

**21.46** Total annual consumption of Factor VIII concentrates in Scotland between 1970 and 1990 is shown in Figure 21.4. The data are set out in Table 21.1 in the Appendix to this chapter.

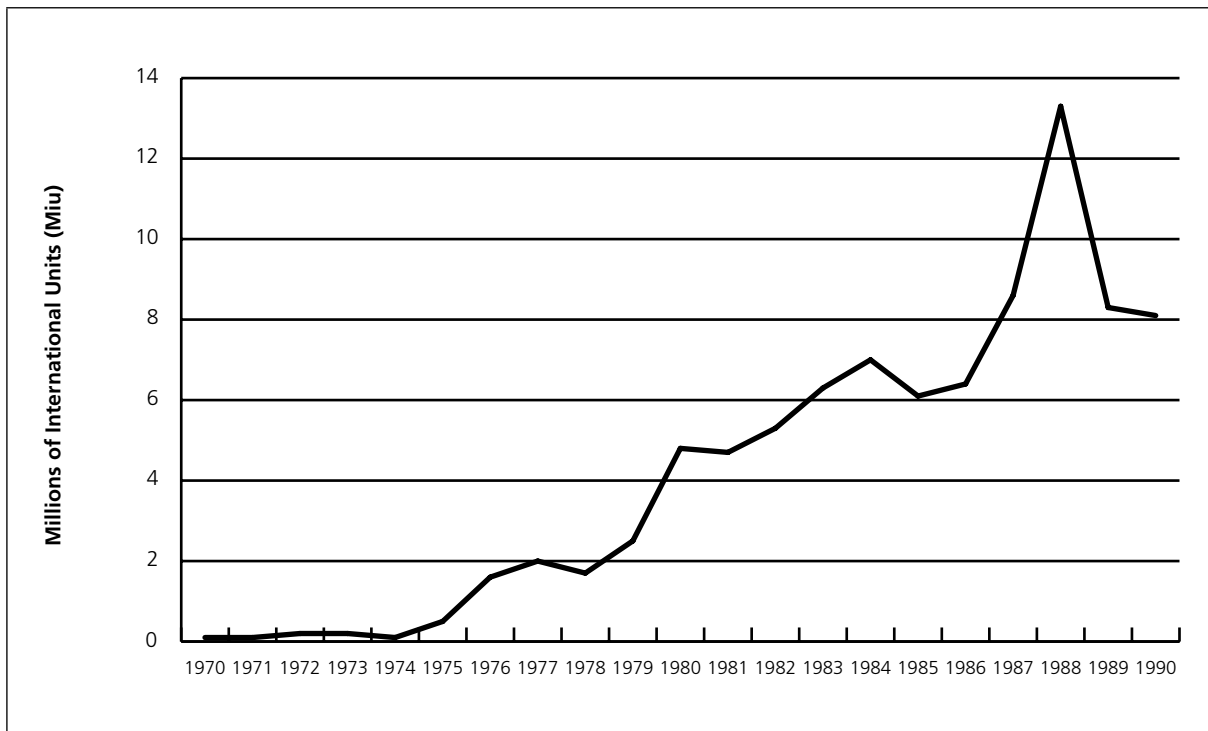
<sup>28</sup> DHSS letter of 24 December 1974 to Regional Administrators [DHF.002.9393] at 9393–94

<sup>29</sup> Note of meeting of Working Party on Products Containing Factor VIII and IX, 21 September 1972 [SNB.007.2128]

<sup>30</sup> Minutes of Central Consultative Committee on Blood Transfusion, 15 March 1975 [SNB.010.2011]

<sup>31</sup> Ibid [SNB.010.2011] at 2013

<sup>32</sup> Letter from CMO to Scottish Senior Administrative Medical Officers, 28 March 1973 [SGH.002.9309]; see paragraph 21.17 for the English letter of 6 March 1973

**Figure 21.4: Annual consumption of Factor VIII concentrates in Scotland, 1970–1990**

**21.47** Information provided to the Inquiry by the United Kingdom Haemophilia Centre Doctors' Organisation (UKHCDO) for this period is not complete.<sup>33</sup> There are gaps in some early years which affect the reliability of the data until the mid-1970s. But the trend in consumption of Factor VIII concentrates is sufficiently well defined for comparison with the rest of the UK.

**21.48** As in the rest of the UK, the data show sustained growth in use of Factor VIII concentrates from about 1975 onwards. Figure 21.4 shows a significant spike in consumption in 1988. This is accounted for by a major rise in demand at the Royal Hospital for Sick Children (Yorkhill) in Glasgow, and is discussed further at paragraph 21.292 below.

**21.49** There is no obvious explanation for the dip in consumption of Factor VIII concentrates in 1985 and 1986. It cannot be related to a switch to cryoprecipitate in response to the threat of AIDS, as was the position in 1983 in the rest of the UK. Effective viral inactivation had been introduced at the beginning of 1985. Nor do SNBTS figures for the amount of frozen plasma collected through this period suggest any supply constraints.<sup>34</sup>

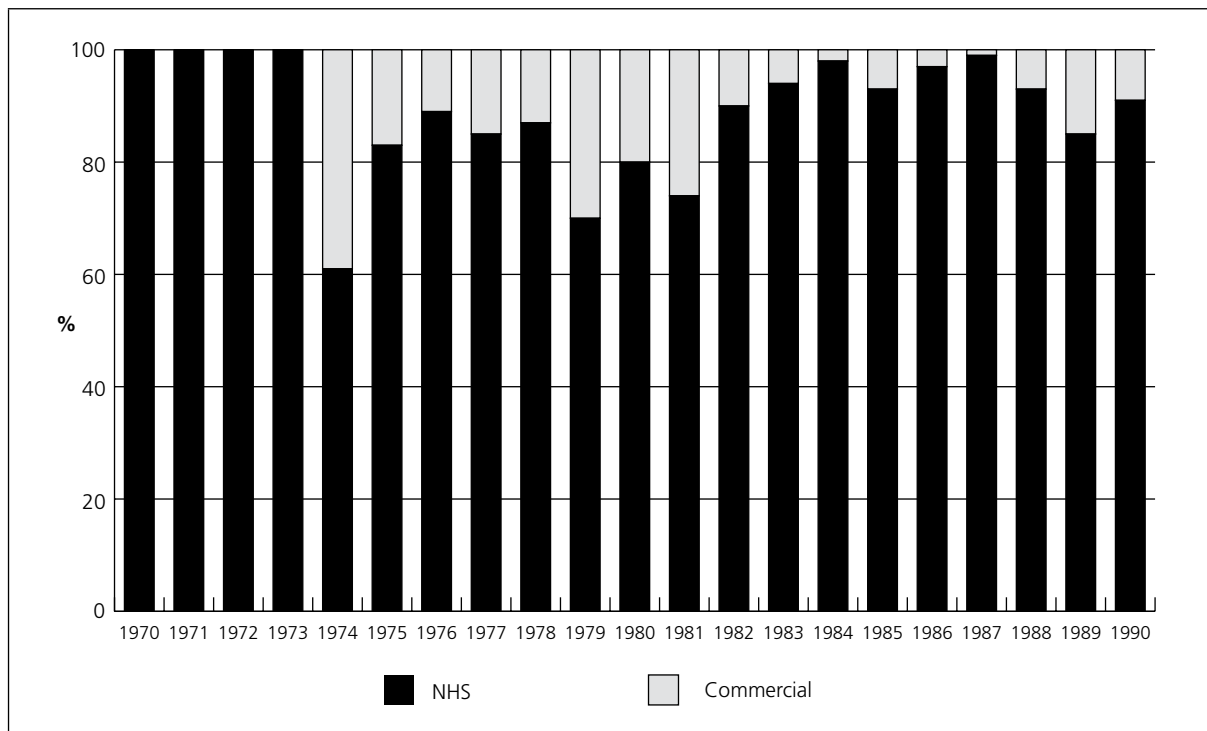
**21.50** Scotland, in common with the UK as a whole, experienced a rise in demand for Factor VIII concentrates from the beginning of the Inquiry's reference period until the late 1980s that was far in excess of what those involved in planning at the beginning of the 1970s could have expected. The inability of NHS sources to supply demand inevitably led to the importation of commercially prepared products from North America from 1972. Nevertheless, in comparison with the rest of the UK, Scottish production met a substantial proportion of the demand for Factor VIII concentrates.

<sup>33</sup> *National Haemophilia Database: Bleeding disorder statistics for the Penrose Inquiry*, UKHCDO, April 2012 [PEN.019.0927] at 0933-34

<sup>34</sup> SNBTS paper, *Self-Sufficiency and the Supply of Blood Products in Scotland*, February 2011 [PEN.013.1125] at 1158–59

**21.51** Figure 21.5 shows the percentage of total Scottish Factor VIII concentrate consumption met from NHS and from commercial supplies in each year from 1970 to 1990. The data are contained in Table 21.1 in the Appendix to this chapter.

**Figure 21.5: Percentage of Scottish Factor VIII concentrate consumption from commercial and NHS sources, 1970–1990**



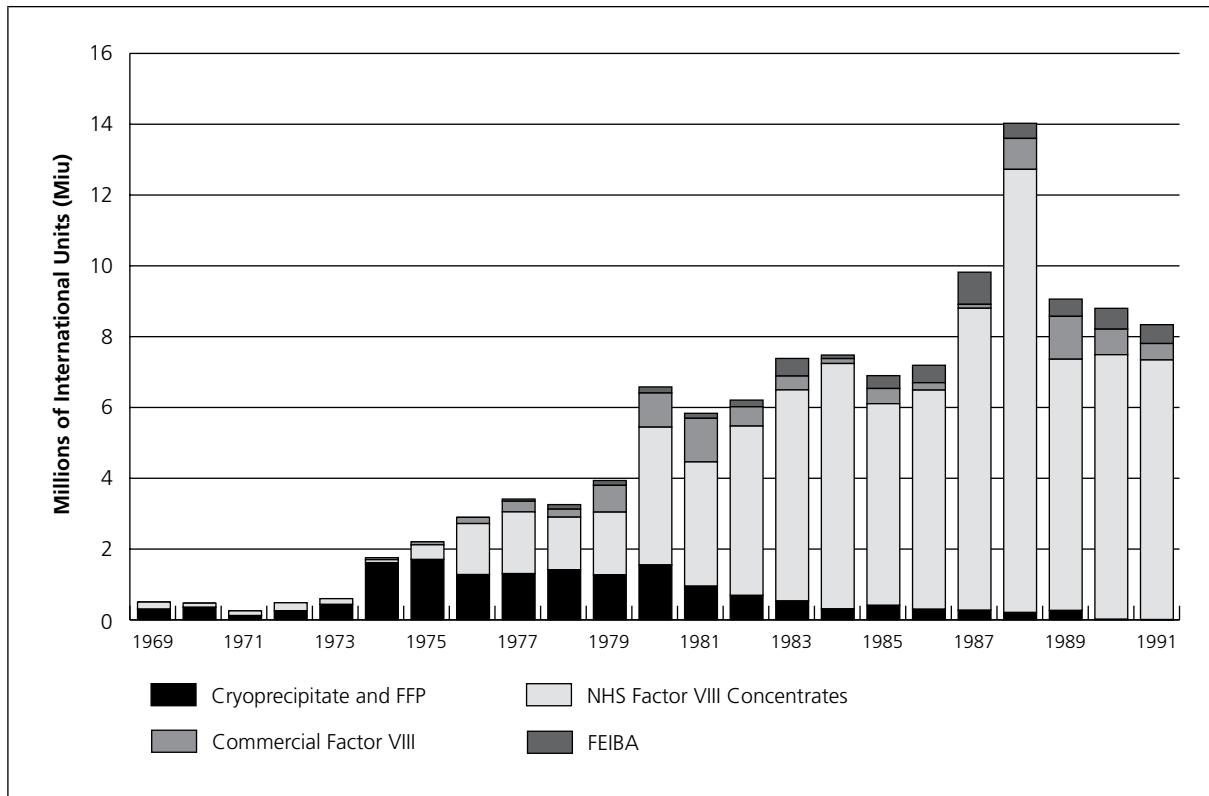
**21.52** As is apparent from Figure 21.5, total use of NHS concentrates far exceeded use of commercial Factor VIII products throughout the period, even in 1974 when the PFC's production was disrupted by the move to Liberton. In Figure 21.5, NHS data include some material sourced from the BPL for Scottish use. But the amounts were relatively small, in total, and do not materially affect the position. As already indicated in paragraph 21.41, production facilities in Scotland had considerably more capacity relative to total domestic demand than was available in England and Wales.

### Choice of therapeutic products

**21.53** The comparative exercise discussed above, as between Scotland on the one hand and the rest of the UK on the other, does not take account of all therapeutic materials used for Haemophilia A therapy over the period 1969–91, and it is necessary to turn to that topic at this stage in order to describe fully what happened in Scotland. As already indicated, for all of the period there was some use of cryoprecipitate, very small amounts of fresh frozen plasma, and FEIBA in addition to Factor VIII concentrates. Cryoprecipitate and fresh frozen plasma were prepared from single donations (though usually administered in pools or in succession in larger numbers) and, for present purposes, can conveniently be grouped. FEIBA was not used exclusively in treatment of patients with Haemophilia A, but had a significant place in the treatment of Factor VIII deficient patients with inhibitors. There are no data to enable the allocation of total FEIBA between Haemophilia A, Haemophilia B and other blood coagulation disorders. From 1979 onwards there was some limited use of DDAVP, but the quantities were insignificant in relation to total use and have not been noted at this stage.

**21.54** Figure 21.6 shows the use of Factor VIII replacement products in Scotland between 1969 and 1991. The data are set out in Table 21.2 of the Appendix to this chapter.

**Figure 21.6: Scottish use of Factor VIII replacement products in Millions of International Units (Miu) – 1969–1991**



**21.55** As noted above, some caution must be used when looking at the data for the early part of the period. At that time, cryoprecipitate and fresh frozen plasma were the principal therapeutic products in use. NHS Factor VIII concentrate then grew in significance, and remained the principal product in use throughout the period. Commercial Factor VIII concentrate remained a small proportion of the total, as did FEIBA.

**21.56** In practice, individual haemophilia clinicians exercised a degree of autonomy in the selection and prescription of products, if they had independent funds or if the relevant health authority supported the choice. Within Scotland there were significant variations between regions, which will be discussed later in this chapter. There were, however, a number of general factors that had an influence on product choice.

**21.57** The PFC's move to Liberton interrupted production in the early part of this period. Bulk stocks of intermediate Factor VIII were prepared at the RIE to carry over the transitional period. In addition, to effect a smooth changeover from cryoprecipitate to intermediate Factor VIII in the treatment of haemophilia an initial stockpile of about one million units was required, and stocks were built up in anticipation of that change.<sup>35</sup>

**21.58** Two observations are appropriate. First, the total issues of Factor VIII concentrates before the PFC was commissioned were relatively small: there was not much AHG available for issue to regions until the PFC was fully in operation, when there was a rapid build-up

<sup>35</sup> Minutes of SNBTS Directors Meeting, 15 October 1974 [SNB.002.4952]

of output. Secondly, although there was a major increase in use of cryoprecipitate and fresh frozen plasma in 1974 and 1975, coinciding with the transitional period at the PFC, use of cryoprecipitate continued to be significant for the rest of the decade until falling away after 1980.

**21.59** Some clinicians, however, were beginning to express views, as early as 1974, on the future availability of products to meet changes in clinical practice. On 18 December 1974, Dr Howard Davies, then Director of the haemophilia centre of the RIE wrote to Professor Cash (copying in John Watt of the PFC) stating that he hoped that sufficient supplies of human intermediate Factor VIII concentrate would be available in Edinburgh in January 1975 to cover the operative needs of his haemophilia patients and enable him to start some of them on home therapy.<sup>36</sup> In response, John Watt sent a telex to Professor Cash on 23 December 1974 suggesting that Dr Davies needed to be a little patient a little longer. He explained that production of Interate<sup>37</sup> had not yet started and he envisaged that volume problems would continue until supplies of fresh frozen plasma increased to a reasonably stable figure above 500 donations per week. He estimated that regular output would not be available until April.<sup>38</sup> However, timetable apart, it appears clear that clinicians' choice of product would become a more significant issue once the PFC was in full production.

**21.60** Scottish clinical practice was entering a period when clinicians' choice would be made against a background of more ample supplies of therapeutic products than had previously been available. Already, however, Dr Davies had pointed to two aspects of practice that were to increase pressure on supplies: elective surgery and the move to home treatment.

**21.61** Whether Scotland achieved self-sufficiency in the events that happened is, to some extent, dependent on the definition of demand. In an environment in which individual clinicians were free to select commercial products, given appropriate funding by local health authorities, by industry or by charities, actual demand for NHS products cannot be a reliable measure of total demand. Where available supplies are known to be limited, clinicians may have accepted the reality and avoided making demands on the NHS facilities that could not be met. Dr Peter Foster commented:

I think if you go back into the 1970s, when PFC was really still getting going and usually doctors were moving forward with home therapy, there is clearly correspondence where SNBTS is really saying, 'Look, we can't provide more at the moment, and the choice is for you', and they decide to buy commercial product because they want to do home therapy. So there is a period when clearly there is a discontinuity between the aspirations of the clinicians and what we can provide.<sup>39</sup>

**21.62** In the mid-1970s the Scottish internal market had not settled, and choice may not have been real. However, Dr Foster prepared a report on 'Self Sufficiency and the Supply of Blood Products in Scotland', with particular reference to the treatment of Haemophilia A which is helpful.<sup>40</sup> He tabulated the amounts of Factor VIII available from the SNBTS

<sup>36</sup> Dr Davies' letter of 18 December 1974 to Dr Cash [SNB.007.2254]

<sup>37</sup> Interate was the new PFC Factor VIII product.

<sup>38</sup> Mr Watt's telex of 23 December 1974 to Dr Cash [SNB.007.2255]

<sup>39</sup> Dr Foster – Day 22, pages 129–130

<sup>40</sup> SNBTS paper, *Self-Sufficiency and the Supply of Blood Products in Scotland*, February 2011 [PEN.013.1125]

compared with the amounts used clinically (as understood from UKHCDO data available before revision for the purposes of the Inquiry) in the period 1975–88. The data, expressed in terms of million units per head of population at each year, are reproduced below.<sup>41</sup>

Year	Total SNBTS FVIII Available (Miu per pop.)		Proportion of Clinical Use Matched by Available FVIII from SNBTS (% average UK use per pop.)	
	Incl. Cryo	Excl. Cryo	Incl. Cryo	Excl. Cryo
1975/76	0.97	0.21	202	111
1976/77	0.86	0.33	134	103
1977/78	0.99	0.39	129	100
1978/79	1.11	0.44	134	70
1979/80	1.27	0.69	136	89
1980/81	1.49	0.99	141	109
1981/82	1.48	1.14	123	105
1982/83	1.80	1.55	138	129
1983/84	1.94	1.71	149	142
1984/85	2.85	2.60	204	197
1985/86	2.56	2.23	180	163
1986/87	2.75	2.50	177	166
1987/88	2.20	1.93	138	125

**21.63** Dr Foster’s data and the UKHCDO data were prepared on different bases, with reference to overlapping periods: they cannot be correlated precisely. However presented, the data paint a very different picture from that shown for England, Wales and Northern Ireland so far as concerns the balance between use of NHS product and commercial product. It is necessary to bear this in mind when considering comments on the supply position in the ‘United Kingdom’, particularly in documents recovered from UK departments. Throughout the UK (including Scotland), however, there was a similar increase in demand overall. In the early 1980s, annual consumption of Factor VIII concentrate in Scotland, as registered by the UKHCDO, more than doubled in comparison with the late 1970s.

**21.64** In relation to his data, Dr Foster concluded:

The data in Table 18 [reproduced at paragraph 21.62 above] indicate that at any point in time the SNBTS had available sufficient Factor VIII to meet average UK clinical practice, if cryoprecipitate was considered to be suitable to supplement Factor VIII concentrate. If cryoprecipitate is excluded then, with exception of the two year period 1978/9 – 1979/80, the availability of Factor VIII concentrate from the SNBTS was sufficient to meet average UK clinical use throughout this period.<sup>42</sup>

**21.65** It was suggested to Dr Foster that the figures in his table for the years 1978–79 and 1979–80 indicated that clinical demand was ahead of the Factor VIII concentrate available from the SNBTS at that time. Figures for the following years did not indicate difficulties

<sup>41</sup> Ibid [PEN.013.1125] at 1184. The expression of production and use data in terms of units per head of population was common at this period. In this table the unit of measurement of available supply is relevant only to the comparison with demand for coagulation therapy, expressed on a consistent basis. The final two columns show the percentage relationship of available SNBTS supplies to average demand, as assessed on a UK basis.

<sup>42</sup> SNBTS paper, *Self-Sufficiency and the Supply of Blood Products in Scotland*, February 2011 [PEN.013.1125] at 1184



of supply. Dr Foster agreed, and said that they were quite clear that they were not able to produce enough concentrate. He told the Inquiry: 'We couldn't meet the aspirations and we were always chasing this moving target'.<sup>43</sup> Dr Foster's assessment of the practical position is accepted: however one presents the available data, he was intimately involved in the production process, and his opinion is reliable.

**21.66** However, it does not present the whole picture. There remains the necessary caveat in relation to any assessment of the balance of supply and demand for products: individual choice was an aspect of practice, and would have differed not only within Scotland but as between Scottish centres and centres in England and Wales. Averaging of UK demand patterns necessarily concealed such differences. 'Self-sufficiency' might imply a capacity to satisfy the demand for NHS products as distinct from the total demand for concentrates where there was a preference for the commercial product that existed independently of whether NHS products were available.

**21.67** It was the view of some witnesses, for example Dr Frank Boulton, that Scotland had become largely self-sufficient by the early 1980s notwithstanding that some commercial product was still being used in Edinburgh and possibly more so in Glasgow.<sup>44</sup> However, Dr Boulton thought that, without there being an actual ban on importation of commercial material, self-sufficiency was a lovely ideal and one to which transfusion services should aspire at all times, but that 'absolute' self-sufficiency was not achievable. There would always be special needs that could not be serviced from local materials.<sup>45</sup> It became a matter of definition. For him, the expression 'absolute self-sufficiency' meant that the community would be able to supply every single vestige of blood or blood products from within that community, with no dependence on outside agencies at all. A more realistic definition, short of perfection, would be that the NHS could service with local products that part of total demand for which clinicians sought NHS products, subject to such regulatory constraints on freedom of prescription as might be in force.

### **Increasing demand for Factor VIII products**

**21.68** At the beginning of the reference period two closely related matters drove increasing demand: the inherent attractiveness of Factor VIII concentrates in haemophilia therapy generally, and, shortly thereafter, a change in clinical practice towards home therapy. As discussed in Chapter 14, *Knowledge of Viral Hepatitis 1*, the late 1960s and early 1970s saw increasing emphasis on blood component use in surgery, and, arising from that, promotion of a policy of total fractionation as the ideal towards which the transfusion services should aim.<sup>46</sup> Best use of the available scarce resource of whole blood was the driver of the SNBTS's research and development of fractionation. A wider range of more effective therapeutic products became available to haemophilia clinicians.

**21.69** A lively debate began on the best approach to clinical practice. As noted above, in the UK as a whole the use of imported Factor VIII concentrate began before products were first licensed for use and quickly became established. At a joint meeting of the UKHCDO and Blood Transfusion Directors on 31 January 1974, there was a wide-ranging discussion about the relative merits of cryoprecipitate and freeze-dried concentrates. With the exception of Inverness, every Scottish region was represented. Mr Watt represented

<sup>43</sup> Dr Foster – Day 22, page 130

<sup>44</sup> Dr Boulton's statement on the use of blood product concentrates [PEN.015.0054]

<sup>45</sup> Dr Boulton – Day 24, pages 77–79

<sup>46</sup> Paragraph 14.53

the PFC. Factors taken into consideration were: ease of manufacture, recovery from the original plasma, ease of administration, and recovery of activity in patients. Those present at the meeting expressed a clear preference for freeze-dried concentrate if it was available.<sup>47</sup>

**21.70** The question of how much material was likely to be needed led to discussion, with different data and methods being employed by different contributors. A consensus was reached, to the satisfaction of the chairman, Professor Blackburn of Sheffield, on a recommendation to the DHSS as a basis for planning future requirements for Factor VIII in the UK. It was felt that once the new fractionation laboratories in Edinburgh and the Lister Institute were in full production, the needs of the country should be met provided sufficient plasma was available. This view was soon to be confounded in relation to England and Wales, as Figures 21.2 and 21.3 above show. But it appears to be clear that, at this stage, the consensus among the Haemophilia Centre Directors as a group was that the UK was on the brink of self-sufficiency. The rapid increase in demand that was to come about was not anticipated.

**21.71** There were, however, already indications that increasing demand might develop. Several contributors stressed that home therapy was becoming more accepted and widespread, improving the quality of patients' lives. It was recognised that cryoprecipitate was not ideal for that use. Some directors were already buying commercial AHG for home therapy.<sup>48</sup> The minute does not reflect any appreciation that this might affect total demand or demand for NHS products.

**21.72** A paper entitled 'Optimum Use of Available Factor VIII' was considered by the Expert Group on Treatment of Haemophilia at a meeting on 11 October 1974. This paper acknowledged that those present at the last meeting of the Haemophilia Centre Directors were unanimous in preferring freeze-dried concentrate to cryoprecipitate.<sup>49</sup>

**21.73** The disadvantages of cryoprecipitate were again stated: the material must be stored at minus 30°C or below<sup>50</sup> and its potency could not be known before use; it was tedious and time-consuming to make up for use; and to prepare clinical doses, packs or bottles could only be pooled after each had been handled individually. Advantages of the concentrates were known potency and no requirement for freezing. However, there was not sufficient NHS freeze-dried material for wide distribution. Commercial concentrates could be readily purchased but were expensive.

**21.74** Cryoprecipitate was widely available at this time and its use was recommended for the routine treatment of early bleeding in joints and muscles. It was generally thought not to be suitable for home treatment, for which there was a growing requirement. NHS freeze-dried concentrate was recommended for routine surgery and cover for dental extraction, and for home treatment when more material could be made available.

<sup>47</sup> Minutes of Joint Meeting of Haemophilia Centre and Blood Transfusion Directors, 31 January 1974 [SNB.007.2190] at 2194–95

<sup>48</sup> Ibid [SNB.007.2190] at 2196–97

<sup>49</sup> Minutes of Expert Group on the Treatment of Haemophilia, 11 October 1974 [DHF.002.3161]; 'Optimum Use of Available Factor VIII' [DHF.002.3406]

<sup>50</sup> In a hospital setting cryoprecipitate might be stored at minus 70°C: Forbes et al, 'Cryoprecipitate Therapy in Haemophilia', *Scottish Medical Journal*, 1969; 14/1: 1–9 [LIT.001.4018]. For home therapy, Jones et al, 'Haemophilia A Home Therapy in the United Kingdom 1975–6', *British Medical Journal*, 3 June 1978, 1447–50 [LIT.001.0258] required only domestic deep-freeze facilities. See also: Jones P. *Haemophilia Home Therapy*, Pitman Medical 1980, page 78. Other recommendations included minus 18°C. There was no consistency in specifying a maximum temperature for safe storage of cryoprecipitate at this stage.

**21.75** Until NHS supplies of concentrate became adequate, commercial material was recommended for use in three areas:

- For heroic surgery and major trauma; also in the management of serious bleeding in the face of anti-VIII antibodies.
- As back-up when NHS materials temporarily ran out. It was stressed that commercial Factor VIII should only be ordered after all reasonable attempts had been made to obtain NHS materials.
- For the immediate provision of home treatment (in the absence of NHS concentrate) in suitable cases who lived too far from a haemophilia centre to be adequately treated there.<sup>51</sup>

**21.76** As in other areas, control was in the hands of haemophilia clinicians. If the last recommendation might have restricted growth in demand, it failed. When giving oral evidence, Professor Charles Forbes commented that it was not carried out in practice. The advantage of home treatment was that it could be given immediately by the person who had a bleed or their family. He did not think it would have been a good idea that only people who lived a long way from a haemophilia centre should be eligible for home treatment.<sup>52</sup>

**21.77** Professor Ludlam agreed that the last recommendation did not reflect practice in the early 1970s. In his experience, each patient was considered individually, and he did try to help some patients who had severe haemophilia and who travelled very long distances by putting them on to home treatment.<sup>53</sup> However, he did not think that the recommendation had ever operated as a way of rationing treatment.

**21.78** These views reflected a movement in thought towards wider use of home therapy, irrespective of distance to the patient's home. But it was dependent on the availability of concentrate. Efficacy and ease of use of concentrates, coupled with the change to home therapy became closely related aspects of growing demand, both for concentrates generally, and for particular products.

**21.79** Among matters that influenced choice, Professor Ludlam noted that early concentrates (Factor VIII and Factor IX), whether NHS or commercial, were relatively impure and contained large amounts of plasma proteins other than those required for therapy. They were also difficult to dissolve. He told the Inquiry:

[T]he volume of reconstitution was relatively large. The early concentrates were only slightly more purified than freeze-dried cryoprecipitate. The volume of a single infusion might be 200–300mls of concentrate, as compared to 1–5mls with recombinant clotting factors today.<sup>54</sup>

**21.80** For particular patients, this could affect the choice of therapeutic material. In the course of this period the PFC continued to produce Factor VIII and IX concentrates of what was termed 'intermediate purity' while commercial companies began to produce more

<sup>51</sup> Optimum Use of Available Factor VIII [DHF.002.3406]; and Minutes of Expert Group on the Treatment of Haemophilia, 11 October 1974 [DHF.002.3161]

<sup>52</sup> Professor Forbes – Day 17, pages 38–39

<sup>53</sup> Professor Ludlam – Day 18, page 65

<sup>54</sup> Professor Ludlam's report Edinburgh Haemophilia Treatment Policy [PEN.015.0375] at 0378; and Professor Ludlam – Day 18, pages 42–44

highly purified products. For some patients, the commercial products were preferable to NHS products on clinical grounds. At a meeting of Directors of the SNBTS and Haemophilia Directors on 30 January 1981 held in Edinburgh, reasons for the continued use of commercial products in Scotland were discussed.<sup>55</sup> Haemophilia directors stated that sometimes only a commercial product was available. On other occasions, a high purity product was required and some directors said that the slower solubility of the PFC intermediate Factor VIII was a disadvantage. Some patients experienced more side-effects with the PFC products than with the commercial products. Mr Watt from the PFC acknowledged that there was a solubility problem and expressed hope that an improved product would be available soon.

**21.81** On the other hand, some clinicians were clearly influenced by the view that American concentrates were prepared from blood that was more likely to be contaminated. When asked what the prevailing view was in Edinburgh regarding the difference between US concentrates and NHS concentrates, Dr Boulton referred the Inquiry to Richard Titmuss' book *The Gift Relationship* which was published in 1970. He said:

[I]t very clearly describes the risk of using blood from donors who are paid, that is the profit-making donor centres and the blood from the non-profit-making donor centres, who used volunteer donors in America .... The book very clearly established the greater risk from using blood – this is not fractionated products but just straight blood – from donors who are paid compared with donors who are not paid, and although there has been more than one magnitude of difference drop in the risk of paid and non-paid blood donors, that debate is still going on to this day, as far as I know.<sup>56</sup>

**21.82** By 1980, Dr Boulton thought that one would be very aware of the problems of using blood and fractionating plasma from donors who were paid. For him, the 1975 World in Action programme described later highlighted a known problem:

[I] think that one was certainly aware that there were risks associated with using commercially obtained plasma from companies who were bleeding their donors and paying them in America or indeed, on reflection, in Austria.<sup>57</sup>

**21.83** The data on use of products overall have to be understood as subject to these, and other factors, affecting individual clinical choice. The selection of products for home therapy reflected a complicated mixture of influences: it was not necessarily straightforward, and individual clinicians might reasonably differ in their views and preferences.

## The development of home treatment

### *Early to mid-1970s*

**21.84** As matters developed, the move towards home treatment accelerated throughout the UK because haemophilia clinicians thought it to be in the best interests of individuals who would benefit from it. In oral evidence Dr Mark Winter outlined a typical example of a patient's experience of treatment in hospital with cryoprecipitate.<sup>58</sup> The problem would arise out of hours. There would be a good chance that the haemophilia centre would

<sup>55</sup> Minutes of meeting of SNBTS Directors and Haemophilia Directors, 30 January 1981 [SNB.001.5055] at 5055–56

<sup>56</sup> Dr Boulton – Day 24, pages 17–18

<sup>57</sup> Ibid page 18

<sup>58</sup> Dr Winter – Day 15, pages 79–80

be closed so that the patient would have to attend a hospital casualty department. It would be extremely unlikely that the doctor seeing him would know anything about haemophilia so there would be a delay while the doctor found out. After consulting the on-call consultant haematologist, the blood transfusion department would be contacted and asked for cryoprecipitate to be prepared. So the patient could be in the hospital for 6–8 hours before the doctor tried to inject the cryoprecipitate with a very large needle rather than the small butterfly needle which was perfectly suitable. Dr Winter said:

[I] have laboured this point because it was a very harrowing experience. I have never, in all my years of haemophilia, ever heard a patient say, 'I went to casualty with a bleed and everything went well'. It never does, for pretty obvious reasons. These departments are very busy. The doctors know nothing about the condition, and haemophilia is rare.

So not only was cryoprecipitate not a very good medical treatment, for the patients it was a pretty dreadful experience having to go to hospital to have the treatment. So that was why, when one spoke to patients or you went to residential Haemophilia Society weekends, there was a very strong, very strongly expressed view from the patients of, 'We want concentrate, not cryoprecipitate and we want it to be British concentrate, not American'.<sup>59</sup>

**21.85** Some haemophilia patients could react to protein impurities in the cryoprecipitate resulting in quite an unpleasant experience for the patient. Dr Winter said: 'Over the period of an hour they might shake and shiver and run a fever and have muscle aches and feel generally unwell'.<sup>60</sup>

**21.86** He said that it was a major revolution when concentrates became available: they were so much easier to use than cryoprecipitate and unlike cryoprecipitate did not need to be deep frozen. At this early period, nobody had a freezer in their homes. Factor VIII and IX concentrates could be kept in small volumes in a domestic refrigerator so home therapy became possible.

**21.87** Home therapy could start from the age of about three, depending on the state of the child's veins and the competence of the parents, who were taught how to inject the patient with concentrate. The patient would then go on home therapy for the rest of his life with a comprehensive clinical review every two to three months, depending on the severity of the disorder. Dr Winter said:

Prior to that, schooling in particular had been so variable an experience for children with haemophilia that there was actually a dedicated boarding school in Hampshire for patients with haemophilia, called the Lord Mayor Treloar School, where many of my patients went. When the concentrate came in, the boarding aspect of that school was no longer deemed to be necessary.

So this was a very major breakthrough. It enabled patients to get control back over their lives, to be on home therapy, and in retrospect we now call this period 'the golden interval'. This would be sort of 1973 until we entered the years of viral contamination problems, say five or six years later.

---

<sup>59</sup> Ibid page 80

<sup>60</sup> Ibid pages 80–81

In retrospect it seems like a golden time where there was a disease which for 2000 years had had no treatment and then suddenly there had been this enormous quantum leap forward. People were getting decent jobs, having a decent amount of time at school, getting early treatment at home for their bleeds. That was causing less joint problems.

**21.88** Parents were taught how to recognise an episode of bleeding. For joint bleeding, heat was a good indicator that there was bleeding. Parents were taught to compare, for example, knees – the knee with a joint bleed would be a lot hotter than the other one. A child would not want to move the joint if there was a joint bleed so it should be pretty obvious that the child had a bleed.

### *First assessments of consequences of home treatment*

**21.89** By 1975 home treatment programmes were being run by several haemophilia centres. Over 1975 and 1976, Drs Jones,<sup>61</sup> Forbes, Fearn and Stuart compiled data on home treatment for patients with haemophilia, including information about access to treatment. Questionnaires were completed by Haemophilia Directors throughout the UK. The number of patients on or in training for home treatment increased from 267 to 488 in the two years, and a further 241 haemophiliacs were considered suitable for home therapy by the end of 1976. About 60% of patients with Haemophilia A were receiving or being considered for home treatment in 1976. Home treatment had become a major part of the programme of therapy. In 1978, they published a paper in which they noted that:

- The related demand was more than half the estimated total national requirement.
- There were many variables requiring research.<sup>62</sup>

**21.90** It was also noted that there was a rise in prophylaxis, expected to be sustained in 1977. There was a continued shortfall in the production of NHS concentrate from the voluntary donor system of the blood transfusion service. In 1976 there were still some areas in the UK where home treatment had not been implemented.

**21.91** The paper proceeded:

Home treatment for many of the haemophiliacs in the United Kingdom would have been impossible without recourse to factor VIII concentrates prepared by pharmaceutical companies. About 55% of the blood product used for home treatment in 1976 was imported, importation being necessary because of continued shortfall in the production of NHS concentrate from the voluntary donor system of the Blood Transfusion Service .... In 1976 the Department of Health announced that the UK requirement for factor VIII concentrate would be met from NHS sources by mid-1977 after the grant of an additional £0.5m to the Blood Transfusion Service.<sup>63</sup> This target has clearly not been met, nor could it have been in the absence of the necessary financial aid to increase fractionation capacity .... The difficulty of implementing home treatment in

<sup>61</sup> Peter Jones was then a consultant paediatrician working at the Newcastle Haemophilia Reference Centre, Royal Victoria Infirmary, Newcastle upon Tyne; he was also Chairman of the UKHCDO's working party on Home Therapy. His handbook for haemophilia patients entitled *Haemophilia Home Therapy* was published in 1980.

<sup>62</sup> Jones et al, 'Haemophilia A home therapy in the United Kingdom 1975-6', *British Medical Journal*, 3 June 1978; 1447-50 [LIT.001.0258]

<sup>63</sup> HC Hansard, Vol 884, col 392, 26 February 1975 [PEN.012.0183]

some areas is reflected in the continued use of cryoprecipitate, which, despite its disadvantages, remained the only product available for 15% of haemophiliacs in 1976.<sup>64</sup>

**21.92** Professor Forbes advised the Inquiry that he and his co-authors wanted to document the enormous long-term advantage to individual patients who had been on home therapy.<sup>65</sup> Home therapy reduced complications and bleeds. In relation to the high number of patients on or awaiting home therapy at the end of 1976, Professor Forbes commented:

Yes, it was a very popular move and this, of course, is before all the horrendous complications came on stream. So this was the golden age, in which we actually seemed to be doing something valuable for these patients.<sup>66</sup>

**21.93** In the Discussion section of the article it was commented that: 'Perhaps the most disturbing aspect of the 1976 inquiry was the lack of adequate follow-up in some centres'.<sup>67</sup> Professor Forbes said that they were looking at follow-up of the number of joint bleeds and joint deterioration and so on but of more concern trying to ascertain whether all these plasma products had a downside. It was to become clear that they did, but that was for the future. Liver function tests were among the follow-up tests carried out. Professor Forbes thought that these tests would have been part of good follow-up. He said:

I'm pleased that we had put that in. We had no idea what would happen. And that was major concern for hepatitis, and for perhaps other infections that we didn't know about.<sup>68</sup>

**21.94** The paper reflected clearly that so far as haemophilia clinicians were concerned, the expectation was of continued and increasing use of factor products, including use in home therapy, with a significant dependence on imported products. Cryoprecipitate was not expected to meet the demand. Commentators, such as Professor Forbes, were sufficiently concerned about risk to recommend follow-up of concentrate therapy by liver function tests, but they had no means of knowing at that stage what the risks were.

### *Home therapy mid-1970s to 1982*

**21.95** Support for home therapy strengthened in the remainder of this period. Home treatment was discussed in Dr Michael Willoughby's textbook on paediatric haematology written in 1976 and published in 1977. Dr Brian McClelland advised the Inquiry that he knew Dr Willoughby's book very well. He said that, although out of date, it was an extremely good book where you could still find the information that you wanted when you wanted it.<sup>69</sup> The textbook offered the Inquiry a useful perspective on the treatment of children with haemophilia in the 1970s.

<sup>64</sup> Jones et al, 'Haemophilia A home therapy in the United Kingdom 1975-6', *British Medical Journal*, 3 June 1978; 1447-50 [LIT.001.0258] at 0260

<sup>65</sup> Professor Forbes – Day 17, page 57

<sup>66</sup> Ibid page 58

<sup>67</sup> Jones et al, 'Haemophilia A home therapy in the United Kingdom 1975-6', *British Medical Journal*, 3 June 1978; 1447-50 [LIT.001.0258] at 0260-61

<sup>68</sup> Professor Forbes – Day 17, page 60

<sup>69</sup> Dr Brian McClelland – Day 21, page 124; for excerpts from Dr Willoughby's book see [PEN.016.1062]

**21.96** In his book Dr Willoughby commented that commercial and NHS concentrates had advantages over cryoprecipitate in respect that they could be stored at 4°C and could be carried by the patient when travelling – extending the meaning of ‘home’, but giving emphasis to the flexibility of the product.<sup>70</sup> In respect of home treatment, he referred to programmes of home transfusion in the early 1970s in the UK and the USA. In a 1970 study carried out in the USA, patients’ preliminary experience showed a reduction in the number of school or work days lost as the patients were spared frequent ‘time-consuming and psychologically undesirable’ visits to hospital.<sup>71</sup> A pilot study was carried out in 1972 in the UK for patients suffering very frequent haemorrhage (at least once every two weeks). Dr Willoughby wrote:

Le Quesne *et al* (1974) in the UK and Levine (1974) in the US have similarly come to the conclusion that home treatment is highly efficacious in reducing the morbidity of haemophilia and improving the quality of life. No increase in utilization occurred except in patients previously undertreated.<sup>72</sup>

**21.97** Professor Forbes agreed with the suggestion that in the late 1970s home treatment was thought to be the way ahead. Most people who were on home treatment programmes eventually had better joints and were less crippled. Patients who had a bleed could get their treatment instantly rather than wait for an ambulance, be taken to an inappropriate casualty department, wait to be assessed and many hours later get treatment.<sup>73</sup>

**21.98** Home treatment also improved patients’ experience of life. Expectations of haemophilia patients were discussed at the meeting of the UKHCDO in January 1977.<sup>74</sup> Mr John Prothero from the Haemophilia Society said that the society aimed to encourage those with haemophilia to lead a full life within a reasonable range of activities. As treatment improved, the patients’ expectations widened. Mr Prothero said that home therapy had helped a great deal, permitting patients to go on holiday away from their centre and to travel on business. Education was discussed and it was noted that some local education authorities and headmasters had not allowed a boy with haemophilia to go to an ordinary school. Mr Prothero thought that by early 1977 the majority of haemophilia patients were not barred from attending ordinary schools.

**21.99** Dr Charles Rizza talked about 13 severely affected Christmas disease patients who had received prophylactic treatment with Factor IX concentrate and commenced home treatment.<sup>75</sup> He said the treatment had been very effective enabling two of his patients, young twin brothers, to never miss school.

**21.100** Several publications were available or in preparation at this point providing guidance to patients and clinicians on home therapy, including a handbook by Dr Jones, Newcastle, and a Haemophilia Society handbook.<sup>76</sup>

<sup>70</sup> Willoughby, MLN. *Paediatric Haematology*, 1977, Churchill Livingstone, Edinburgh, London, New York, page 321 [PEN.016.1062] at 1065

<sup>71</sup> *Ibid* [PEN.016.1062] at 1068; Rabiner & Telfer, ‘Home Transfusion for patients with haemophilia A’, *New England Journal of Medicine*, 1970; 283:1011

<sup>72</sup> Willoughby, MLN. *Paediatric Haematology*, 1977, Churchill Livingstone, Edinburgh, London, New York [PEN.016.1062] at 1068

<sup>73</sup> Professor Forbes – Day 17, pages 37 and 39

<sup>74</sup> Minutes of UKHCDO meeting, 13 January 1977 [SNB.001.7117] at 7136–7138

<sup>75</sup> *Ibid* [SNB.001.7117] at 7138–39

<sup>76</sup> *Ibid* at 7139–40



*The early 1980s: An Edinburgh insight*

**21.101** As the figures earlier in this chapter show, there was increasing demand for Factor VIII concentrate in 1979–82 (rest of the UK) and 1980–82 (Scotland). As more fully discussed below from paragraph 21.260 onwards, there were variations in practice across Scotland. A practical illustration of what was happening in Edinburgh and south east Scotland at the time was given by Professor Ludlam and Dr Boulton. Dr Davies, Professor Ludlam’s predecessor, had consistently used cryoprecipitate and PFC Factor VIII, predominantly cryoprecipitate.

**21.102** When Professor Ludlam and Dr Boulton arrived in Edinburgh in 1980, increasing demand for concentrates for home therapy became a significant issue. Professor Ludlam told the Inquiry that in Edinburgh, in contrast to Glasgow under Drs Forbes and Willoughby, there was no particular policy in relation to home treatment. When there was a plentiful supply of Factor VIII, home treatment was for anyone who was competent to give it to themselves and bled sufficiently frequently that they needed it.<sup>77</sup> However, it was clear that home treatment was in demand, and it was increasingly provided over time.

**21.103** In a written statement, Professor Ludlam noted that at the beginning of 1980 there were only six patients on home treatment out of a population of 187 patients registered with Haemophilia A. He said: ‘There was a lot of enthusiasm for home treatment and I was continually being asked about it’.<sup>78</sup> The number on home treatment in Edinburgh increased from six in 1980 to 47 in 1989.

**21.104** Professor Ludlam and Dr Boulton did not favour cryoprecipitate for home treatment. Dr Boulton agreed with the view expressed by other clinicians that cryoprecipitate was very difficult for home therapy. He said:

It was not totally unsuitable. It could be used. But the patients, and if they were a young boy, the patient’s family, the parents, would need quite careful and specific training and monitoring so to do. And so it was only really practical in families (a), who were relatively well trained and (b), probably in fairly close proximity to the hospital in case things went wrong.<sup>79</sup>

**21.105** Professor Ludlam said that he was not prepared to take the risk of giving patients cryoprecipitate at home.<sup>80</sup> Storage requirements and the inconvenience of administration made it an unsuitable material, in his view. The patient would have to have a deep-freeze and a water bath that could be heated to 37°C to melt the individual frozen units of cryoprecipitate. Professor Ludlam emphasised the need for a clean, if possible sterile, environment, and careful control of temperature for optimal results.<sup>81</sup> If the water was too hot the proteins in the frozen plasma would congeal, a bit like egg white. Professor Ludlam described to the Inquiry what the patient at home would have to do:

They ... would take out of the deep freeze 15 packs of cryoprecipitate, put them in the water bath. They take about a quarter of an hour to melt. And then each of those packs has to have a tube put into it and the melted cryoprecipitate rolled out. Because they are polythene bags, you can roll them up and squeeze the cryoprecipitate out. You do that repeatedly 15 times, squeezed out into a

<sup>77</sup> Professor Ludlam – Day 18, page 65

<sup>78</sup> Ibid page 89; and Professor Ludlam’s statement on the use of blood product concentrates [PEN.015.0445] at 0458

<sup>79</sup> Dr Boulton – Day 24, page 15

<sup>80</sup> Professor Ludlam – Day 18, page 72

<sup>81</sup> Ibid pages 32–36

bigger bag. You would then have to hang that up, connect it to a drip set, like giving a conventional blood transfusion, the patient would then have to put the needle into their vein and connect up the transfusion set to the tubing on the needle. And it would take about half an hour/40 minutes to run in.<sup>82</sup>

**21.106** He said that treatment with cryoprecipitate was straightforward in hospital:

But in a home setting, well – I wasn't prepared to let patients have treatment at home with cryoprecipitate for all these reasons. But perhaps the most important reason ... is the reactions. A lot of patients getting cryoprecipitate had reactions. Often these were mild and they would take an antihistamine beforehand, but I was looking at some information a day or two ago, suggesting that actually cryoprecipitate should only be given where adrenaline is available, and adrenaline is when you get an acute life-threatening allergic reaction, what's called an anaphylactic reaction. So for these reasons I wasn't keen and I did not have a home therapy programme based on a cryoprecipitate. I concede other places did and it seemed to work for them, but it was logistically difficult.<sup>83</sup>

**21.107** In a paper provided to the Inquiry after the Oral Hearings,<sup>84</sup> Professor Ludlam stated that home therapy critically depended on a ready and reliable supply of concentrate. If there was a reduction in the availability of concentrate, hospitals could adapt by substituting cryoprecipitate for treatment. This was not an option for those on home therapy. If there was a lack of concentrate, home therapy had to be discontinued. Professor Ludlam noted that this was very disturbing and disruptive for patients (and their families) and was to be avoided if at all possible. Many of his patients could not get home therapy because there was not an adequate supply of concentrate. In England the majority of patients were treated with both NHS and commercial products. He preferred not to expose patients who had only received NHS concentrate to commercial product.

**21.108** Professor Ludlam said that home treatment could start from the age of four or later, depending on the child. He explained the difficulties of treating babies:

A child with severe haemophilia usually starts to bleed around the age of nine months when they start to crawl around and walk and fall over. And so to begin with, they only get occasional bleeds, perhaps every month or so, and so they need treatment and the baby is distressed from the pain of the bleed and that makes their veins constrict a bit. They have very small veins, they may have chubby arms, and it is not easy to treat small babies, give them an intravenous infusion of anything. The clotting factor concentrate is of some volume and therefore it can be very traumatic for everybody, treating very small babies.<sup>85</sup>

**21.109** He maintained Dr Davies' policy of using NHS material for the treatment of children.<sup>86</sup> He commented on his predecessor's preference for NHS concentrates:

[Dr] Davies had a policy of not using commercial concentrates because of the uncertainty about hepatitis viruses in the concentrates derived from plasma

---

<sup>82</sup> Ibid page 35

<sup>83</sup> Ibid pages 37–38

<sup>84</sup> Professor Ludlam's paper, 'Clinician's perspective on availability and use of clotting factor concentrates for treating haemophilia in Scotland ....' [PEN.019.1003]

<sup>85</sup> Professor Ludlam – Day 18, pages 76–77

<sup>86</sup> Ibid pages 76–77; see paragraphs 21.261 onwards for an explanation of Dr Davies' policy.

collected in the United States and elsewhere .... The disadvantage of this policy was that there was relatively little factor VIII concentrates available and this [was] significantly delaying the introduction of home treatment for many eligible patients. I impressed upon SNBTS my desire to have more factor VIII concentrate.<sup>87</sup>

**21.110** But Professor Ludlam pressed ahead with home treatment. His policy in commencing home treatment at age four or later was different from Dr Winter's, but not materially.

**21.111** Jones and colleagues expressed a similar view about the wider picture.<sup>88</sup> Concentrate was needed to support home treatment: it was not until freeze-dried concentrates were more freely available that large-scale home treatment programmes became possible, in their view. Given the limited supplies of NHS product, Dr Jones thought that home treatment for many of the haemophilia patients in the UK would have been impossible without recourse to commercial Factor VIII. In Scotland, that was the position for a short time in the early 1980s.

### Prophylactic treatment of haemophilia

**21.112** The practice of prophylaxis was also initiated in the 1970s although Dr Winter thought that the prophylactic programme did not really get going until the 1980s.<sup>89</sup>

**21.113** In his textbook on paediatric haematology, Dr Willoughby discussed prophylactic treatment.<sup>90</sup> He wrote:

Prophylactic administration of Factor VIII or IX in severely affected patients has met with greater success. Clearly this is reserved for patients with quite exceptionally severe and frequent haemorrhages ....

The rationale for intermittent prophylactic replacement therapy is that spontaneous haemorrhage is only seen in patients with Factor VIII levels below 1–2 per cent and infusions of concentrates at 36 to 48-hour intervals can keep the concentration above this level for most of the time ....

**21.114** At the UKHCDO meeting on 13 January 1977 there was a discussion about a trial of prophylactic treatment of severely affected haemophilic boys at Lord Mayor Treloar School, Hampshire.<sup>91</sup> The boys were treated with cryoprecipitate, Kryobulin and Hemofil. All but one of the boys had a fairly substantial reduction in the number of bleeds. Not all of them preferred prophylaxis to 'on demand' treatment but it was suggested that the two boys with good results who wanted to stop prophylaxis might have forgotten what a bad bleed was like. Professor Stewart from the Middlesex Hospital in London commented that prophylactic treatment for haemophilia patients should not be entered into on a large scale until there was sufficient evidence that it was beneficial to the patients. The trial was said to be aimed at providing information for future discussion, and not with the

<sup>87</sup> Professor Ludlam's report, 'Edinburgh Haemophilia Treatment Policy' [PEN.015.0375] at 0379

<sup>88</sup> Jones et al, 'Haemophilia A home therapy in the United Kingdom 1975-6', *British Medical Journal*, 3 June 1978; 1447–50 [LIT.001.0258]

<sup>89</sup> Dr Winter – Day 15, pages 72–75; Prophylaxis, as pioneered by Swedish physicians, is the regular administration of Factor VIII or Factor IX for severely affected patients to prevent spontaneous episodes of bleeding.

<sup>90</sup> Willoughby, MLN. *Paediatric Haematology*, 1977, Churchill Livingstone, Edinburgh, London, New York, page 324 [PEN.016.1062] at 1068

<sup>91</sup> Minutes of UKHCDO meeting on 13 January 1977 [SNB.001.7117] at 7125–26

intention of immediate implementation. It was, in the event, the beginning of a new form of demand for therapeutic products that was heavily dependent on factor concentrates.

**21.115** When Professor Forbes was asked why he thought some people appeared to have reservations about prophylaxis, he replied: 'I think the concern was that it was the huge amount of exposure to plasma products that it would entail'.<sup>92</sup>

**21.116** At a meeting of the UKHCDO on 20 and 21 November 1979, Dr Jones presented a report from the Home Therapy Working Party. Professor Stewart asked whether there had been any move to find out if prophylactic treatment really did any good. Dr Jones responded by saying: '[F]or haemophilia A patients, limited prophylaxis was very effective indeed but it must be for a very good reason. One could spend less on prophylactic treatment than on on demand treatment in some instances'.<sup>93</sup>

**21.117** Professor Forbes commented on Dr Jones' remarks:

This was a very interesting concept because people thought it would be very expensive giving routine treatment but in fact it reduced the amount of bleeding so that over a period of time the number of units of factor VIII given reduced, and of course, the joint damage and the other things reduced as well. So it seemed to be a very efficient and effective way of proceeding.<sup>94</sup>

**21.118** Professor Ian Hann, who took up the position of Consultant Paediatric Haematologist and Oncologist at the Royal Hospital for Sick Children, Yorkhill, Glasgow in January 1983, told the Inquiry that he thought that his predecessor Dr Willoughby was well ahead of his time with regard to his belief that prophylaxis was the way forward. There was a great deal of scepticism over whether it was efficacious or practical, a view shared at that time by Professor Hann. He now considered that Dr Willoughby was right.<sup>95</sup>

**21.119** At Yorkhill, Professor Hann carried out short-term prophylaxis in patients who had bursts of bleeding problems or a very severe bleed which did not settle down. He said:

So we carried out short-term prophylaxis, usually for several months or a little longer, during which we could verify a supply and then, in almost all of these cases, we had to discontinue prophylaxis.<sup>96</sup>

**21.120** They never had enough product to carry out long-term prophylaxis. There was also doubt at the time whether long-term prophylaxis would work.

**21.121** When Professor Hann was working at the Royal Free Hospital in London (prior to taking up the post in Glasgow)<sup>97</sup> his colleagues were worried initially that early prophylaxis might increase the risk of developing inhibitors, the antibodies to factor proteins which make a patient resistant to treatment. It took years, probably until nearly 1990 or thereafter, for people to accept that prophylaxis worked. Professor Hann moved to Great Ormond Street Hospital in London in 1987 and his unit was the first to get all patients onto recombinant prophylaxis in about 1990.

---

<sup>92</sup> Professor Forbes, Day 17, pages 56–57

<sup>93</sup> Minutes of UKHCDO meeting on 20–21 November 1979 [LOT.003.5015] at 5033–34

<sup>94</sup> Professor Forbes – Day 17, pages 67–68

<sup>95</sup> Professor Hann – Day 21, page 28

<sup>96</sup> *Ibid*, pages 32–33

<sup>97</sup> Professor Hann was a lecturer in haematology at the Royal Free Hospital from May 1980–December 1982.

**21.122** The evidence indicates that the emergence of prophylactic treatment had begun to influence demand at this period in some cases, but there is insufficient evidence to suggest that it had made a huge impact on total demand by 1982.

**21.123** The discussion so far shows that there was persistent and significant growth in the use of Factor VIII products throughout the period to 1988, and points to some of the factors driving that growth:

- Meeting the hidden demand related to patients' needs for treatment with coagulation factor products that had not previously been available, or available in sufficient quantity, to provide for the treatment of all haemophilia patients.
- Changing patterns of provision as new products became available.
- The ability to develop therapy regimes, and in particular home treatment, as concentrates became more readily available.
- To some extent, the start of prophylactic therapy.

**21.124** In parallel with these developments, there was growing understanding that there was a price to pay. In Professor Cash's colourful expression, there were no therapeutic roses without thorns.

### Transmission of hepatitis

**21.125** The first part of that price was exposure to risk of transmission of homologous serum jaundice or serum hepatitis.<sup>98</sup> The risk was widely recognised, but little understood by haemophilia clinicians and commentators on therapy in the early part of the period.<sup>99</sup> The second part of the price was exposure to the risk of developing inhibitors. By the end of the 1960s both risks were the subject of comment. At this stage, before the licensing and general importation of commercial concentrates, Factor VIII concentrate therapy was provided by cryoprecipitate and early forms of AHG.

**21.126** In 1967, the Haemophilia Centre Directors decided at a meeting of representatives of all 36 of the haemophilia centres that then existed to set up a study of the incidence of transfusion hepatitis and the incidence of inhibitors<sup>100</sup> – 'two most alarming, but unrelated, complications of treatment of patients with coagulation defects' – in patients treated for Haemophilia A and B.<sup>101</sup> The study appears to have been taken forward by the Cryoprecipitate Working Party of the MRC Blood Transfusion Research Committee.<sup>102</sup> A progress report, most likely prepared by Dr Rosemary Biggs, was presented to the Haemophilia Centre Directors on 5 April 1971.<sup>103</sup> The study represented a significant initiative in the late 1960s and early 1970s in hepatitis research.

<sup>98</sup> The early history of developing knowledge of the risk of transmitting hepatitis associated with therapeutic products is discussed in Chapter 14, *Knowledge of Viral Hepatitis 1*.

<sup>99</sup> See, for example, Maycock et al, 'Further Experience with a Concentrate Containing Human Antihæmophilic Factor', *British Journal of Haematology*, 1963; 9:215 [LIT.001.0063]. The focus was on short-term reactions to treatment, especially jaundice, reflecting a lack of understanding of the natural history of transfusion transmitted hepatitis. Dr Smith suggested that manufacturers of therapeutic products had a distinctive appreciation of the risks of virus transmission: Dr Smith's statement on viral inactivation to 1985 [PEN.012.1551] at 1554

<sup>100</sup> Antibodies inhibiting the efficacy of factor therapy.

<sup>101</sup> Agenda for meeting of Haemophilia Centre Directors, 5 April 1971, Appendix 1 [DHF.001.1811] at 1812

<sup>102</sup> Ibid [DHF.001.1811]

<sup>103</sup> The letter [DHF.001.1810] covering the Agenda for the meeting of Haemophilia Centre Directors on 5 April 1971 came from the Oxford centre, where Dr Biggs was then Director. The letter says 'I have prepared a written report...'. The report, [DHF.001.1811] at 1812, contains introductory material almost identical to the 1974 article by Dr Biggs discussed at paragraph 21.139. It therefore seems likely that Dr Biggs was responsible for the report to the 5 April 1971 meeting.

**21.127** The progress report presented data for 1969 (and therefore before imported commercial concentrates had arrived in the UK). So far as disclosed in the report, prior structured research into hepatitis in haemophilia appears to have been very limited. The narrative provides an insight into contemporary thinking:

Transfusion hepatitis is thought to be a virus infection transmitted to the recipient by the donor plasma. There is every reason to suppose that the virus is contained in the various protein fractions used to treat haemophilia and Christmas disease (cryoprecipitate, human antihaemophilic globulin ... and factor-IX concentrate). The incidence of the virus in the donor population may be of the order of 1 per 1000 ....<sup>104</sup>

**21.128** By this stage, a number of preparations had been introduced, and there are difficulties with the terminology used to identify them. In the late 1960s, AHG (in Scotland largely Cohn Fraction I) was a low potency product sometimes called 'concentrate'. In the early 1970s, commercial pharmaceutical companies introduced a true concentrate, of variable but increasing potency, sometimes referred to as AHG. Where possible, the distinctions will be noted.

**21.129** Clinicians were asked to record the varieties and amounts of therapeutic materials used and 'the incidence of inhibitors and jaundice'.<sup>105</sup> Progress with the study is discussed in Chapter 14, *Knowledge of Viral Hepatitis 1*, paragraphs 14.16 to 14.19. The focus was on 'clinical jaundice'. No attempt was made to record sub-clinical hepatitis since it was thought that the important feature from the point of view of the patients was clinical illness. For 1969, it was reported that 29 patients (2.8%) were jaundiced.<sup>106</sup> Three patients had died. Two of the three had been treated with cryoprecipitate only. The third had been treated with cryoprecipitate and 'concentrate' (in this case AHG, the low potency product).<sup>107</sup> A more detailed examination of the records of haemophilia patients in Oxford showed that seven had developed jaundice.<sup>108</sup> Other data, derived from 60 patients treated at the Oxford centre, indicated the incidence of Hepatitis B associated antigen and antibody. It was reported that, of the sample of 60 patients, 11 had a positive test for Hepatitis B antigen or antibody and that of these only one developed 'clinical hepatitis'.<sup>109</sup> In retrospect, it is very likely that the vast majority of these jaundiced patients had been infected with the Hepatitis B virus (HBV). During the period covered by the data reported (1969 and 1970), the first, insensitive, tests for the so-called 'Australia antigen', later to be identified as the Hepatitis B antigen (HBsAg), were available. The antigen had been identified in 1967 as associated with serum hepatitis virus.<sup>110</sup>

**21.130** The reports identified a fundamental dilemma for clinicians that was to persist, in one form or another, for decades:

The clinical value of free and early treatment of haemophilic patients in the saving of life and the prevention of crippling is now well established. This treatment is known to carry two main hazards: (1) the transmission of viral

<sup>104</sup> Agenda for meeting of Haemophilia Centre Directors, 5 April 1971, Appendix 1 [DHF.001.1811] at 1812

<sup>105</sup> Ibid [DHF.001.1811] at 1812

<sup>106</sup> Ibid [DHF.001.1811] at 1813

<sup>107</sup> Ibid [DHF.001.1811] at 1814

<sup>108</sup> Ibid [DHF.001.1811] at 1815

<sup>109</sup> Ibid [DHF.001.1811] at 1816

<sup>110</sup> Blumberg et al, 'A Serum Antigen (Australia Antigen) in Down's Syndrome, Leukemia, and Hepatitis', *Annals of Internal Medicine*, 1967; 66:924-931 [PEN.002.0764]

hepatitis; (2) the development of specific antibodies against coagulation factors.<sup>111</sup>

**21.131** At this early stage, the risks were thought to be low. On the basis of the data from the 60 Oxford patients, it was reported that whereas about 18% of individuals had evidence of infection with HBV at this time, only 2.8% had overt illness. The view expressed was that:

Although the surveys do not involve large numbers it is likely that the prevalence of hepatitis virus in the materials used to treat haemophiliac patients is approximately as expected. The overall low incidence of clinical illness is presumably due to the fact that the patients became immunized in childhood.<sup>112</sup>

**21.132** The research findings led to the incorrect conclusion that patients with coagulation defects were very resistant to clinical infection with the HBV. For haemophilia clinicians, concerned to balance the advantages of therapy with the materials available against the risks of transmission of infection, the emphasis on what they could observe in treating patients is clear. As in cases of post-transfusion hepatitis, the focus in discussing hepatitis in haemophilia patients treated with blood products (cryoprecipitate or concentrate of any generation) was on acute, clinically observed, hepatitis, and in 1971 it was thought that this was largely due to HBV infection.<sup>113</sup> A low number of diagnosed cases was taken to indicate a low risk overall. However, an infection that escaped identification on the screening tests available could not be taken into account. The possibility of any form of chronic disease was ill understood and little appreciated.<sup>114</sup> At this time (up to the early 1970s) it was thought and hoped that development of good (screening) tests for HBV would lead to a very great reduction in post-transfusion hepatitis or its equivalent in haemophilia patients.

**21.133** So far as concerns the second hazard, the author, Dr Biggs, had reservations about data on the development of specific antibodies against coagulation factors (inhibitors): it was thought to be fragmentary and inconclusive. There was, to that date, no evidence of a steady increase in patients with antibodies. Of the patients seen at the centres in 1968, 5.47% had antibodies, and in 1969 the figure was 6.1%, but those were the only two years for which there were data.<sup>115</sup>

**21.134** The progress report stated:

Hepatitis transmission must be related to the number of 'donor exposures' of the patients. This number will increase with the use of dried concentrates made from large pools of donors. These concentrates have advantages in treatment in that the potency is known and they are convenient to make up and administer. The problem in recommending an increased manufacture of these lies in the possible increase in hepatitis and antibodies. From the point of view of clinical hepatitis this danger seems to be small though the high

<sup>111</sup> Agenda for meeting of Haemophilia Centre Directors, 5 April 1971, Appendix 1 [DHF.001.1811] at 1820

<sup>112</sup> Ibid [DHF.001.1811] at 1816

<sup>113</sup> In respect of clinically observed hepatitis, largely in patients with jaundice, it was probably correct that the majority of cases were indeed due to Hepatitis B. As was learned much later, a far smaller proportion of patients with NANB Hepatitis/HCV presented with overt jaundice.

<sup>114</sup> Some commentators noted long-term sequelae, eg prolonged viraemia: see 'More about Australia Antigen and Hepatitis', *The Lancet*, 15 August 1970; 347–349 [DHF.002.7334]

<sup>115</sup> Agenda for meeting of Haemophilia Centre Directors, 5 April 1971, Appendix 1 [DHF.001.1811] at 1821

incidence of Australian antigen and antibody in haemophiliacs suggests that they do become infected. We feel that the increased risk of clinical illness is not so great as to overbalance the advantages of the use of concentrates.<sup>116</sup>

**21.135** In practice, haemophilia therapy had come to be dependent on blood products. Before the discovery of cryoprecipitate (in the mid-1960s) fraction concentrates (introduced in the late 1950s) were in short supply and usually reserved for surgery and the treatment of major complications in hospital. Most haemophilia patients had received fresh frozen plasma for the routine management of haemorrhage. The introduction of cryoprecipitate allowed outpatient treatment for all but the most severe bleeding episodes.<sup>117</sup>

**21.136** Changes in clinical practice inevitably increased the numbers of patients exposed to blood products at a time when knowledge of the risks had not developed. The discovery of the Australia antigen, in Professor Cash's words in 1972, heralded an explosive research effort in which clinicians, biochemists, geneticists, microbiologists and immunohaematologists all made important contributions to developing knowledge.<sup>118</sup> At the same time, the ready availability of large-pool concentrates heralded an explosion in their use.

**21.137** The WHO scientific group's report 'Viral Hepatitis' reflected progress in the understanding of the clinical, epidemiological and immunological behaviour of Hepatitis B.<sup>119</sup> One aspect of that progress was developing understanding that not all cases of post-transfusion hepatitis were caused by Hepatitis B infection, and that, as more Hepatitis B carriers<sup>120</sup> were eliminated from serving as blood donors, the proportion of cases due to other types of hepatitis would increase.<sup>121</sup> The report noted that some carriers had been found to have liver abnormalities ranging in severity from minor changes in the nucleus of the cell to severe hepatitis and cirrhosis. There was also a changing picture of the prevalence of HBsAg in apparently healthy blood donors. Prevalence was said to vary with such factors as the socio-economic status and sex of the donor, whether he was a volunteer or paid, and whether he lived privately or in an institution. Antigen had been detected most frequently in males in the younger age-groups. And the association between a history of clinical jaundice and a chronic HBsAg carrier state was breaking down.<sup>122</sup>

**21.138** In Scotland, the report of the joint symposium held by the Royal College of Physicians of Edinburgh and the Royal Society of Edinburgh in 1972 indicated the state of knowledge among transfusion specialists at that time. The risks of transmitting serum hepatitis and of inducing antibodies (inhibitors) associated with Factor VIII products were recognised as established.<sup>123</sup> Other BTS studies in the early 1970s, in England and Scotland, sought to determine the prevalence of Hepatitis B infection in the general population,

<sup>116</sup> *Ibid* [DHF.001.1811] at 1820–21

<sup>117</sup> Jones et al, 'Haemophilia A home therapy in the United Kingdom 1975-6', *British Medical Journal*, 3 June 1978; 1447–50 [LIT.001.0258]

<sup>118</sup> Cash, 'Principles of effective and safe transfusion', *Proceedings of the Royal Society of Edinburgh*, 1972; (B) 71 (Supplement) [PEN.002.0559] at 0563

<sup>119</sup> 'Viral Hepatitis: Report of a WHO Scientific Group' World Health Organization Technical Report Series, 1975, No. 512 [SGH.002.9746]. See Chapter 14, *Knowledge of Viral Hepatitis*, paragraphs 14.31–14.42

<sup>120</sup> Individuals with persistent evidence of the presence of HBsAg in their blood.

<sup>121</sup> 'Viral Hepatitis: Report of a WHO Scientific Group', World Health Organization Technical Report Series, 1975, No. 512 [SGH.002.9746] at 9754

<sup>122</sup> *Ibid* [SGH.002.9746] at 9761

<sup>123</sup> Douglas AS, 'Plasma coagulation factors', *Proceedings of the Royal Society of Edinburgh* 1972; (B) 71 (Supplement):65 [PEN.002.0575]



and in specific cohorts such as prisoners, in connection with blood collection policy.<sup>124</sup> In transfusion circles, there was increasing interest in the relationship between transfusion and hepatitis infection.

**21.139** The second published report of Dr Biggs' study, in 1974, again related to the incidence of jaundice in patients treated for Haemophilia A and B (Christmas disease). The period covered was 1969 to 1971.<sup>125</sup> By the date of publication, with the benefit of improved testing and screening for HBV, it was thought that more than one blood-borne virus might be responsible for post-transfusion hepatitis. But the focus for haemophilia doctors, exemplified in Dr Biggs' report, remained on clinically apparent disease and on Hepatitis B.<sup>126</sup> The diagnostic features of clinical jaundice identified were identical to those reported at the Haemophilia Centre Directors' meeting on 5 April 1971, and related to the acute illness. The possibility of chronic liver disease arising from one or more of the post-transfusion hepatitis viruses was barely recognised by haemophilia doctors in the early 1970s, even as late as 1974.

**21.140** The paper recognised the clinical value of treatment of haemophilia patients, and the known hazard of transmission of serum hepatitis. It stated:

The data on hepatitis suggest that severely affected and multi-transfused patients with coagulation defects do not have a high incidence of clinical illness associated with jaundice. Present calculations suggest that if all of the patients were exposed to virus contained in pools of plasma 4–5% of them might develop clinical illness. The proportion of patients exposed to virus is likely to decrease in future rather than to increase since donations grossly infected with Hepatitis B antigen will be excluded by universal donor screening.<sup>127</sup>

**21.141** It was still thought that patients developed some immunity to the virus from multiple transfusions.<sup>128</sup> The paper also suggested that large donor pools might be a positive advantage because the virus would be diluted and would also contain Hepatitis B antibodies (conferring passive immunity to HBV infection with these antibodies).<sup>129</sup>

**21.142** The incidence of anti-HBs found by Dr Biggs in haemophilia patients treated with blood products showed that a proportion did become infected by HBV. Dr Biggs' 1974 paper recognised that factor concentrates generally were associated with a risk of transmitting hepatitis. It was the nature and the scale of the problem that were not captured. The publication of the MRC study (chaired by Dr Maycock) in 1974 helped to continue the erroneous perception among haemophilia clinicians that post-transfusion hepatitis was rare in the UK.<sup>130</sup> Others took a different view,<sup>131</sup> but the balance of opinion in the UK seems clearly to have been reflected in these major studies.

<sup>124</sup> See Chapter 14, *Knowledge of Viral Hepatitis 1*, paragraphs 14.20–14.26

<sup>125</sup> Biggs, 'Jaundice and antibodies directed against Factors VIII and IX in patients treated for haemophilia or Christmas Disease in the United Kingdom', *British Journal of Haematology*, 1974; 26:313 [LIT.001.0099]. See Chapter 14, *Knowledge of Viral Hepatitis 1*, paragraphs 14.16–14.19

<sup>126</sup> Biggs, 'Jaundice and antibodies directed against Factors VIII and IX in patients treated for haemophilia or Christmas Disease in the United Kingdom', *British Journal of Haematology*, 1974; 26:313 [LIT.001.0099] at 0102

<sup>127</sup> *Ibid* [LIT.001.0099] at 0111

<sup>128</sup> This was indeed correct in some patients who lost HBsAG, but retained HBsAB, in their blood. But this distinction was not understood for some years after the date of this paper.

<sup>129</sup> Biggs, 'Jaundice and antibodies directed against Factors VIII and IX in patients treated for haemophilia or Christmas Disease in the United Kingdom', *British Journal of Haematology*, 1974; 26:313 [LIT.001.0099] at 0111

<sup>130</sup> See Chapter 14, *Knowledge of Viral Hepatitis 1*, paragraphs 14.20–14.26

<sup>131</sup> Buchholz, 'Blood Transfusion: Merits of Component Therapy', *The Journal of Pediatrics*, 1974; 84/2:165–172 [LIT.001.0141] at 0145

**21.143** Generally, however, in the early 1970s the increased risk of clinical illness was thought by clinicians to be insufficient to overbalance the advantages of the use of cryoprecipitate and concentrates in clinical treatment of haemophilia.<sup>132</sup> By 1974 many haemophilia patients receiving cryoprecipitate or Factor VIII concentrate had already become infected with the HBV but subsequent studies were to show that the vast majority of these individuals did not sustain long-term liver damage from that source of infection.

**21.144** However, the focus on Hepatitis B which had largely characterised the approach to assessing transfusion-associated transmission of infection until this time was about to shift. The Hepatitis A virus (HAV) was identified in 1973 and it became apparent that this was a water-borne, not blood-borne virus.<sup>133</sup> From 1974, research began to indicate that HBV accounted for a relatively small proportion of cases of post-transfusion hepatitis. On epidemiological and, subsequently, serological grounds, it became clear that HBV and, now, HAV could not account for the majority of cases of post-transfusion hepatitis as had been implied in earlier discussion. In 1974 Prince and others postulated the existence of an additional hepatitis virus or viruses, distinct from HAV and HBV.<sup>134</sup> The putative existence of non-A, non-B (NANB) Hepatitis was suggested by serological analysis published in 1975.<sup>135</sup>

### *1975 and growing understanding of risk of transmission*

**21.145** Developing knowledge of hepatitis thereafter is discussed in Chapter 15, *Knowledge of Viral Hepatitis 2 – 1975 to 1985*. In Europe, Dr Mannucci and colleagues at Milan were among the leading commentators. In February 1975, they published a paper on the incidence of asymptomatic liver disease in haemophilia patients treated with cryoprecipitate, commercial factor concentrates, and, in the case of the older patients, fresh frozen plasma.<sup>136</sup> The authors reported asymptomatic liver abnormalities, and suggested that there was a need for long-term prospective evaluation of any possible relationship between these abnormalities in haemophilia patients and the development of overt hepatic dysfunction. It was a suggestion that the condition occurring in haemophilia patients (which came to be recognised as NANB Hepatitis) might be more than just a benign condition.

**21.146** Dr Garrott Allen, Stanford, a campaigner for volunteer donation in the USA, wrote to Dr Maycock on 6 January 1975. He commented on the ineffectiveness of screening for the HBV antigen and said that at least half of the cases of post-transfusion hepatitis were caused by an unknown agent other than Hepatitis A or B.<sup>137</sup> He remarked that this unknown agent still seemed to be more frequently encountered in the lower socio-economic groups of paid and prison donors. Dr Allen had raised an issue over the selection of donors that was to become significant in relation to the choice of therapeutic product as the period progressed.

<sup>132</sup> A powerful statement of the balancing of interests and the need to continue use of concentrates was set out in a letter by Kasper and Kipnis in *Journal of the American Medical Association*, 31 July 1972; 221/5:510 [LIT.001.0098]

<sup>133</sup> Feinstone et al, 'Hepatitis A: Detection by Immune Electron Microscopy of a Viruslike Antigen Associated with Acute Illness', *Science*, 1973; 182:1026 [PEN.010.0110]. See Chapter 14, *Knowledge of Viral Hepatitis 1*, paragraphs 14.64–14.66

<sup>134</sup> Prince et al, 'Long-incubation post-transfusion hepatitis without serological evidence of exposure to Hepatitis-B virus', *The Lancet*, 1974; 2:241–46 [LIT.001.0363]

<sup>135</sup> See Chapter 14, *Knowledge of Viral Hepatitis 1*, paragraphs 14.65–14.67

<sup>136</sup> Mannucci et al, 'Asymptomatic liver disease in haemophiliacs', *Journal of Clinical Pathology*, 1975; 28:620–624 [LIT.001.0132]. See Chapter 15, *Knowledge of Viral Hepatitis 2 – 1975 to 1985*, paragraphs 15.37–15.39

<sup>137</sup> Dr Garrott Allen's letter of 6 January 1975 to Dr Maycock [SGH.004.6061]

**21.147** From 27 July to 1 August 1975, a symposium, organised by the World Federation of Hemophilia and the International Society of Blood Transfusion, took place in Helsinki. Topics included problems related to adverse effects of coagulation concentrates. The reports of proceedings at the symposium showed that concentrates were frequently associated with adverse effects which might include liver disease, thromboembolism and hepatitis. It was agreed, however, that the occurrence of these adverse effects, albeit of clinical relevance, did not justify withdrawal or reduction of the very effective and life-changing use of concentrates.<sup>138</sup> For a period this became the prevailing view among clinicians, and total consumption of Factor VIII concentrates continued to grow in the UK, as shown in Figure 21.1 above.

**21.148** In his evidence to the Inquiry Professor Forbes agreed that this was a view he shared around this time. Although aware of these risks, he advised that the risk of dying of bleeding was always much greater and that was what drove him and his colleagues to use these products despite the possible downside.<sup>139</sup> It appears, however, that there was now growing acceptance at international level that clinically relevant liver disease could be associated with the use of human blood products. The risk/benefit balance was about to become more problematical.

**21.149** There were two publications concerning concentrates and hepatitis in *The Lancet* of August 1975. The first, by Dr John Craske et al, reported an outbreak of jaundice associated with three out of four batches of a commercial brand of freeze-dried Factor VIII concentrate (Hemofil) at the Bournemouth Haemophilia Centre the previous year.<sup>140</sup> Dr Craske was then based at the Public Health Laboratory in Poole, Dorset.<sup>141</sup>

**21.150** Out of the 18 patients who had received the commercial concentrate nine became ill. Five patients had ‘non-B hepatitis’, two had Hepatitis B and two had both. In the introduction, Dr Craske commented on the huge improvement brought by concentrate treatment: concentrates were not associated with pyrexia and urticaria which occasionally occurred with cryoprecipitate, and they had made home treatment more practicable and major operations on haemophilia patients much easier.<sup>142</sup> But, on the authors’ findings, the risk of transfusion-associated hepatitis was greatly increased over single donor preparations. When blood for transfusion was prepared from commercial donations the risk increased the frequency of jaundice between three and nine times. In respect of concentrates, the article said:

There seems to be a pronounced increase in the risk of post-transfusion hepatitis when some batches of commercial freeze-dried factor-VIII concentrates are used. This must be balanced against the undoubted advantage that the freeze-dried product has over cryoprecipitate.<sup>143</sup>

**21.151** The article noted that the pool size might be critical in Factor VIII concentrates since transfusion hepatitis was a known hazard with large-pool products prepared from volunteer donors in the UK.

<sup>138</sup> Mannucci, ‘Side effects of antihemophilic concentrates’, *Scandinavian Journal of Haematology Supplement*, 1977; 30:1–5 [LIT.001.0150]

<sup>139</sup> Professor Forbes, Day 17, pages 46–47

<sup>140</sup> Craske et al, ‘An outbreak of hepatitis associated with intravenous injection of factor-VIII concentrate’, *The Lancet*, 2 August 1975; 2:221–223 [LIT.001.0360]

<sup>141</sup> Dr Craske’s fellow authors were from the Bournemouth Haemophilia Centre.

<sup>142</sup> Pyrexia is a fever and urticaria is a skin rash.

<sup>143</sup> Craske et al, ‘An outbreak of hepatitis associated with intravenous injection of factor-VIII concentrate’, *The Lancet*, 2 August 1975; 2:221–223 [LIT.001.0360] at 0362

**21.152** Measures to reduce the frequency of jaundice were suggested:

- The first recommendation was that commercial Factor VIII concentrates should be reserved for the treatment of life-threatening bleeds in all haemophilia patients and for covering major operations.
- The second recommendation was to reserve commercial concentrates for severely affected haemophilia patients '[S]ince they are more likely to be immune to hepatitis A and B'.<sup>144</sup>

**21.153** When giving evidence, Dr Winter commented that the first recommendation was not feasible in England at that time because there was not enough NHS concentrate to sustain the haemophilia population. In relation to the second recommendation he said that as the major hepatitis risk was transmission of Hepatitis C (NANB Hepatitis), the fact that the more severely treated patients might be immune to Hepatitis A or B would not actually be relevant.

**21.154** But Dr Winter thought that the paper generally stated exactly what would be expected: if haemophilia patients were given Factor VIII concentrate at that time, they would nearly all get abnormal liver function tests, yet only a minority of them would get clinical symptoms.<sup>145</sup>

**21.155** The second publication in *The Lancet* of August 1975, a letter by Dr Dane and Dr Cameron from the Middlesex Hospital Medical School in London, reported the testing of batches of commercial Factor VIII concentrate (including one of the batches referred to by Dr Craske in the first article) using the authors' own solid phase radioimmunoassay (RIA) test.<sup>146</sup> All three batches were found to be HBsAg positive (and therefore infectious for Hepatitis B). The authors believed that if donations were screened by RIA (a more sensitive test than employed by the manufacturers of the concentrates for routine screening) the final product would be much more likely to be safe. The letter from Drs Dane and Cameron did not refer to 'non B hepatitis' – the expression adopted in the Craske letter to distinguish unidentified cases from cases of HBsAg positivity.

**21.156** It was suggested to Dr Winter that the test used by Drs Dane and Cameron might be leading people in the wrong direction because it was creating a kind of reassurance: if there was better screening for Hepatitis B, the problem would be solved. He agreed, as Hepatitis C (HCV) was to become a much greater problem than Hepatitis B.<sup>147</sup>

**21.157** The papers by Drs Mannucci, Craske, Dane and Cameron in *The Lancet* of August 1975 marked a transition point in the information available to haemophilia clinicians that had a bearing on the selection of therapeutic products. While screening of donated blood for HBsAg had already substantially reduced the risk of post-transfusion Hepatitis B, the tests for screening each donor for HBsAg were, until the late 1970s, relatively insensitive. Many commercial Factor VIII concentrates contained contributions from thousands of donors, and were still infectious for Hepatitis B (as demonstrated by these studies). From 1975, as tests for Hepatitis B became increasingly sensitive, the realisation grew that one or more other infectious agents were responsible for a very high prevalence of liver blood test abnormalities in recipients of concentrates since evidence for past exposure

<sup>144</sup> Ibid [LIT.001.0360] at 0362

<sup>145</sup> Dr Winter – Day 15, pages 96–99

<sup>146</sup> Dane and Cameron, 'Factor-VIII concentrate and hepatitis', *The Lancet*, 16 August 1975 [LIT.001.0358]

<sup>147</sup> Dr Winter – Day 15, pages 99–100

to Hepatitis B was becoming less common. Biopsy results were to become an important factor in the debate.

**21.158** Awareness of NANB Hepatitis grew in the second half of the 1970s and particularly in association with blood product concentrates. Dr Winter said:

I think it was very well established by 1975, the group in Milan of Professor Mannucci had actually done liver biopsy studies which had demonstrated histological hepatitis in these patients as well, and it was for that reason by, you know, the mid 1970s that UKHCDO were starting to approach DOH with a view to persuading them to initiate moves toward self-sufficiency. It was the hepatitis argument that was obviously driving this initiative.<sup>148</sup>

**21.159** As noted above (paragraph 21.84), Dr Winter said that haemophilia patients expressed a very strong preference for concentrates. Compared with cryoprecipitate, concentrate offered very significant improvements in their quality of life. But they would also state that they did not want to have any concentrate of US origin. They wanted concentrate of British origin because of the perception that British donors were voluntary donors and were therefore acting out of altruistic motives whereas the commercial donors were donating for financial reasons and were more likely to be infected with viruses. This simplistic argument was very strong within the haemophilia community. Because of this perception, it took a lot of work in Dr Winter's clinic to persuade patients in some cases to continue to receive commercial concentrate.

**21.160** Dr Winter said there was a 'Tarzanoid' philosophy in relation to concentrates around this time: UK product good, US product bad.<sup>149</sup> The whole issue was about to move into the glare of media publicity.

### *'World in Action' television programmes*

**21.161** 'World in Action', a television programme in two parts shown in 1975, investigated the manufacture of blood products in the USA and the concept of self-sufficiency in the UK. A DVD of the programme was shown to the Inquiry and sent to several clinicians for their comments.<sup>150</sup>

**21.162** Part one, broadcast on 1 December 1975, featured three haemophilia patients whose lives had improved significantly since using commercial concentrates. One of these patients had experienced severe hepatitis, associated with Hemofil manufactured by Hyland, then a US drug company. Professor Arie Zuckerman, then recognised as an authority on hepatitis, was interviewed, as was Dr Craske. The documentary included footage of Hyland Donor Centres including centres in San Jose and downtown Los Angeles. The 'World in Action' team found that Hyland's paid donors included alcoholics and down-and-outs. It was suggested that, because of their lifestyles, many of these donors from 'Skid Row' areas were likely to be carriers of hepatitis viruses.

**21.163** Dr J Garrott Allen, the campaigner against the paid donor system in the USA already mentioned, was interviewed on the programme and he said that a number of studies carried out in the previous decade had indicated that the risk of hepatitis was 60–70 times greater from paid donors than from a volunteer source such as friends and relatives.

<sup>148</sup> Ibid pages 104–105. Dr Winter was wrong in suggesting that Mannucci and colleagues had done liver biopsy studies by 1975. Mannucci's first liver biopsy study came out in 1978: Mannucci et al, 'A clinicopathological study of liver disease in haemophiliacs', *Journal of Clinical Pathology*, 1978; 31: 779–783 [LIT.001.1624] at 1627–28

<sup>149</sup> Dr Winter – Day 15, pages 107–108

<sup>150</sup> For a transcript of the programme see [PEN.013.1400]

**21.164** Dr Richard Wilbur, the senior Vice President for Medical Affairs at Baxter Laboratories (then owner of Hyland), was also interviewed. Dr Wilbur's reaction to hepatitis infection in England following use of Hemofil was that the reported cases occurred from earlier batches made before their new techniques for screening donors for hepatitis were in place.<sup>151</sup> He considered that the risk-benefit ratio of taking Factor VIII concentrate compared with 'this relatively mild' disease was a good one for the patient.<sup>152</sup> When asked about the type of donors who sold their plasma to Hyland, Dr Wilbur said:

[W]e would prefer that all of the plasma were available from better sources and we do not deliberately seek out as a source of plasma the unfortunate people in the country. As I said before, we would vastly prefer to have it from voluntary donors just as everyone would like to have blood transfusions from voluntary donors.<sup>153</sup>

**21.165** This part of the programme ended with the investigation team commenting that Hemofil carried a high risk for three reasons: the use of paid donors, its production from large plasma pools, and the inadequacy of hepatitis tests.<sup>154</sup>

**29.166** Part two, broadcast on 8 December 1975 focused more strongly on the supply of concentrates in the UK. Patients and the Haemophilia Society both indicated their preference for UK material. Dr Maycock, then senior advisor to the Department of Health on blood transfusion policy, was interviewed, as was Mr John Watt, of the PFC.<sup>155</sup>

**29.167** Dr Maycock was asked about the decision to import concentrates in 1973, given the known hepatitis risk of paid donors. It was suggested that the Department of Health had been somewhat complacent about these risks. Dr Maycock did not agree: he thought the quality of the material was controlled, both in the UK and the USA. His view was not shared by Professor Zuckerman who believed that it was well recognised that the commercial donor carried a considerably greater risk of transmitting hepatitis than the volunteer donor. But it was reported that British-made concentrates were not entirely free of risk either. Since the previous year, Professor Zuckerman had also detected a surprising number of infected batches of English concentrate.

**29.168** Dr Maycock said he hoped that self-sufficiency would be achieved by mid-1977. He rejected the suggestion that there might not be sufficient production capacity or enough donors. He stressed that there was certainly no lack of donors.

**29.169** Mr Watt told the presenter that the new plant in Edinburgh, the PFC, should be able at capacity, to produce more than the need for all plasma fractions for Scotland by the spring of the following year (1976). After that it would depend on government policy. Mr Watt agreed with the presenter that making concentrates in the UK should be very much cheaper than importing foreign concentrates. As well as cost, Mr Watt talked about the ethics of importing Factor VIII concentrates from impoverished countries. He said:

I know of one Middle Eastern country where a haemophiliac patient may travel 300 miles and wait for several days outside the clinic looking for treatment and

---

<sup>151</sup> This would have been a reference to improved screening of donor blood for HBsAg.

<sup>152</sup> World in Action transcript [PEN.013.1400] at 1411

<sup>153</sup> Ibid [PEN.013.1400] at 1413

<sup>154</sup> Ibid

<sup>155</sup> John Watt was introduced in the programme as Scientific Director of the Scottish Blood Transfusion Association but at this time he was the Scientific Director of the PFC, Liberton.

it's not because the clinic doesn't want to take them in, it's because they don't have enough beds and they don't have enough material. The Factor VIII isn't there. It's all gone to the more affluent parts of the world.<sup>156</sup>

**29.170** Dr David Owen, then Secretary of State for Health, also appeared on the programme and was asked how long it would take before Britain could stop being dependent on imported concentrate. He replied: '[A]s fast as buildings can be set up and equipment purchased .... We've brought it down to two years and maybe we can improve even on that'.<sup>157</sup> He agreed with the journalist interviewing him that paid donors were a greater health risk than volunteer British donors. But he said there was always some risk from any use of blood from donors.

**29.171** In relation to the world trade in plasma Dr Owen said: 'I think there's a very strong moral case for once you are self-sufficient, ensuring that you use only your own national sources and freeing up those resources in other nations for their needs'.<sup>158</sup>

**29.172** Dr Winter viewed the documentary and provided the Inquiry with a statement in which he commented:

The opening scenes, with various British teenage haemophiliacs and their families, are especially important since they underscore the very great improvement in quality of life afforded by the new concentrates, as compared with the use of cryoprecipitate, which was clumsy, time consuming, associated with side effects and in particular had to be administered in hospital.<sup>159</sup>

The programme had looked at the case of one boy who, before home therapy, had made 98 visits to hospital in one year and had three months off school.<sup>160</sup>

**29.173** Dr Winter noted in his statement that the programme set out visually what was already clear at the time: blood products derived from commercial donations were significantly more likely to be associated with viral infections.<sup>161</sup> Near the beginning of the programme it was revealed that paid donors had six to 13 times the risk of having hepatitis.

**29.174** The programme showed people waiting to give blood with bottles of alcohol sticking out of their pockets, but Dr Winter advised the Inquiry that the major consideration to prevent a batch being infected was the viral status of a donor: whether the donor was underweight or drank alcohol would be of less significance to the risk of virus infection of the donation.<sup>162</sup>

**29.175** Dr Winter said that it was his understanding that the pool size in commercial manufacture would be at least 20,000 and sometimes higher by the mid-1970s. Haemophilia doctors thought at the time that if the patient received Factor VIII concentrate in the 1970s, particularly from US donor plasma, it was inevitable that he was getting a number of different hepatitis infections.<sup>163</sup>

---

<sup>156</sup> World in Action transcript [PEN.013.1400] at 1424

<sup>157</sup> Ibid [PEN.013.1400] at 1422

<sup>158</sup> Ibid [PEN.013.1400] at 1424

<sup>159</sup> Dr Winter's statement on the use of blood product concentrates [PEN.015.0292] at 0293

<sup>160</sup> World in Action transcript [PEN.013.1400] at 1401

<sup>161</sup> Dr Winter's statement on the use of blood product concentrates [PEN.015.0292] at 0293

<sup>162</sup> Dr Winter – Day 15, page 85

<sup>163</sup> Ibid pages 82–83

**29.176** In Dr Winter's opinion, Professor Zuckerman and the others were really talking about Hepatitis B in the programme. In the mid-1970s after two or three years of concentrate use, many patients with haemophilia were displaying blood tests suggestive of a hepatitis-like pattern in their liver function blood tests. They were by and large very well. Maybe 5% or perhaps higher had circulating levels of Hepatitis B and about 20% could be shown to have antibodies against Hepatitis B; a small percentage could be demonstrated to have Hepatitis A but for the majority of these other patients, who clearly had a hepatitis-like picture on their liver function blood tests, all the standard Hepatitis A and B markers were negative. So it was for this reason that haemophilia doctors came to think that there was a third type of hepatitis which was called 'non-A, non-B Hepatitis'.

**29.177** Dr Winter advised that a patient who got NANB Hepatitis could become clinically unwell, but that was not necessarily a very common event and not as common as clinical illness in Hepatitis A or B. In case of infection with either of those viruses, the patient normally felt thoroughly unwell at the time of the infection. NANB Hepatitis was more likely to get into the blood stream and inflame the liver. The focus for discussion in the documentary should have been NANB Hepatitis, because it was (in retrospect) by far the most relevant type of hepatitis for these patients.<sup>164</sup>

**29.178** It has to be noted that while, in retrospect, Dr Winter was correct in his comment about the incidence of NANB Hepatitis it was only in 1975 that the first suggestions of the existence of NANB Hepatitis (first postulated in 1974) were beginning to be accepted. And, beyond the observation that many individuals with haemophilia were beginning to have persistent, usually mild, blood test abnormalities, nothing was known about NANB Hepatitis/HCV-related chronic liver disease, still less about its impact on infected haemophilia patients 10 or more years later. The documentary could not have dealt with NANBH/HCV at the time: it was really concerned with Hepatitis B.

**29.179** In the programme Professor Zuckerman said:

[H]epatitis, or jaundice, is a particularly interesting infection because the severity of the illness ranges from a very mild form of infection, perhaps with trivial symptoms, to an attack of jaundice with quite a lot of disability which may last for some weeks or perhaps even months, and it is associated with a significant death rate. In addition, in a number of cases it may progress to chronic liver damage and may end up in a condition such as chronic active hepatitis or cirrhosis of the liver.<sup>165</sup>

**29.180** A professor of medicine at the University of Southern California, Dr Mosley, was asked in the programme to quantify the risk of getting hepatitis from a clotting factor concentrate and his response was: 'probably 100 per cent if the individual is susceptible'.<sup>166</sup> Dr Winter suggested that 'susceptible' in this context probably meant that the individual did not already have antibodies to HBV.<sup>167</sup>

**29.181** One of the committee members from the Haemophilia Society interviewed in the programme said that people with haemophilia were not too bothered about where the blood came from as long as they had blood concentrate to keep them going, and in some

---

<sup>164</sup> Ibid pages 86–87

<sup>165</sup> World in Action transcript [PEN.013.1400] at 1402

<sup>166</sup> Ibid [PEN.013.1400] at 1408

<sup>167</sup> Dr Winter – Day 15, pages 91–92



cases to keep them alive; of course they would prefer that blood was donated voluntarily and not from people who were undernourished and alcoholic.<sup>168</sup> Dr Winter recognised that sentiment. In his centre the supply of NHS concentrate was very limited and at least 90% of the concentrate was commercial in origin. This was due to the capacity of the plant at Elstree to produce the concentrate, and a policy of preferential supply to certain hospitals.<sup>169</sup>

**29.182** One of the patients featured on the programme who had contracted hepatitis while using Hemofil talked about how he was vomiting really badly and wondered whether it was worth using the concentrate. Two days later, he had a bleed in his elbow and said he had no hesitation in going to the fridge and injecting the Hemofil because he knew it would stop the bleeding and the pain from the bleed was going to be so much worse than any of the pain he had suffered with hepatitis.<sup>170</sup>

**29.183** Dr Winter was not surprised by what this patient had said and commented:

That's a mirror of, as I have been trying to reflect in my comments, the quite extraordinary change of quality of life for these people whose existence had really been pretty miserable, regular bleeding into joints and muscles, poor schooling, lifelong pain, no sport, limited ability to get jobs because of poor education, and suddenly there was this white powder they could give at home and it had an enormous difference. So for all these reasons, when faced with this variable data with variable opinions by doctors, their view was 'Well, we are extremely reluctant to consider not using this product any more because of the quality of life it has given us'.<sup>171</sup>

**29.184** Professor Forbes said that he had not watched the programme when it was shown in 1975 but had seen it twice since then. He remembered when it was broadcast that it was the talk of the haemophilia part of the hospital. He thought that there was a gasp of disbelief when they showed the types of donors that were being used to give plasma in commercial centres. Professor Forbes was appalled when he watched the programme recently; there was no monitoring at all of these paid donors and even if they were asked questions, they denied they had any problems whatsoever but clearly they did have. He thought it was incredible to see the donors drinking alcohol immediately before they gave blood.<sup>172</sup>

**29.185** Although Professor Forbes could not remember any specific details in relation to practitioners' reactions to the programme, he stated that people felt this was not the way to go. Commercial concentrates of all kinds, probably not just Hemofil (featured in the programme) but the other ones too, were all 'tarred with the same brush'.<sup>173</sup>

**29.186** Having watched the 'World in Action' programme, Professor Cash wrote to *The Lancet* at the beginning of January 1976 stating:

There is no doubt that the import into the United Kingdom of factor VIII concentrates derived from external sources, however well screened for hepatitis viruses, represents an unequivocal pathway by which the level of a potentially

<sup>168</sup> World in Action transcript [PEN.013.1400] at 1418

<sup>169</sup> Dr Winter – Day 15, pages 92–94

<sup>170</sup> World in Action transcript [PEN.013.1400] at 1415

<sup>171</sup> Dr Winter – Day 15, pages 94–95

<sup>172</sup> Professor Forbes – Day 17, pages 30–31

<sup>173</sup> Ibid page 32

lethal virus into the *whole* community is being deliberately increased. Although the absolute magnitude of this problem was exaggerated and over-dramatised by the television programmes, nobody with direct or indirect responsibilities for this phenomenon would wish to belittle the serious nature of the moral and practical dilemmas which face us all.

Perhaps the most misleading feature of the second television programme was the impression given that the recent and specific injection of £500,000 by the DHSS into the blood transfusion services will have worked its way through by mid-1977 and by that time the necessity to purchase further supplies of factor VIII concentrates will be eliminated. Our own experience indicates that this will not occur, not least because the present NHS production target for factor VIII concentrates is too low.<sup>174</sup>

**29.187** Professor Cash was asked about the letter when he appeared at the Inquiry and it was suggested to him that he had been something of a prophet, in commenting on risk of a 'potentially lethal virus' in the early 1980s. His response was:

[B]ut I wouldn't see myself as some prophet, a prophet of doom ... in 1969 I did my own World in Action. I had a WHO travel fellowship and spent three and a half months in the States looking very carefully at all aspects of their transfusion service, made a lot of hugely important friends over there that were immensely important in the later years. And one of the things I did when I was in California was to go into the Cutter – it was Cutter, not Hyland – skid row area, and this is San Francisco, as I recall, and – I mean, I thought the film was pretty gentle on that. What I saw was obscene. It was just obscene.<sup>175</sup>

**29.188** Professor Cash went on to say that he thought the film had exaggerated the situation because not all plasma that was used in commercial concentrates was coming from 'Skid Row'. There were some companies who claimed (and Professor Cash said he believed them at this time) that they did not use these sorts of donors at all but used 'university campus people'. He pointed out that PCR Hepatitis C studies were carried out many years later on old batches of commercial concentrate and some of them were negative.<sup>176</sup>

**29.189** Dr Boulton who was working as a Director of the Liverpool Haemophilia Centre at this time told the Inquiry that he did not see the programme but he remembered conversations after it was broadcast.<sup>177</sup> He felt at the time that the programme had exaggerated the problem but he admitted that he was then a young and inexperienced doctor. A year or so before the programme, in 1973 or 1974, Dr Boulton was working at the London Hospital and had seen a haemophilic patient who needed Factor VIII over Christmas for a fairly major dental problem. There was not enough NHS cryoprecipitate or NHS Factor VIII in stock to cover the surgery safely so Dr Boulton ordered in a small amount of commercial Factor VIII and this mild haemophilic man in his 50s received some. The man got both Hepatitis B and NANB Hepatitis. Dr Boulton said that he had a rather rude awakening into the dangers of hepatitis from commercial (in this case US) Factor VIII.

<sup>174</sup> Cash, 'Commercial and NHS factor VIII concentrates', *The Lancet*, 24 January 1976; 221 [LIT.001.0245]

<sup>175</sup> Professor Cash – Day 25, page 75

<sup>176</sup> *Ibid* pages 75–76

<sup>177</sup> Dr Boulton – Day 24, pages 9–11; Dr Boulton took up the post of Consultant and Honorary Lecturer in Haematology and Blood Transfusion, BTS, Edinburgh in 1980; he became Deputy Director in 1982.

**29.190** Dr Boulton said that when he was working in Liverpool (after October 1975), commercial Factor VIII was bought from Austria not the USA. There was clearly a concern then that US products were to be avoided and he believes that this was a legitimate or at least understandable reaction to his experience of treating and giving a patient NANB Hepatitis. Dr Boulton was asked if the plasma used for the Austrian commercial product was Austrian. He replied that it was quite possible that some of the plasma came from the USA but he did not know that at the time; he was under the impression, and had been told by Immuno's director, that the material was Austrian in origin. But it was clearly from paid donors.<sup>178</sup>

### ***Commercial concentrate production in the mid- to late-1970s***

**29.191** As the 'World in Action' programme revealed, one of the first concentrates used in the UK was Hemofil, manufactured by Hyland. It was not the only product on the market. By the late 1970s four major companies controlled most of the world's plasma. Based in the USA they were:

- Cutter Laboratories of Berkeley, California.
- Alpha Therapeutic Corporation of Los Angeles.
- Armour Laboratories of Chicago.
- Hyland in a suburb of Los Angeles.

**29.192** International pressure against exploiting developing countries had restricted the supply of plasma from 'the Third World plasma mills',<sup>179</sup> and foreign firms were keen to have access to the lucrative American drug market. By the end of the 1970s only Hyland remained in American hands; it belonged to Baxter Travenol Laboratories, based in Chicago. Alpha Therapeutic had been bought by a Japanese company (Dr Naito's Green Cross Company); the German pharmaceutical company, Bayer AG, had taken over Cutter Laboratories; and Armour was in the hands of the French multinational Rhone-Poulenc.<sup>180</sup>

**29.193** Concentrates available at or about the time of the programme were:<sup>181</sup>

#### Factor VIII products

<b>Manufacturer</b>	<b>Trade name</b>	<b>FDA licence granted</b>	<b>Last release</b>
Armour Pharmaceutical Company	Factorate	1973	1985
	Factorate Generation II	1977	1985
Alpha Therapeutic Corporation	Profilate	Licence transferred in August 1978 from Abbott Laboratories	Not available
Hyland Division, Baxter	Anti-haemophilic Factor (Human)	May 1966	Not available
	Hemofil	January 1968	Not available
Cutter Biological (later Miles, Inc.)	Koate	January 1974	October 1984

<sup>178</sup> Dr Boulton – Day 24, pages 10–11

<sup>179</sup> Starr, D. *Blood*, 2002 (2nd edition), Perennial, New York, 258 [LIT.001.2920] at 2928

<sup>180</sup> Ibid

<sup>181</sup> Kasper et al, 'Recent evolution of clotting factor concentrates for hemophilia A and B', *Transfusion*, 1993; 33:422–434 [SGH.002.1947]

Factor IX Products

<b>Manufacturer</b>	<b>Trade name</b>	<b>FDA licence granted</b>	<b>Last release</b>
Hyland Division, Baxter	Proplex	July 1970	Not available
Cutter Biological (later Miles, Inc.)	Konyne	December 1968	May 1985

*Increasing evidence of the risk of hepatitis in the late 1970s*

**29.194** Notwithstanding Professor Cash's reservations about their accuracy, the 'World in Action' programmes could have left no interested observer in doubt that at least some clinical specialists believed that commercial factor products carried an unacceptable risk of transmitting hepatitis virus infection in comparison with the NHS products in manufacture at the time. The accounts of reactions among hospital staff, for example by Professor Forbes, indicate that these were extreme. Some experts, in addition to Professor Cash, could draw on personal observation and experience.

**29.195** Dr McClelland was appointed to the SNBTS in 1977. Sometime after his appointment, he visited the Cutter Company in San Francisco. In his statement provided to the Inquiry, he wrote:

I also remember very clearly an experience that has coloured my thinking about the use of blood from commercial donors throughout my career, and I cannot think of any reason why this would not have influenced my own views about commercial Factor VIII during the early 1980s. Shortly after my appointment to the SNBTS in 1977 (I do not have a record of the dates) I visited the Cutter Company in San Francisco. During this trip I visited their Oakland plasma centre. I have a very clear recollection of being amazed to find that there were no donors in the centre and that I asked one of the two staff in evidence why the centre was empty. I recall her response, which was that this was typical for that day of the week, because it was the day for collection of social security cheques. I also recall that I took away a copy of a notice displayed in the centre [reproduced at Figure 21.7 below]. This stated the fees for a plasma collection – \$US 16.

This visit left me in no doubt that even in this relatively favoured part of the USA, the company depended very heavily on the provision of plasma by people of low income. One implication of this that was clear to me at that time was that plasma was being collected from individuals who might be dependent on the payments from the plasma centre and who would therefore have an incentive to conceal any aspects of their health that might make them unsuitable as donors.<sup>182</sup>

<sup>182</sup> Dr McClelland's statement on the use of blood product concentrates [PEN.015.0307]. See also Dr McClelland – Day 21, pages 88–91

Figure 21.7



**21.196** Dr McClelland referred to the 'World in Action' programme when giving evidence about haemophilia patients keeping abreast of developments in therapy. He was very impressed with the common sense knowledge that a lot of the patients and some of the parents featured on the programme expressed about the infection risks and the safety and effectiveness of the products.<sup>183</sup>

**21.197** Dr McClelland told the Inquiry that when he was on-call for the BTS, professionals who happened to be haemophilia patients would visit and they would very often have their own specific personal views about which product they had chosen to be treated with.<sup>184</sup> He said:

There were some individuals who would only accept to be treated with cryoprecipitate, even accepting all the inconvenience. There were some who would not accept treatment with imported Factor VIII. There are some who had a very strong preference for particular products and it would be quite wrong, I think, to say that these were idiosyncratic preferences. These patients almost certainly had extremely good reasons, which they could probably explain very articulately in many cases, why they chose a particular approach to their own treatment, and my recollection is that that was evident among some, not all, but some of the haemophilia patients early on in my career.<sup>185</sup>

<sup>183</sup> Dr McClelland – Day 21, pages 161–162

<sup>184</sup> Dr McClelland started working for the BTS in Edinburgh in 1977.

<sup>185</sup> Dr McClelland – Day 21, pages 159–160

**21.198** When asked if the patients' expertise related to their perception of the effectiveness of the different products, Dr McClelland replied:

In the broad sense – well it depends how you define 'effectiveness'. Strictly speaking, I would define clinical effectiveness as essentially describing the balance of benefit and disbenefit. So safety is actually, in that sense, part of effectiveness, but it may be easier to separate them out and say were they concerned about the safety, which, if you think might be: what will this do to me in the long term? Will I get something nasty in two, five, ten years' time? As opposed to: will this stop my bleed and control my pain now, better than other products?

And of course, the third factor that to some patients mattered a lot, is inconvenience. Will it take me an hour fiddling around with syringes and needles and jars of salt water and other things to get my dose, or can I go to the fridge, take it out, stick a syringe in and that's it? All those factors and many others would have influenced their choices.<sup>186</sup>

**21.199** In the Inquiry's view Dr McClelland's impressions reflected a realistic assessment of the position. In the meantime, more structured investigations continued.

**21.200** At the meeting of the UKHCDO held on 13 January 1977 (referred to above), Dr Craske presented a report on his continuing study of hepatitis in haemophilia patients treated with Hemofil.<sup>187</sup> Three hundred and seventy one patients had been followed up. One had died with cause of death possibly attributable to Hepatitis B. Dr Craske proposed an extension of his study over two years. He suggested that:

This continued study would include a follow up of patients who had had Hemofil associated hepatitis to study the incidence of chronic sequelae, and a comparison of jaundice associated with NHS Factor VIII and commercial products.<sup>188</sup>

**21.201** The discussion reflects a degree of scepticism among the haemophilia clinicians. As minuted:

Prof Stewart said that jaundice would always occur and there were difficulties in specific identification of the causal agents. Dr Dane [a virologist] said there were problems with the sub-typing. This was possible with samples from patients but was difficult with the concentrates because of the very small amounts of virus present in the samples. Tests for HBsAg could not pick up trace amounts of antigen. Hepatitis B was uncommon in the general population in patients under 14 years of age.<sup>189</sup>

**21.202** Dr Craske was challenged on how he distinguished between Hepatitis B and non-B types. At the same meeting, Dr Biggs reported data returned from haemophilia centres on the incidence of jaundice. There was no action proposed in response to Dr Craske's study, which continued in any event, and his Working Party reported in due course.

---

<sup>186</sup> Ibid pages 160–161

<sup>187</sup> Minutes of meeting of UK Haemophilia Centre Directors, 13 January 1977 [SNB.001.7117] at 7127; Report [SNB.001.7004]

<sup>188</sup> Minutes of meeting of UK Haemophilia Centre Directors, 13 January 1977 [SNB.001.7117] at 7127

<sup>189</sup> Ibid [SNB.001.7117] at 7127

**21.203** The meeting discussed the supply of Factor VIII. At earlier meetings of the Reference Centre Directors it had been established that the BTS could supply sufficient plasma for fractionation to provide a minimum of 40 million units of Factor VIII per year. However there was a hold-up in the expansion of the fractionation process in the UK.

**21.204** Dr Macdonald (Glasgow Royal Infirmary) talked about supplies of Factor VIII concentrate in the west of Scotland. He said that the PFC at Liberton had the capacity to make 60 million units of Factor VIII per year but to reach this figure, the centre would need about £25,000 for new equipment and extra running costs including payment for staff to operate a 24-hour shift system of working. He advised that, in 1976, 14% of all Factor VIII used in the west of Scotland was commercial and 46% of Factor VIII used was freeze-dried NHS intermediate potency concentrate (from the PFC at Liberton).<sup>190</sup>

**21.205** The meeting was informed of a joint plan by the DHSS and the SHHD to divert plasma from south of the border to Liberton for fractionation and return to England and Wales once the Liberton PFC was fully operational: it was not known at this time when that would be.<sup>191</sup>

**21.206** Once more, it was Professor Mannucci and his colleagues who moved the debate forward in an editorial published in 1977 on the work of the Helsinki Symposium, 27 July–1 August 1975, as noted above at paragraph 21.147.<sup>192</sup> The work of this team, as published in 1975, on the natural history of NANB Hepatitis is discussed in Chapter 15, *Knowledge of Viral Hepatitis 2 – 1975–1985*, at paragraph 15.37. The 1977 editorial contained an important analysis of papers discussing the known side-effects of the use of concentrates and an assessment of their significance. It pointed to the advent of home therapy as a factor that might be significant, especially in the light of the observations by Jones et al which emphasised the possibility that complications might develop far from the control of specialised centres. But the editorial did not expand on it. The material part of the paper carried forward the group's analysis of the consequence for haemophilia patients of long-term exposure to 'the agent(s) implicated in *post-transfusion hepatitis*'. They noted that the incidence of clinical illness associated with jaundice was surprisingly low in people with haemophilia. But they commented:

[T]he research of Hasiba et al and Yannitsiotis et al suggests that the observed abnormalities are likely to be related to the frequent and repeated exposure to the agent contaminating the blood derivatives. The observation of Hasiba et al that abnormal liver function was more frequent in patients treated with commercial concentrates than in those treated with blood-bank cryoprecipitate is rewarding, because it clearly shows a way in which prevention can be attempted.<sup>193</sup>

**21.207** The position remained, however, that the clinical and prognostic significance of the observed anomalies in patients was unknown, and that the great majority of the patients were asymptomatic and free of physical signs of liver involvement. It was concluded that until an answer could be provided by long-term prospective evaluation, it appeared unjustified to withdraw or reduce the very effective and life-changing use of concentrates. The same view was emphasised in the discussion:

<sup>190</sup> Ibid [SNB.001.7117] at 7132

<sup>191</sup> In the end this plan did not proceed. See Chapter 19, *Production of Blood Products – Facilities*.

<sup>192</sup> Mannucci, 'Side-effects of antihemophilic concentrates', *Scandinavian Journal of Haematology*, 1977; 30:1–5 [LIT.001.0150]

<sup>193</sup> Ibid [LIT.001.0150] at 0151

[A]nti-hemophilic concentrates are frequently associated with side effects which may be of clinical relevance. However, they do not justify withdrawal or limitation of replacement therapy, which would be accompanied by a consistent deterioration of the present pattern of life of hemophiliacs.<sup>194</sup>

**21.208** In April 1977, Mannucci and colleagues reported on the use of 1-Deamino-8-D-Arginine Vasopressin (DDAVP) to promote Factor VIII properties in patients with moderate and mild haemophilia and von Willebrand's disease undergoing surgery, without use of plasma concentrates.<sup>195</sup> In his review of this period in the paper 'AIDS, hepatitis and hemophilia in the 1980s: memoirs from an insider', Professor Mannucci stated that the advantages of DDAVP in reducing the risk of blood-borne infection in mild haemophilia were immediately appreciated in Italy, where the early use of DDAVP led to a significantly lower rate of infection in Italian patients with mild Haemophilia A when compared to patients with mild Haemophilia B which was unresponsive to DDAVP.<sup>196</sup>

**21.209** SNBTS researchers were aware that there was a rise in Factor VIII activity after infusion of DDAVP. The effect had first been described by SNBTS staff using peptides synthesised in Czechoslovakia.<sup>197</sup> However, there was reluctance to trial the preparation in UK patients, and the intelligence was shared with Italian colleagues who published the 1977 paper referred to. In the circumstances, Mannucci's confirmation of the effectiveness of DDAVP might have been expected to lead to increased use of DDAVP in the UK and Scotland in particular. There was no reference to DDAVP therapy in the minutes of the UKHCDO for 1977, after Mannucci had published, as bearing on the treatment of haemophilia patients. Scotland was well represented at the meetings, but the representatives do not appear to have raised the subject.

**21.210** Towards the end of the 1970s there was an increasing awareness that use of concentrates carried a high risk of hepatitis, particularly in previously untreated patients or in patients who had been treated infrequently.

**21.211** Papers in late 1977 and 1978 by Lesesne,<sup>198</sup> Spero,<sup>199</sup> Mannucci<sup>200</sup> and Preston added significantly to the debate about the relationship between concentrate use and hepatitis. All of these papers were based on the results of liver biopsies which was new evidence. Developing thought is discussed in Chapter 15, *Knowledge of Viral Hepatitis 2 – 1975–1985*.

**21.212** What was to prove in time a significant development in the UK was reported on 16 September 1978. Preston and colleagues (Sheffield) published 'Percutaneous liver biopsy and chronic liver disease in haemophiliacs'.<sup>201</sup> Having dealt with HBV, the paper commented:

<sup>194</sup> Ibid [LIT.001.0150] at 0153

<sup>195</sup> Mannucci et al, '1-Deamino-8-D-Arginine vasopressin: a new pharmacological approach to the management of haemophilia and von Willebrand's disease', *The Lancet*, 1977; 869–72 [LIT.001.0354]

<sup>196</sup> Mannucci, 'AIDS, hepatitis and hemophilia in the 1980s: memoirs from an insider', *Journal of Thrombosis and Haemostasis*, 2003; 1:2065–69 [LIT.001.1101]

<sup>197</sup> See, for example: Gader et al, 'A new vasopressin analogue and fibrinolysis', *The Lancet*, 22 December 1973; 1417–18 [SNB.014.2443]; Prowse et al, 'Specificity in the Factor VIII response to vasopressin infusion in man', *British Journal of Haematology*, 1979; 41:437–447. [SNB.014.2934]

<sup>198</sup> Lesesne, 'Liver biopsy in hemophilia A', *Annals of Internal Medicine*, 1977; 86/6:703–707 [LIT.001.3712]

<sup>199</sup> Spero et al, 'Asymptomatic structural liver disease in hemophilia', *New England Journal of Medicine*, 1978; 298/25 [LIT.001.0177]

<sup>200</sup> Mannucci et al, 'A clinicopathological study of liver disease in haemophiliacs', *Journal of Clinical Pathology*, 1978; 31:779 [LIT.001.1624] at 1629

<sup>201</sup> Preston et al, 'Percutaneous liver biopsy and chronic liver disease in haemophiliacs', *The Lancet*, 16 September 1978; 592–594 [LIT.001.0387]



In addition, non-A, non-B hepatitis may well be an important factor and observations in four of our eight patients support this possibility.

**21.213** Among other conclusions, the paper stated:

A wide spectrum of chronic liver disease was demonstrated, including chronic aggressive hepatitis and cirrhosis. The liver pathology bore no relation to clinical history or to biochemical findings .... The high incidence of chronic liver disease seems to be a recent development and is probably related to factor-concentrate replacement therapy.

**21.214** The immediate impact of this research in the UK, and in particular of the Preston publication, was not great. At the time, Sheffield was not a noted centre of excellence in research in this field, and the significance of the findings of Preston et al was not appreciated. Lesesne, Spero and Manucci had not recommended an immediate change in therapeutic practice. Nor had Preston. As Table 21.1 in the Appendix to this chapter shows, growth in concentrate usage accelerated after 1978.

**21.215** After the initial outbreak of hepatitis following infusion of Hemofil Factor VIII concentrate in 1975, Dr Craske and his colleagues had been charged by the Haemophilia Centre Directors with forming a working party to survey more closely the overall incidence of hepatitis following the use of Hemofil and all other Factor VIII products used in the UK. In addition, the survey was originally aimed at analysing the different types of hepatitis that occurred, whether due to Hepatitis B virus or non-B (subsequently non-A non-B) virus or viruses. It was also to begin to assess the possibility that some attacks of hepatitis could lead to chronic liver disease.

**21.216** Although the survey was far from perfect, partly because knowledge of the putative NANB Hepatitis virus became progressively more definite during the two years of the survey period, the results and the conclusions drawn by Dr Craske and his colleagues were important. The full results of the incidence of hepatitis following use of all Factor VIII products were disclosed to the Haemophilia Centre Directors in August 1978. The report was published in November 1978.<sup>202</sup>

**21.217** There were returns from 24 haemophilia centres. Overall 207 overt episodes of hepatitis (symptoms of hepatitis and abnormal liver test results) were reported. All Factor VIII products were implicated. One hundred and thirty five cases (65.2% of the total) were thought to be non-B and 72 (34.8% of the total) were thought to be Hepatitis B related. Hepatitis was again defined by symptoms. There was no systematic measurement of liver function tests carried out on all recipients. From these studies Craske and colleagues concluded that there were probably two different organisms responsible for 'non-B' Hepatitis, based upon incubation times and the occurrence of apparent multiple attacks in some patients.

**21.218** Although no evidence was produced by the survey as to the likelihood of development of chronic liver disease following an acute attack, the report also referred to a visit by Dr Craske to Dr Roberts and his colleagues at the Department of Medicine at the University of North Carolina. One hundred liver biopsies had been carried out on patients there who had been treated for up to 10 years with Factor VIII concentrates. Chronically elevated serum transaminases were recorded, and nearly 50% had histological changes compatible with cirrhosis, chronic active or chronic persistent hepatitis. The report noted:

<sup>202</sup> Report of the Haemophilia Centre Directors' Hepatitis Working Party – 1978 [SNB.001.7192]

There is controversy as to whether these changes are the sequel to acute virus hepatitis, or are due to some other cause, but Dr Roberts and many other physicians are of opinion that virus hepatitis is the main factor. The elucidation of this problem, therefore, remains the most urgent one from the patient's point of view.<sup>203</sup>

**21.219** Unlike post-transfusion hepatitis, in respect of which different views were held at this time as between the USA and the UK/Europe, in the case of chronic hepatitis in haemophilia patients there was a consensus among US and European investigators. Despite cautious reports, the general view remained in 1978 that the disease in people with haemophilia, while inevitable in a high proportion of patients, was, to a great extent, probably benign. This view was to change very gradually over the next 10 years, as discussed later.

**21.220** The possibility that further work might show whether more than one agent was involved, canvassed by Dr Craske and his colleagues, was taken up in a letter to *The Lancet* of 11 November 1978: 'Evidence for existence of at least two types of Factor-VIII-associated non-B transfusion hepatitis'.<sup>204</sup> Comparison of observations following infusion of a number of commercial products suggested that at least two agents might be involved. The finding was said to emphasise the need for further work to attempt to isolate the infective agents involved.

**21.221** Discussions about the risk of transmission of hepatitis continued throughout 1979. Only now, more attention came to be focused on NANB Hepatitis. The issue was raised in a meeting at the MRC on 12 February 1979.<sup>205</sup> At this meeting it was decided that a major UK study of post-transfusion hepatitis should not be supported by the MRC.<sup>206</sup>

**21.222** The decision that a survey of post-transfusion hepatitis was not warranted was to have longer-term consequences. In the US studies had contributed to the understanding that the prevalence of infection in a given community was an important factor in assessing risk. Lack of similar research contributed to the perpetuation of error about the prevalence of infection in the UK.

**21.223** On 10 March 1979, Wyke and others (including Zuckerman), published 'Transmission of NANBH to chimpanzees by Factor IX concentrates after fatal complications in patients with chronic liver disease'.<sup>207</sup> Seventeen patients at the liver unit, King's College Hospital, received concentrate from four different batches of commercial and non-commercial concentrate. Six cases of NANB Hepatitis resulted. The chimpanzees were infused with batches of Factor IX (from commercial and non-commercial sources) which were associated with the transmission of NANB Hepatitis to the infected patients, and with blood from implicated donors. All the chimpanzees had developed hepatitis. It was suggested that, until there was a screening test for the NANB Hepatitis agent, concentrates should be restricted:

<sup>203</sup> Ibid [SNB.001.7192] at 7197

<sup>204</sup> Craske et al, 'Evidence for existence of at least two types of Factor-VIII-associated non-B transfusion hepatitis' *The Lancet*, 1978; 2:1051-52 [LIT.001.0392]

<sup>205</sup> Minutes of meeting, 12 February 1979 [DHF.002.4842]. See Chapter 15, *Knowledge of Viral Hepatitis 2 – 1975 to 1985*.

<sup>206</sup> Chapter 15, *Knowledge of Viral Hepatitis 2 – 1975–1985*.

<sup>207</sup> Wyke et al, 'Transmission of NANBH to chimpanzees by Factor IX concentrates after fatal complications in patients with chronic liver disease', *The Lancet*, 10 March 1979; 520-524 [LIT.001.0378]

Until blood-donors can be screened for the non-A non-B hepatitis agent, it would seem wise to restrict the use of both commercial and non-commercial concentrates to life-threatening situations. In particular, their use in patients with chronic liver disease should be avoided, as the risk of a serious illness resulting appears to be increased.

**21.224** That advice was not followed. The Haemophilia Reference Centre Directors met again on 15 October 1979.<sup>208</sup> The Hepatitis Working Party had produced a report in relation to liver disease in patients with haemophilia which had been circulated to all the Reference Centre Directors in advance of the meeting. One hundred and seventy nine patients with severe Haemophilia A were studied. Following physical examination of the patients and analysis of their liver function tests, results showed that in spite of multiple transfusions and very large numbers of grossly abnormal liver function tests, very few patients showed any stigmata of chronic liver disease. Patients treated with different types of Factor VIII (NHS and commercial) showed no significant difference in either their liver function tests or viral hepatitis markers.<sup>209</sup> There was discussion regarding the details in the report but this was not recorded in the minutes. Dr Craske invited the Centre Directors to let him have their comments on a draft form (Form C3) asking for information on patients thought to have developed chronic hepatitis.

**21.225** At the 10th meeting of the UKHCDO on 20–21 November 1979, an updated version of Dr Craske's Hepatitis Working Party report was presented.<sup>210</sup> There was much discussion on the contents of the report including (apparently for the first time at a UKHCDO meeting) the prevalence of chronic hepatitis in haemophilia patients. Age appeared to be a very relevant factor. The average attack rate of hepatitis in patients over 40 was six times that for those aged up to 40. Dr Craske commented that most patients thought to have developed chronic hepatitis had not previously had an overt attack of hepatitis. Professor Stewart of the Middlesex Hospital suggested that samples of liver should be obtained from all haemophilia patients who went to post-mortem. Causes of hepatitis were said to be uncertain: the meeting was reminded to keep an open mind. The directors were again asked to report cases of chronic hepatitis by completing the working party's approved version of the new Form C3.<sup>211</sup> Dr Craske stated that there were two types of non-A, non-B Hepatitis, a more confident assertion than previously. In a wide-ranging discussion over two days, including a scientific session, there was, so far as recorded, no discussion of change in practice relating to the prescription of Factor VIII.

**21.226** On 30 April 1980, the Council of Europe, Committee of Ministers, made a number of recommendations including No R(80) 'concerning blood products for the treatment of haemophiliacs'.<sup>212</sup> The recommendations stated that Member States should pursue the goal of self-sufficiency in anti-haemophilia products and in blood plasma for their preparation. The appendix set out recommendations the Council considered desirable for each Member State including:

[T]o give the necessary information to all concerned in haemophilia therapy regarding the problems arising from the procurement and rational use of

<sup>208</sup> Minutes of 9th meeting of UK Haemophilia Reference Centre Directors, 15 October 1979 [LOT.003.2997]

<sup>209</sup> Hepatitis Working Party Report (October 1979) – Appendix 1 [SNB.001.7207]

<sup>210</sup> Minutes of UKHCDO meeting on 20–21 November 1979 [LOT.003.5015]

<sup>211</sup> Ibid [LOT.003.5015] at pages 5024 and 5032–33

<sup>212</sup> Council of Europe Committee of Ministers, 'Recommendation No R(80) 5 of the Committee of Ministers to Member States Concerning Blood Products for the Treatment of Haemophiliacs'. (Adopted by the Committee of Ministers on 30 April 1980 at the 318th meeting of the Ministers' Deputies) [DHF.001.0507]

products; it must be realised that a balance should be achieved between the available resources and the justified needs of haemophiliacs.<sup>213</sup>

**21.227** On 30 September 1980, the UK Haemophilia Centre Directors met in Glasgow.<sup>214</sup> Dr Craske presented the report of the Hepatitis Working Party for 1979. The report set out the results of surveillance for 1978 and 1979. It narrated:

This year has seen the completion of the first year of the surveillance programme financed by a grant from the Department of Health and Social Security. This is part of a three year programme. The second part of the project consists of an investigation for evidence of chronic liver disease in haemophiliacs on long term factor VIII therapy.<sup>215</sup>

**21.228** The report stated:

The prevalence of hepatitis in 1978 and 1979 has had about the same level as that observed in 1976-77. There has been an increase in the proportion of cases of N/A, N/B hepatitis reported in patients with mild coagulation defects receiving concentrate for the first time to cover operations .... The observed increase in mild haemophiliacs contracting hepatitis is probably due to the fact that most severe haemophiliacs have already been exposed to viruses present in all brands of concentrate and are therefore immune to re-infection. Patients with mild haemophilia have not so been exposed; therefore there is no evidence to suggest that the contamination rate of different brands or batches of concentrate with N/A, N/B viruses has diminished.<sup>216</sup>

**21.229** The main conclusions of the working party were that:

1. Transaminitis is unrelated to current factor VIII therapy and the level of anti HBs antibody.
2. Transaminitis is unrelated to a previous history of overt hepatitis.

This is supported by the observation that in 6 out of 7 cases of jaundiced patients observed at Oxford in the past year, the liver function tests quickly returned to normal after the acute attack ....

These results suggest that if transaminitis is related to viral hepatitis, the patients who become carriers and develop chronic liver disease will only contract mild or symptomless acute hepatitis, and the most overtly jaundiced patients will fully recover. This is supported by our observations of hepatitis B infections in haemophiliacs ....<sup>217</sup>

**21.230** 'Transaminitis' was emerging as a descriptive condition identified by biometric abnormalities. At this time it seems that there was some ambiguity in the use of the expression. It is not clear whether those who used the term associated 'transaminitis' with ongoing liver inflammation (hepatitis) or with more established liver damage. However, these conclusions show that among haemophilia doctors, as among hepatologists, there was increasing realisation that chronic liver disease might be associated with persistent

---

<sup>213</sup> Ibid [DHF.001.0507] at 0509

<sup>214</sup> Minutes of UKHCDO meeting, 30 September 1980 [SNB.001.7296]. Substantially the same material was repeated by Dr Craske at an International Symposium held on 1 and 2 October 1980 at the Royal College of Physicians, Glasgow, on Unsolved Problems in Haemophilia [DHF.003.0649]

<sup>215</sup> Report of the Haemophilia Centre Directors' Hepatitis Working Party, 1979 [LOT.003.5679] at 5680

<sup>216</sup> Ibid [LOT.003.5679] at 5680

<sup>217</sup> Ibid [LOT.003.5679] at 5684

mild liver test abnormalities – ‘transaminitis’ – and possibly a carrier state. Furthermore, it was now realised that liver damage and disease might arise in the absence of symptoms.

**21.231** The minute of the UKHCDO meeting on 30 September 1980 stated:

Large pool concentrates appeared to give a higher risk of hepatitis than small pooled concentrates and Dr Craske felt that increased usage of small pooled concentrates would help to reduce the incidence of hepatitis in the haemophilic population. First-time exposure to large pooled factor VIII concentrate resulted in many cases of hepatitis, especially in von Willebrand’s disease patients. Professor Bloom wondered whether cryoprecipitate would be a better product to use for mild haemophiliacs and von Willebrand’s disease but pointed out that there was a problem over the amount of factor VIII in these materials. Dr Craske agreed and he said that the NHS product was certainly better than the Commercial products because of the screening of the blood donors and the regular donor panels which were used in the U.K. The screening procedures for donors of plasma used to make Commercial factor VIII is radioimmunoassay but because of the unstable population and the poor social background, it is likely that there will be a higher incidence of carriers of the hepatitis virus than in the U.K. volunteer blood donors.<sup>218</sup>

**21.232** There was no reported discussion, in the Hepatitis Working Party Report, or at the meeting on 30 September 1980, of the need or desirability for a fundamental reassessment of, or change in, the Haemophilia Directors’ approach to product selection. In Scotland, over the next six months there were discussions relating to the use of cryoprecipitate, but records do not disclose serious concern among haemophilia clinicians of adverse consequences from the use of the PFC concentrates.

**21.233** At a meeting of Directors of the SNBTS and Haemophilia Directors on 30 January 1981 held in Edinburgh, Professor Cash spoke about cryoprecipitate and emphasised that it should be seriously considered for home therapy.<sup>219</sup> Home therapy was increasing and would place such a strain on resources that all options had to be included. The Haemophilia Directors were generally not in favour of using cryoprecipitate for home therapy as they considered the risks of side-effects were too great. They were prepared to use cryoprecipitate in hospitals.

**21.234** When Professor Cash appeared at the Inquiry he explained his reason for recommending cryoprecipitate to meet the therapeutic needs of haemophilia patients. He said:

As a person responsible for self-sufficiency, so I thought, I was drawing attention to my colleagues, not just saying, ‘Keep going with cryoprecipitate chaps’, but cryoprecipitate was much higher yielding than John Watt’s PFC’s concentrates, and that applies across the world. So if you switched fast from cryoprecipitate to concentrate, from the point of view of self-sufficiency, you were going to need a lot more plasma to stay still. And I actually suggested we gave just a thought before we rushed down that track, and that’s all that that was really about.<sup>220</sup>

<sup>218</sup> Minutes of UKHCDO meeting, 30 September 1980 [SNB.001.7296] at 7305

<sup>219</sup> Minutes of meeting of SNBTS Directors and Haemophilia Directors, 30 January 1981 [SNB.001.5055] at 5056

<sup>220</sup> Professor Cash – Day 25, page 113

His advocacy of cryoprecipitate was not based on apprehension of risk related to Factor VIII concentrate.

**21.235** At the joint meeting on 30 January 1981, Dr Albert Bell of SHHD introduced paper 81/2, regarding the Council of Europe recommendation concerning blood products for the treatment of haemophilia.<sup>221</sup> The Directors agreed that policy and practice in Scotland were consistent with the recommendations urging Member States to become self-sufficient and to follow guidelines for the preparation and use of blood products. Professor Forbes told the Inquiry that he was not aware of this recommendation and admitted he knew nothing about the Council of Europe and their role in relation to blood products at that time.<sup>222</sup>

**21.236** Concern was expressed again at a meeting of the Scottish Haemophilia and Blood Transfusion Working Group held on 4 March 1981 about the level of commercial material being purchased.<sup>223</sup> It was agreed that the aim must be for the NHS in Scotland to be self-sufficient. This could be achieved with good planning and steps had been taken to improve the input of plasma. Professor Cash again spoke in favour of cryoprecipitate highlighting two factors:

- The increased yield.
- The increased pool size (although acknowledging that there was a school of thought in the UK that the larger pool size may increase the risk of hepatitis).

**21.237** Professor Cash urged members to bear in mind the allergic reactions and side-effects which could arise. He commented that the majority of home therapy patients had no problems when using cryoprecipitate and in Belgium it was used extensively. Professor Cash did not develop the argument, and the context indicates that his primary concern at this stage was still related to supply.

**21.238** The meeting then agreed that Professor Cash and Dr Foster would monitor ongoing studies in relation to the improvement of the yield of intermediate Factor VIII and the development of a product of higher potency. Dr Foster also drew attention to the importance of reporting adverse reactions to the PFC products. This was necessary to meet the requirements of the product licence but also gave the PFC the opportunity to withdraw other material of the batch giving rise to suspicion pending investigation. The discussion reported gave no indication that the Haemophilia Directors present considered that there were serious risks of adverse reactions: the discussions related to procedural difficulties in devising a reporting system.

**21.239** On 4 July 1981, an editorial in the *BMJ* set out the risk to haemophilia patients in rather more stark terms. It narrated:

Despite advances in screening donors and in blood fractionation, post-transfusion hepatitis remains the major complication of the modern treatment of haemophilia. The diagnosis is usually inferred from abnormalities in the results of hepatic biochemical tests rather than from clinical evidence. Surveys in haemophiliacs have shown changes in the liver architecture consistent with previous viral assault, including those of chronic persistent and chronic active

<sup>221</sup> Minutes of meeting of SNBTS Directors and Haemophilia Directors, 30 January 1981 [SNB.001.5055] at 5057

<sup>222</sup> Professor Forbes – Day 17, pages 83–84

<sup>223</sup> Note of meeting of Haemophilia and Blood Transfusion Working Group, 4 March 1981 [SNB.001.5064]

hepatitis and of cirrhosis. Indeed, in some cases early death from liver disease might prove to be the price paid by haemophiliacs for the improved quality of life afforded by the easy availability of clotting-factor concentrates.

So while no one doubts that the only way to treat haemorrhage in severe haemophilia is by rapid replacement of the relevant clotting factor, considerable thought is being given to reducing the risks. Attention has focused on three practices: the risks of collecting plasma from paid as opposed to volunteer donors; the optimum size of the plasma pool; and attempts at removing the several viruses of hepatitis from blood products.

The risks of viral contamination are certainly increased if plasma is obtained by plasmapheresis of paid donors. True, the sensitivity of testing for hepatitis B has been improved so that its incidence in patients given multiple transfusions is about the same from either paid or volunteer sources, but hepatitis B is a relatively minor problem.<sup>224</sup>

**21.240** The article went on to identify NANB viruses (at least two) as the main cause of chronic liver disease in patients with haemophilia. In relation to the volunteer/paid donor issue, the editorial provided relevant evidence of a material reduction in risk when a hospital changed from commercial to volunteer blood. In relation to the second factor, there was again relevant evidence. The final paragraph stated:

Thirdly, is it likely that the recipients of multiple transfusions can be immunised, or that the threat of hepatitis can be removed from donated blood entirely? Immunisation against hepatitis B is certainly a possibility, but, in the absence of specific markers for non-A, non-B hepatitis, overall protection against hepatitis appears remote. A more likely possibility is that hepatitis-free blood products will become available ...<sup>225</sup>

**21.241** The editorial referred to three recent reports dealing with heat-inactivation,  $\beta$ -propiolactone, and wet-heat treatment processes as more likely to achieve the removal of viral contamination.

**21.242** The third and final Annual Report of the three-year retrospective study financed by the DHSS (project no J/S240/78/7) was produced by the Oxford Haemophilia Centre on behalf of the UK Haemophilia Centre Directors for the year 1980–81.<sup>226</sup> The report, written by Dr Craske and dated 24 September 1981, covered a series of cases of Factor VIII and IX related hepatitis in the UK. Haemophilia Centre Directors had reported 283 episodes of hepatitis relating to 253 patients. Of those, 197 episodes were non-B Hepatitis and were therefore thought probably to be non-A, non-B incidents. There were 86 incidents of Hepatitis B. The incidence of Hepatitis B continued to decline as the sensitivity of screening tests for infectious HBV improved. As published, the report was little different in its terms from the report presented to the UKHCDO Hepatitis Working Party at Glasgow on 30 September 1980. The final report stated:

The question of the significance of chronic hepatitis observed by several groups of workers in liver biopsies of patients with chronically elevated transaminases is still unanswered. Current investigations are attempting to relate the results

<sup>224</sup> 'Post-transfusion hepatitis', *British Medical Journal*, 1981; 283/6283: 1–2 [LIT.001.0227]

<sup>225</sup> Ibid [LIT.001.0227]

<sup>226</sup> Haemophilia Centre Directors' Hepatitis Working Party report for 1980–81 [DHF.001.1711]

in different groups of patients to their transfusion history, and there is strong evidence that different types of non-A, non-B hepatitis are related to different products .... Most patients in this group are still entirely symptomless. The natural history of the disease in non-haemophiliacs is still not known ....<sup>227</sup>

**21.243** The incidence of overt NANB Hepatitis infection associated with US commercial concentrates was 4–20 times higher than that associated with the NHS product. There had been no further deaths directly or indirectly attributable to liver disease in the past year. This report was very significant because it implied that, by 1981, the vast majority of severe and moderately severe haemophilia patients already had NANB Hepatitis. It stated:

The chief finding is that 70-80% of cases of non-A, non-B hepatitis were associated with the first dose of concentrate that the patient received.<sup>228</sup>

**21.244** This was subsequently shown to be the case. The corollary was thought at the time to be that:

Most of the patients treated with any batch of concentrate will be immune to non-A, non-B hepatitis, since batches of concentrate of any brand are contaminated with one (or more) serotypes of these agents.<sup>229</sup>

**21.245** Dr Craske presented this report at the 12th meeting of the Haemophilia Centre Directors on 9 October 1981.<sup>230</sup> He recommended continued surveillance; a study of sub-clinical hepatitis; collection of data on batch numbers; need for post-mortem liver samples; and hepatitis-free concentrates.

**21.246** This report summarised the findings of the survey. Dr Craske had several recommendations to make including:

- Surveillance should continue.
- A multi-centre prospective study of hepatitis in first time/seldom treated patients was planned. This group seemed to have a higher risk of contracting NANB Hepatitis whatever type of material was used for their treatment.
- The working party to continue to collect data on the batch numbers of materials received by patients who developed hepatitis.
- Some commercial firms had claimed that a hepatitis-free Factor IX concentrate was available. Dr Craske thought this may well be true but there were problems in proving the safety of each batch of concentrate as only a limited number of laboratory animals were available for testing the materials.

**21.247** There was some critical comment on Dr Craske's methodology. He had still not overcome the scepticism of some members of the group. Nevertheless, this report shows that enormous progress in understanding the size and nature of the problems of hepatitis in haemophilia patients had occurred in the three years since the initial survey report of 1978.

---

<sup>227</sup> Ibid [DHF.001.1711]

<sup>228</sup> Ibid [DHF.001.1711] at 1712

<sup>229</sup> Ibid [DHF.001.1711] at 1712

<sup>230</sup> Minutes of meeting of UK Haemophilia Centre Directors, 9 October 1981 [SNB.001.7354] at 7372



**21.248** Paragraph 6.79 of the Preliminary Report commented:

Throughout this period there was a debate taking place in the medical community. On one side the view was held (mainly by virologists and public health doctors) that haemophilia patients should not be given concentrates because it was not known what viruses were being transmitted to them. The contrary view (mainly held by the Haemophilia Society and haemophilia doctors) was that concentrates should continue to be given because they transformed the lives of haemophilia patients and hepatitis appeared to be a relatively benign condition.

**21.249** When Professor Forbes appeared at the Inquiry he was asked whether he thought this summarised the points of view at the time. He replied:

All these papers were highlighting something that we did know and understand, that hepatitis was a problem. How much of a problem we didn't really grasp initially, and it's only as these papers came out – the first was Eric Preston, and I think it was liver biopsy he used, and we were appalled that so many of the patients clearly had liver disease and that was then confirmed by the Mannucci paper and so on. So we were gradually becoming aware that the use of all these blood products was not as benign as we thought it was.

....

We started to feel anxious about the use of the products that we gave, which were so wonderfully life-changing for the patients, and that's why, of course, the Haemophilia Society didn't want to change anything. They wanted to go on and give as much product as possible. Because it was thought that the hepatitis that clearly was there was a pretty benign disease, not so eventually, but there we are. That was the state of play.<sup>231</sup>

**21.250** By 1981, a more cautious use of Factor VIII concentrates made from large plasma pools was beginning to be supported, by haemophilia centre clinicians among others. Professor Mannucci's recommendation of DDAVP has already been noted. A similar point was made in 1981 in a study from the University of Gothenburg, Sweden, reported by Norkrans and colleagues.<sup>232</sup>

**21.251** The search for alternative therapeutic materials reflected a degree of growing concern about the use of large-pool factor concentrates. However, there was as yet no change in practice: as the growing use reflected in Figures 1 and 4 indicates, despite the concern about transmission of hepatitis, haemophilia practice throughout the UK continued to depend largely on the use of concentrates.

### Choice of products

**21.252** As noted at the beginning of this chapter, there were good reasons for the selection of specific products to meet specific needs in some cases. However, the Inquiry was aware of comment that individual haemophilia doctors may have been influenced in their selection of commercial products by factors other than the clinical needs of the

<sup>231</sup> Professor Forbes – Day 17, pages 63–64

<sup>232</sup> Norkrans et al, 'Acute hepatitis non-A, non-B following administration of Factor VIII concentrates', *Vox Sanguine*, 1981; 41:129-33 [LIT.001.0743]

patient. The origin of this view, for the most part, appears to have been Douglas Starr's book *Blood*. It is possible to comment only in relation to practice in Scotland.

**21.253** In *Blood*, the relationship between the commercial companies and treatment providers was described as 'cosy'. Douglas Starr was talking specifically about Germany where almost all of the therapeutic material had been bought from the USA. It cost only a quarter to a third as much as the German-made product. But the suggestion was that this type of relationship appeared to be commonplace throughout the advanced world. Douglas Starr wrote: 'Most of the World Haemophilia Federation's budget was paid for by the fractionation companies, who picked up the tab for its lavish annual meetings ...'.<sup>233</sup>

**21.254** Douglas Starr also commented that the National Hemophilia Foundation in the USA received anywhere from 15–25% of its operating budget from the industry as well as special grants for educational projects. He said:

The doctors and the hemophilia organizations argued that the relationship was appropriate and collegial, not coercive. They saw it as a mutual exchange of medicine, money, and information to help their patients get as much clotting factor as they needed at the best prices. Yet patients would later claim that the financial links between the drug companies and the doctors influenced the treatment providers to be complacent about safety.<sup>234</sup>

**21.255** When giving evidence to the Inquiry, Professor Forbes was asked whether he was aware of a cosy relationship of the kind described. He replied: 'I have never been at any meetings that were lavish. So I must have missed out on that'.<sup>235</sup> In the UK, a Symposium on Haemophilia held in Glasgow on 19 September 1975 was sponsored by Travenol.<sup>236</sup> When asked about sponsorship of this symposium, Professor Forbes replied that he did not remember the detail but must have been there. He thought that the sponsors would support the travel of some of the speakers and they may even have paid for accommodation, if required.<sup>237</sup>

**21.256** The evidence set out at paragraphs 21.301 to 21.306 below, relating to the succession from Dr Willoughby to Dr Hann at Yorkhill shows how, in the exercise of their clinical judgement, haemophilia doctors differed in the selection of therapeutic products. Individual clinicians had their preferences, and, objectively, some preferences may have been based on grounds of varying substance.

**21.257** There was, however, no evidence before the Inquiry that would support a finding that Scottish practitioners were influenced in their choice of therapeutic products by benefits provided by pharmaceutical companies in the way hinted at by Starr.

**21.258** The DoH scheme for England and Wales provided for the distribution of NHS products to regions pro rata to the contributions of plasma made for fractionation. At all material times, NHS output was insufficient to meet total demand. The unmet balance of demand was provided by commercial purchases funded by regional health authorities. That allowed for variations within regions. The arrangements for procuring therapeutic

<sup>233</sup> Starr, D. *Blood*, 2002 (2nd edition), Perennial, New York, page 244 [LIT.001.2901] at 2914

<sup>234</sup> Ibid [LIT.001.2901] at 2914

<sup>235</sup> Professor Forbes – Day 17, page 48

<sup>236</sup> Programme for Symposium on Haemophilia, Royal College of Physicians and Surgeons of Glasgow, 19 September 1975 [SNB.001.6951]

<sup>237</sup> Professor Forbes – Day 17, pages 48–49

products in England, and particularly in London and the south east of England, including Canterbury and Thanet, were described by Dr Winter. In some respects, they were very different from arrangements in Scotland. Dr Winter said that individual Haemophilia Directors exercised autonomy in the selection of therapeutic products.<sup>238</sup> It was for the individual to form a view of NHS and commercial concentrates. They would ascertain how much NHS product was likely to be available for the year, and then enter into negotiations, along with procurement colleagues, with a commercial company for purchase of the concentrate of their choosing.<sup>239</sup> In London and the south east, the position was different. Two major centres, St Thomas' Hospital and Kent and Canterbury, had budgets for commercial purchases while others, perhaps 15 small centres, had little or none. It was agreed to allocate NHS material preferentially to them. As a result, Dr Winter used a relatively small proportion of NHS concentrates in his practice.<sup>240</sup>

**21.259** Dr Winter's evidence indicates that national government policy on distribution of available NHS concentrates might have, at best, an indirect bearing on clinical practice and the risks to which patients were exposed. It also indicates clearly that haemophilia clinicians were closely involved in decisions about the procurement and use of commercial products.

#### *Edinburgh and south east Scotland*

**21.260** UKHCDO data on therapeutic products used in managing patients with Haemophilia A in Edinburgh and south east Scotland are summarised in Table 21.3 in the Appendix to this chapter, and shown graphically in Figure 21.8. In the Figure, cryoprecipitate and fresh frozen plasma quantities have been aggregated. DDAVP values have been omitted since they are insignificant in quantity. The picture that emerges is for the period from 1969–91. It provides a quantified historical account as background to the written and oral evidence available to the Inquiry.

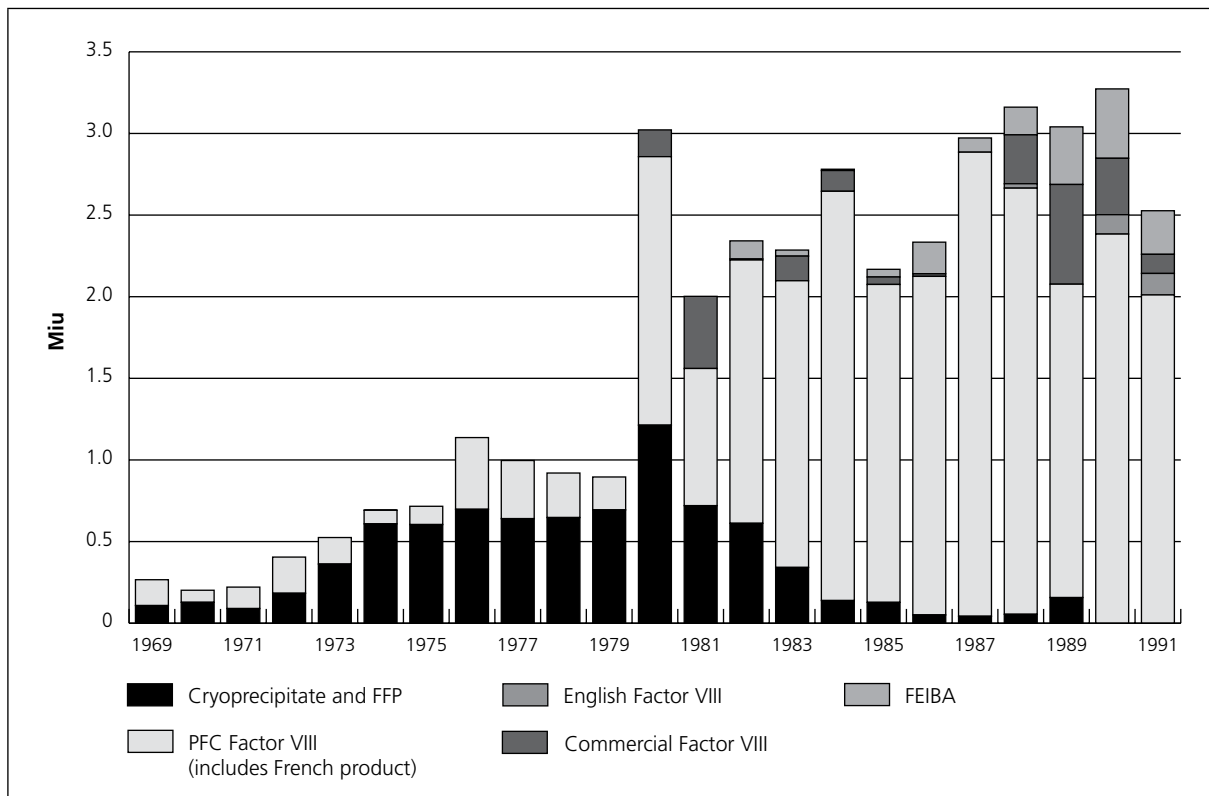
---

<sup>238</sup> Dr Winter – Day 16, page 78

<sup>239</sup> Ibid page 77

<sup>240</sup> Ibid pages 78–79

**Figure 21.8: Edinburgh Haemophilia A Therapy in Million International Units (Miu) – 1969–91**



**21.261** When Dr Davies was in charge, up until 1980, locally produced cryoprecipitate and PFC's concentrates were preferred in the region. As Figure 21.8 demonstrates, Dr Davies clearly made extensive use of cryoprecipitate. He also made not insignificant use of PFC concentrates but took the precautionary view that cryoprecipitate involved fewer donors and was less likely to transmit infections known and unknown. Edinburgh used almost no commercial product under Dr Davies' stewardship.<sup>241</sup> Until 1975, the PFC concentrates were small pool AHF Cohn Fraction I concentrates and for the last three or four years of Dr Davies' period, PFC concentrates made from relatively large pools. Dr Davies used 500 units of commercial Factor VIII in 1974, a unique departure from his general practice, and otherwise prescribed SNBTS products. Professor Ludlam told the Inquiry that Dr Davies had a cautious attitude towards the use of imported commercial Factor VIII concentrate policy. He did not use commercial concentrates because of the uncertainty about hepatitis viruses, in part because he considered the domestic product to be generally safer than concentrates derived from plasma collected in the USA and elsewhere, and in part because he did not want to expose his patients to viruses that might be novel to the local community.<sup>242</sup>

**21.262** Professor Ludlam said that he had tried to follow Dr Davies' policies when he came to Edinburgh in 1980. However, he was interested in introducing home treatment, and was not enthusiastic about home treatment with cryoprecipitate, as discussed earlier at paragraphs 21.101 to 21.106.

<sup>241</sup> Professor Ludlam – Day 18, pages 88–89. See also Professor Ludlam's statement on the use of blood product concentrates [PEN.015.0445] at 0458

<sup>242</sup> Professor Ludlam – Day 19, page 125. Professor Ludlam's report Edinburgh Haemophilia Treatment Policy [PEN.015.0375] at 0379

**21.263** However, in the early 1980s demand for home treatment put pressure on the available supplies of PFC Factor VIII concentrate, and Professor Ludlam said that during 1981 and 1982 a small amount of commercial concentrate was purchased to treat a small number of patients with specific haemostatic therapeutic difficulties, or, in one case, to provide home treatment to one of two patients who lived at some distance. The other was on home treatment for other reasons.<sup>243</sup> In 1980, Professor Ludlam had six patients on home therapy out of 187 registered with his centre. Five per cent of the product used was commercial.<sup>244</sup> By 1983, when Professor Ludlam had transferred most of his patients to concentrates, he had managed to maintain most of them on Scottish product.

**21.264** Following Professor Ludlam's appointment, there was a significant increase in the use of therapeutic materials generally, met in part by commercial purchases. As compared with Dr Davies' practice, use of cryoprecipitate, initially at a peak in 1980, began to fall, reaching a low point in 1987 before rising again in 1989 when there was a major readjustment of the balance between SNBTS and commercial products, and, within the SNBTS range, between cryoprecipitate and PFC Factor VIII. There was an immediate and significant increase in demand for concentrates in 1980 and following years. The shortages of PFC Factor VIII at the beginning of the 1980s described by Dr Foster were reflected in an increase in commercial purchases.

**21.265** So far as commercial products are concerned, use began in 1980 and grew in 1981 as Professor Ludlam's approach to therapy took effect, and then fell until 1988 when there began a significant and sustained increase. There was also a change in the commercial products used after the initial unsettled period, when Factorate was used to make good the limitations in NHS production. From 1982 until 1987 the main products from commercial sources contributing to the total were FEIBA and porcine Factor VIII. From 1988 a wider range of Factor VIII products were purchased including Monoclate, Profilate, Octapharma Factor VIII and Hemofil-M in addition to FEIBA and porcine Factor VIII.

**21.266** Professor Ludlam said that for patients with severe Haemophilia A there were two treatment options: cryoprecipitate and NHS Factor VIII concentrate. Patients were very keen to get onto Factor VIII concentrate and home treatment. Initially, concentrate was in 'desperately short supply'.<sup>245</sup> At that stage he had to delay introducing patients to home treatment because of the lack of NHS concentrates and patients were unhappy about it.<sup>246</sup> A large-scale effort had gone into scaling back cryoprecipitate production and scaling up the manufacture of concentrate to enable patients to be treated at home.<sup>247</sup> Over the period, the SNBTS succeeded in increasing production and meeting demand for Factor VIII concentrate, with commercial purchases reducing as a result until 1988.

**21.267** The graph in Figure 21.8 suggests a more complex picture. The initial surge in use in 1980 to meet Professor Ludlam's new approach to therapy clearly stretched the PFC's capacity. The reduction in use of cryoprecipitate in 1981 was balanced by increasing supplies of the PFC Factor VIII in and after 1982. Dr Foster's evidence indicated that the switch to commercial products in 1980 and 1981 was driven by the need to make good, shortages in the domestic product in order to meet Professor Ludlam's requirements. The first year or two of the 1980s saw a radical change in clinical policy.

<sup>243</sup> Professor Ludlam – Day 18, pages 70–73

<sup>244</sup> Ibid pages 88–89. See also Professor Ludlam's statement on the use of blood product concentrates [PEN.015.0445] at 0458

<sup>245</sup> Professor Ludlam – Day 35, page 28

<sup>246</sup> Ibid page 26

<sup>247</sup> Ibid pages 26–27

**21.268** Overall, the data tabulated for Edinburgh reflect broadly the balance Professor Ludlam was aiming for, though the proportions differ. About 9% of Edinburgh's Factor VIII supplies in 1980 were commercial. That rose to over 34% in the following year before falling back to about 8% by 1983. Commercial purchases were significant as Professor Ludlam introduced home therapy, but fell rapidly at the same time as the risk of AIDS was becoming more firmly associated with a transmissible agent or, on his analysis, progressive immune compromise caused by reaction to antigen overload.

**21.269** Over the same period, from the 1970s to the mid-1980s, therapy for Haemophilia B had progressed from treatment with fresh frozen plasma to Factor IX concentrate, which itself developed over time from a combination product, including several factors, to a concentrate composed of Factor IX alone.<sup>248</sup> Professor Ludlam was able to use Scottish products for most patients.

**21.270** So long as the PFC supplies continued to meet the demand for concentrates among Professor Ludlam's patients, the position in Edinburgh and south east Scotland, as presented by Professor Ludlam, was close to the ideal. Products produced locally from blood donated in Scotland were used more or less exclusively in haemophilia therapy. The Council of Europe Committee of Ministers 'Recommendation No R(80) of 30 April 1980: Concerning Blood Products for the Treatment of Haemophiliacs', stated that Member States should pursue the goal of self-sufficiency in antihemophilia products and blood plasma for their preparation. The Recommendation acknowledged the fact that both the geographical origin and type of donor population had a significant effect on the risks of infectious diseases.<sup>249</sup> Professor Ludlam's arrangements would have satisfied that recommendation if his area of operation had been a state.

**21.271** Dr McClelland joined the service in Dr Davies' period. He said of his early experience:

As a first year junior house officer in 1969, I was privileged to work for the late Dr Howard Davies, an Edinburgh Royal Infirmary consultant physician who cared for patients with haemophilia. Dr Davies was a strong proponent of cryoprecipitate rather than factor VIII concentrate. I remember clearly that his rationale for this struck me as being eminently sensible. It was that by avoiding the use of products made from the blood of thousands of donors, especially those from other corners of the world, one was almost bound to reduce the risks of passing on infections, known or unknown, to the patients.<sup>250</sup>

**21.272** The observation does not quite fit the pattern of use demonstrated in the graph at Figure 21.8, though the contrast was with concentrates prepared from 'thousands' of donations, the position in commercial production rather than at the PFC. Subject to that, Dr McClelland's comments reflect the picture in Figure 21.8.

**21.273** Dr McClelland commented specifically on Dr Davies' preference for local products, rather than imported products, as a way of minimising infection. He told the Inquiry:

[I] think his view was as a sort of matter of fairly elementary biology: the more, as it were, different donors' blood samples contributed to the dose

<sup>248</sup> Professor Ludlam – Day 18, pages 46–48

<sup>249</sup> Council of Europe Committee of Ministers, 'Recommendation No R(80) 5 of the Committee of Ministers to Member States Concerning Blood Products for the Treatment of Haemophiliacs' (Adopted by the Committee of Ministers on 30 April 1980 at the 318th meeting of the Ministers' Deputies) [DHF.001.0507]

<sup>250</sup> Dr McClelland's statement on the use of blood product concentrates [PEN.015.0307]

that one received as a patient, arithmetically the risk of getting something nasty was increased, and the further afield the blood came from, there was a certainly incalculable but reasonable grounds to expect that something new and different and unfamiliar to the indigenous population might be in that blood.<sup>251</sup>

**21.274** As described by Dr McClelland, the reasoning was not complicated, but it explained clearly the pattern of use of materials in Edinburgh during Dr Davies' period. Professor Ludlam was prepared to use commercial products, in particular Armour's Factorate Factor VIII, which was not heat-treated to any extent until 1984.<sup>252</sup> There is no basis in evidence, however, to doubt that the early use of Factorate was a response to shortage of the SNBTS product rather than a matter of choice.

**21.275** Apart from putting pressure on the SNBTS by changing clinical practice, the Edinburgh Centre took steps to protect individual patients when they were away from home. A national system in use since the 1970s provided every patient diagnosed with haemophilia with a card stating what their condition was, the level of severity, which haemophilia centre they were registered with and where to phone in an emergency. Professor Ludlam said:

Patients were individually told to request either cryoprecipitate or an NHS concentrate and to avoid a commercial concentrate if possible. To emphasise the importance of this each patient was supplied with a small statement to this effect, which was placed in their haemophilia card, which they could then show to get treatment at another Centre.<sup>253</sup>

**21.276** This step was initiated because patients might travel to England and if they required treatment there was a possibility they might get an injection of commercial concentrate.<sup>254</sup> It gave added emphasis to the continuing preference for NHS products, where possible, after Professor Ludlam took over from Dr Davies in 1980. Professor Ludlam had a research interest in monitoring a group of his patients treated solely with NHS product. The card system supported monitoring.<sup>255</sup> But there is no reason to treat this as other than an incidental aspect of treatment policy.

**21.277** Dr Boulton took up his post in Edinburgh in 1980. In his oral evidence, he talked about the different forms of therapy available for the patients at that time, comparing perceptions of the SNBTS product then and later:

[A]s time went by, I did become aware of views that there were problems with fractionated product, even from NHS volunteer donors. But I think it was not unreasonable for the newer generation to advocate an increase in usage of Factor VIII.

The problem was that if one were to restrict the use to what, at that time, was felt on good grounds but not on established grounds, to be a safer product, ie a cryoprecipitate that was more difficult to use, less potent, the patients would not have so much protection from joint damage, whereas one would be able,

<sup>251</sup> Dr McClelland – Day 21, pages 153–154

<sup>252</sup> The commercial products used in Edinburgh from 1988 were heat-treated.

<sup>253</sup> Professor Ludlam's report, *Edinburgh Haemophilia Treatment Policy* [PEN.015.0375] at 0380

<sup>254</sup> Professor Ludlam – Day 18, pages 68–69

<sup>255</sup> *Ibid* pages 72–73

with higher doses of smaller volume infusion lyophilised from the freeze-dried fractionated product, be able to embark on a programme of prophylactics for preventing the damage to joints, particularly in boys as they were approaching their teens.<sup>256</sup>

**21.278** The dilemma for clinicians could only be resolved by the exercise of judgement. Dr Boulton pointed out that Professor Ludlam was anxious to increase the use of Factor VIII for the haemophilic patients, particularly the young ones.<sup>257</sup> In Dr Boulton's view, Professor Ludlam was right to move away from cryoprecipitate treatment and towards the use of more Factor VIII for treatment of haemophilia patients. At that time they had no inkling of HIV/AIDS but did of course know about hepatitis.

**21.279** Dr Boulton and his colleagues thought that the process of blood donor selection and testing and ever better hepatitis screenings would result in a quality of plasma sent for fractionation that would be as risk-free as possible.<sup>258</sup> He considered the PFC product to be as good a quality product as could be obtained anywhere in the world and on a par with commercial firms. But the commercial firms developed a very good marketing strategy. The packaging, the literature with attractive pictures etc were of a standard way beyond the budget of the PFC.

**21.280** The change of practice in Edinburgh, including the use of commercial products during the early part of Professor Ludlam's tenure, reflected the state of knowledge at the time. No single factor explains the whole picture, however. There were specific cases where commercial product was preferable for the particular patient. Some patients did not tolerate the PFC intermediate concentrate, for example, and for them a commercial alternative was prescribed. That apart, Professor Ludlam promoted home treatment to a greater extent than Dr Davies and that explains his resort to commercial concentrates in 1980 and the next few years.<sup>259</sup> The PFC had to gear up production to meet increasing demand generated by changes in treatment policy, increasingly towards home treatment.

**21.281** But the picture is complicated by other factors. By the end of the 1970s there were growing and widespread concerns about the use of concentrates related to risk of transmission of NANB Hepatitis. However, there was no evidence of a shift to cryoprecipitate at that stage. Later, in 1982–83, some clinicians in the USA, in particular Dr Oscar Ratnoff, attempted to move patients back to cryoprecipitate, but this was resisted by patients who wished to continue taking concentrates.<sup>260</sup> Figure 21.8 shows use of cryoprecipitate increasing in 1979, peaking in 1980 and then beginning to fall, but on Professor Ludlam's evidence this could not be said to relate to a policy decision relating to transmission risk. He told the Inquiry that he did consider switching his patients from factor concentrates to cryoprecipitate in 1982–83 (as happened in some parts of England and Wales). He discussed the possibility with his colleagues in the SNBTS and they did not look at all favourably upon being able to achieve it within the timescale. He thought the possibility was discussed informally with Dr McClelland and Dr Boulton. He said that all three had offices close together and used to talk about these sorts of things. It may also have been discussed in a more formal context but he could not recall this happening.<sup>261</sup>

<sup>256</sup> Dr Boulton – Day 24, page 16

<sup>257</sup> Dr Boulton – Day 24, page 18

<sup>258</sup> Ibid pages 102–103

<sup>259</sup> See paragraphs 21.103–21.110

<sup>260</sup> Note of a meeting between Professor Ludlam and the Inquiry Team, 19 April 2011 [PEN.012.0774] at 0775; Professor Ludlam – Day 35, pages 30–31

<sup>261</sup> Professor Ludlam – Day 35, pages 29–30



**21.282** The wider picture at the time was of increasing emphasis on scaling up concentrate production at the PFC, not least to meet Professor Ludlam's requirements. The SNBTS was putting all its effort into improving the PFC's plant for concentrate production.<sup>262</sup> The logistics of making the switch to cryoprecipitate would have been huge, and, in treatment terms, it seemed a retrograde step.<sup>263</sup> A large effort had gone into scaling up the manufacture of factor concentrates, which enabled patients to be treated at home.<sup>264</sup> Professor Ludlam would have had enough cryoprecipitate to switch one or two patients back to it but if there was to be a wholesale move back to cryoprecipitate his understanding was that it would have taken some time for the SNBTS to change course in manufacture. It would have required huge changes to the manufacturing practices.<sup>265</sup> It would have taken time to acquire the necessary production equipment, train staff and obtain the required consumables.<sup>266</sup>

**21.283** As Figure 21.8 shows, from 1982–87, use of cryoprecipitate decreased, the SNBTS Factor VIII concentrate was the principal product used, and use of commercial products fell to a very small percentage of total Factor VIII usage. Professor Ludlam was asked about alternatives to the standard treatment options for patients with severe Haemophilia A. The alternatives discussed were:

- i. No treatment (although this was not an option if the patient was bleeding).
- ii. Reducing the amount of factor concentrate (including switching from prophylactic treatment to on-demand treatment).
- iii. Treatment with cryoprecipitate.
- iv. From 1984 onwards, the use of commercial heat-treated Factor VIII concentrate.

**21.284** In Professor Ludlam's view, the first course proposed was not appropriate. He explained that the risks that arose from not treating patients greatly outweighed the risk of transmission of infection, a view generally shared by other haemophilia clinicians. In addition to the practical difficulties already mentioned, switching to cryoprecipitate would not eliminate the risk of transmission of infection entirely.<sup>267</sup>

**21.285** The second option raised a more technical issue. In the period 1982–84, Professor Ludlam had studied abnormalities in the immune systems of patients.<sup>268</sup> When he received the results of immune function tests showing reductions in CD4 counts, he considered whether the results were related to the amount of concentrate the patient had received over the past two or three years. He was very quickly able to go back over several years' worth of transfusion records and there seemed to be no correlation between the immune abnormalities, and the amount of factor concentrate the patient had received. There was nothing to suggest that if patients used less concentrate this would result in fewer immune abnormalities.<sup>269</sup>

---

<sup>262</sup> Ibid page 28

<sup>263</sup> Note of a meeting between Professor Ludlam and the Inquiry Team, 19 April 2011 [PEN.012.0774] at 0775

<sup>264</sup> Ibid

<sup>265</sup> Ibid

<sup>266</sup> Professor Ludlam – Day 39, pages 21–22

<sup>267</sup> Professor Ludlam – Day 35, pages 26 and 31

<sup>268</sup> See Chapter 11, *HIV/AIDS Aetiology*, paragraphs 11.65–11.72

<sup>269</sup> Professor Ludlam – Day 39, pages 16–17

**21.286** Professor Ludlam accepted that it was possible that certain patients might not have seroconverted if the amount of factor concentrate they received had been reduced at an earlier stage. However, the issue was not straightforward. At this period (in the mid-1980s), all treatment at the Edinburgh Haemophilia Centre was on demand, that is in response to the patient suffering a bleed, and usually at home. If patients used less Factor VIII or chose not to treat bleeds as intensively as they might have normally, they might actually require a lot more treatment to settle the bleed. Professor Ludlam explained that bleeds into joints (particularly elbows and knees) can be extremely painful and can last for several days. An untreated knee bleed, for example, will last about a week to 10 days. If not treated from the outset the pain becomes so great that patients may require large amounts of morphine or pethidine. At that point, the patient might opt for treatment and would then require a lot more treatment to settle the bleed than if he had commenced treatment from the beginning. If a bleed was treated very early on then usually a single injection was enough, whereas if the bleed was left to develop over several days, the patient needed an awful lot of treatment and therefore a lot of Factor VIII.<sup>270</sup>

**21.287** Professor Ludlam said that occasionally patients presented with recurrent bleeds into a joint (typically where they had received a short course of treatment in response to a bleed and then had re-bleed). One possible course of treatment under those circumstances was to treat the patient for two or three months, often every day, to try and keep the factor level up to stop the recurring bleeding.<sup>271</sup> Circumstances varied. Professor Ludlam's evidence was that he considered carefully all of the treatment options in selecting the appropriate course before deciding what was in his patients' best interests. The second option, of reducing the amount of concentrate infused, did not provide a generally acceptable approach. The third option, increased use of cryoprecipitate, was subject to the limitations on supply already discussed. More generally, on Professor Ludlam's approach it was one of the range of treatment options to be considered on an individual basis.

**21.288** So far as use of commercial products is concerned, Figure 21.8 reflects a shift in policy in and after 1988, implicit in the pattern of usage. Views were developing at that time about the ease of use of commercial Factor VIII products because of their high purity; relative to the SNBTS product. Professor Ludlam had also observed immune abnormalities in some of his patients that were not associated with viral infection, but were hypothesised to be associated with protein impurities in the PFC products. Until late 1984 there was confidence in the relative safety of the SNBTS product. Steps taken at the end of that year to inactivate HIV in the PFC's intermediate Factor VIII product proved to be successful. The question whether any products were 'safe' from transmission of NANB Hepatitis/HCV is discussed in other parts of this Report.

**21.289** Having regard to the evidence as a whole, there is no basis for a view that Professor Ludlam's general practice was other than as described by him: decisions on therapy were made on an individual basis, with a clear bias towards the use of SNBTS products in most cases, consistently with the policy of his predecessor. Decisions were made on professional grounds. There was no suggestion that he was influenced by any considerations other than his patients' welfare, and there is no basis for inferring that he was. Professor Ludlam's research interests are considered later, in the context of information and advice tendered to patients. However, in the Inquiry's view, these interests did not influence his choice of therapeutic product for the treatment of his patients.

---

<sup>270</sup> Ibid pages 17–18

<sup>271</sup> Ibid pages 19–20

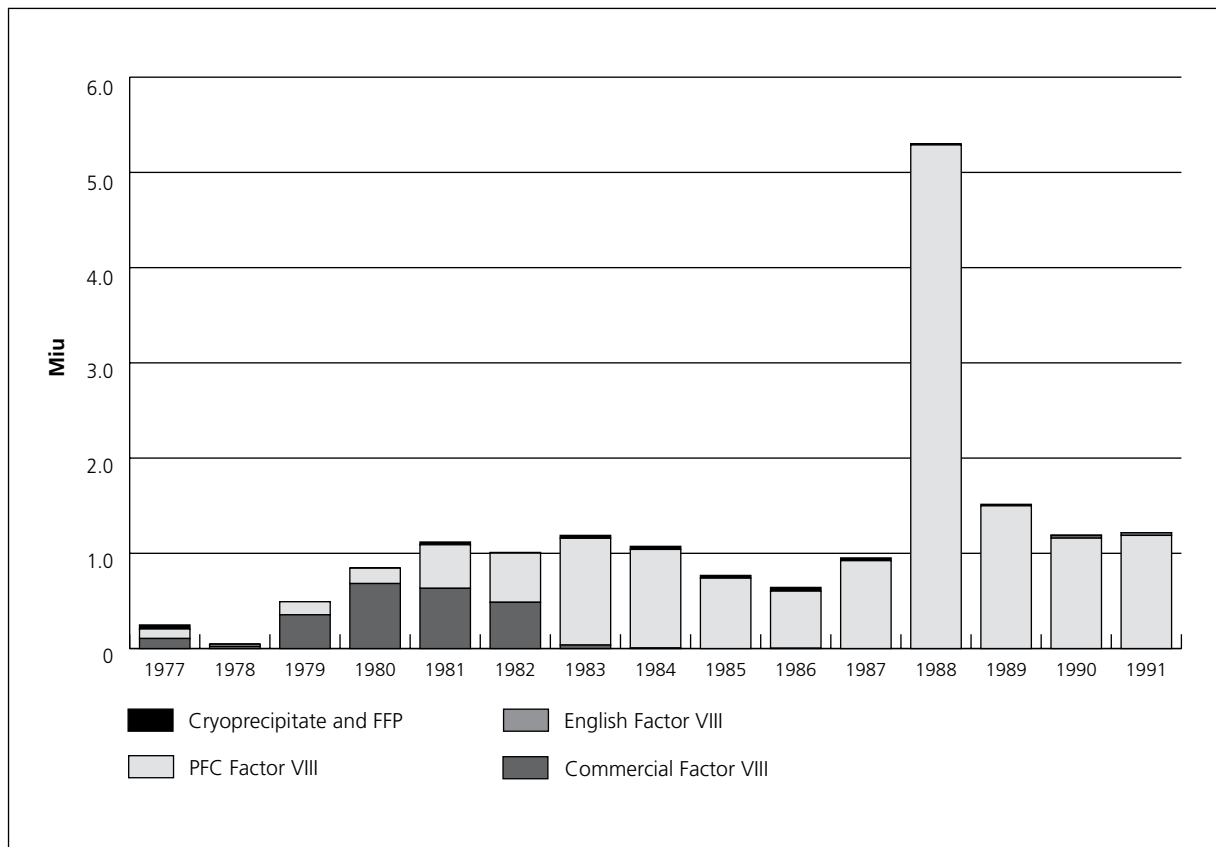
### *Glasgow and west of Scotland*

**21.290** When looking at the picture that emerges in Glasgow and the west of Scotland it is important to take account of the division of clinical responsibility between two treatment centres. Until their teens, children received specialist management of their blood coagulation disorders at West of Scotland Children’s Comprehensive Care Haemophilia Centre at Yorkhill Hospital. Thereafter they were transferred to the GRI. A patient diagnosed with HCV infection while in adult care might have received the infective agent at either hospital, and under very different clinical regimes.

### **Royal Hospital for Sick Children, Yorkhill**

**21.291** Data on Haemophilia A therapy at Yorkhill are summarised in the Appendix to this chapter at Table 21.4, and shown graphically in Figure 21.9. The Figure has been prepared on the same basis as that for Edinburgh and south east Scotland.

**Figure 21.9: Glasgow Yorkhill Haemophilia A Therapy in Million International Units (Miu) – 1977–91**



**21.292** Data are available for Yorkhill from 1977 onwards. The UKHCDO has not reported any use of products up to 1976. Within the period for which data are available, there are variations that reflect changing policy. Cryoprecipitate use varied considerably until 1982, annual quantities ranging from 60 to 41,930 units without discernible pattern. Use of commercial products, already administered in 1977, rose steeply to 1981, fell back in 1982, and from 1983 dwindled to almost zero. 31,000 units of FEIBA were used, exceptionally, in 1991, but made no impression on Figure 21.9 in light of the high value for NHS products. The spike in 1988 reflects an exceptionally heavy use of NHS Factor VIII

concentrates, probably related to one or two unusual clinical events creating exceptional demand. There was no evidence that it reflected a change of policy.<sup>272</sup>

**21.293** Dr Willoughby, who was a haematologist at Yorkhill until the end of 1982, provided the Inquiry with two written statements.<sup>273</sup> He explained that commercial Factor VIII was used in order to make home therapy as easy as possible for the parents of his young patients. He wrote:

It was much easier to reconstitute with its diluent, taking only a few minutes of gentle handling, as I remember it. The volume for a normal dose could be comfortably drawn up into a 10 or 30ml syringe, which could then be easily attached to a slender scalp-vein IV needle for injection (rather than a drip-stand etc.).

Commercial factor products were typically supplied boxed with all the necessary components for immediate and easy use. The material was ordered through the hospital pharmacy and was relatively expensive, but it was considered that the advantages justified the expense.

**21.294** Dr Willoughby explained in his second statement that his prime concern was to treat haemorrhagic events as expeditiously as possible and home therapy avoided the need to travel, often some distance, to hospital. Dr Willoughby was an advocate of prophylactic therapy (see paragraph 21.113). In his statement he said that the aim of prophylactic home treatment was to prevent serious joint and muscle pathology, and to transform the children's quality of life and that of their families. Cryoprecipitate was unsuitable for home therapy due to the 'slow thawing out process in a 37 degree water bath, drip type infusion and somewhat uncertain dosage'.

**21.295** Although the risks of NANB Hepatitis were well known, Dr Willoughby's perception was that all concentrates carried a high risk of transmission, whether NHS or commercial. Pool size was less of a concern than using a product that permitted the establishment of a home therapy programme. Dr Willoughby thought that much more attention was paid to pool size following the discovery of HIV.

**21.296** Though scarcely discernible from Figure 21.9, cryoprecipitate was used at Yorkhill, but, both in absolute and relative terms, in very small quantities.

**21.297** As already indicated Dr Willoughby was a strong supporter of home therapy and of prophylaxis.<sup>274</sup> However, at Yorkhill, very young (and newly diagnosed) patients were usually managed as hospital-based patients (as opposed to home-therapy-based patients).<sup>275</sup> In general, Dr Willoughby considered that commercial and NHS concentrates had advantages over cryoprecipitate in that they could be stored at 4°C and could be carried by the patient when travelling.<sup>276</sup>

<sup>272</sup> The Inquiry contacted clinicians who worked at Yorkhill during the relevant period to see if they could recall the reason for the heavy use of concentrates in 1988. Professor Hann's response [PEN.019.1447], Dr Pettigrew's response [PEN.019.1450], Dr Gibson's response [PEN.019.1452]

<sup>273</sup> Dr Willoughby's first statement on the use of blood product concentrates [PEN.019.1265] and Dr Willoughby's second statement on the use of blood product concentrates [PEN.019.1272]

<sup>274</sup> Paragraphs 21.95 and 21.113

<sup>275</sup> Professor Hann – Day 31, page 27

<sup>276</sup> Paragraph 21.96

**21.298** In his book on paediatric haematology, Dr Willoughby discussed the different products used to treat coagulation deficiencies. He noted that plasma and cryoprecipitate had an advantage over human concentrates in carrying a low risk of transmitting serum hepatitis since each bag was prepared from a single donor, rather than a pool. He noted that commercial Factor VIII and Factor IX concentrates were available as well as similar concentrates being available from many of the UK blood transfusion centres. He commented on the high cost of commercial concentrates. There was nothing to suggest bias in favour of the commercial product.<sup>277</sup>

**21.299** At the UKHCDO meeting held in Glasgow on 30 September 1980, Dr Willoughby said that from his experience of working with children it was clear that using Factor VIII concentrates would give the possibility of non-crippled adults.<sup>278</sup> He clearly favoured use of concentrates. According to Professor Hann, in a statement provided to the Inquiry, Dr Willoughby '[H]ad what appeared to be a preference for commercially (as opposed to NHS-produced) products ....'<sup>279</sup>

**21.300** That preference is reflected in the data for the early years covered by Figure 21.9. In a discussion with Professor Hann just prior to his departure from Yorkhill, Dr Willoughby said that he was generally disillusioned with the health service throughout the UK and felt he had been let down with regard to supplies.<sup>280</sup> He said that commercial concentrate was a better option as it was available, and enabled doctors to treat patients with very severe or life-threatening bleeding without having to rely on cryoprecipitate which was extremely difficult to use in children. He felt that the Scottish concentrate suffered from being of very low purity, difficult to draw up, with significant wastage, and there were also other problems such as infusion-related reactions.

**21.301** Professor Hann became Director of the West of Scotland Children's Comprehensive Care Haemophilia Centre in January 1983, in succession to Dr Willoughby.<sup>281</sup> There was an immediate, and significant, change in treatment policy. So far as recorded, Dr Willoughby had used Travenol Hemofil Factor VIII in 1977 and 1978. Armour Factorate was used in each year from 1977 to 1984, with usage in 1983 falling to 7.6% of the level in 1982, and to just over 1% of the 1982 level in 1984. Professor Hann effectively withdrew commercial concentrates from use on taking up his appointment.

**21.302** Professor Hann did not share Dr Willoughby's preference. He explained that the NHS product was cheaper, and that the risk of transmitting viruses was perceived to be smaller because of the better donor pool. But, he added, there were several caveats to that. One of these was the desire not to 'chop and change' products too much because of the small risk of inhibitor development which could be devastating as it made the patient untreatable in that era. For Professor Hann, the prime reason for choosing NHS product was the lower risk of infectivity.<sup>282</sup> However, he considered that, having discussed the issue with Dr Willoughby, his predecessor made the choice for what he regarded as good reasons. His evidence to that effect is accepted. Dr Willoughby justified his position in discussion with Professor Hann, and there is no evidence that undermines his position. Similarly, Professor Hann did not at that time share Dr Willoughby's belief that prophylaxis

<sup>277</sup> Willoughby, MLN. *Paediatric Haematology*, Churchill Livingstone, Edinburgh, London, New York, page 321 [PEN.016.1062] at 1065

<sup>278</sup> Minutes of UKHCDO meeting, 30 September 1980 [SNB.001.7296] at 7301

<sup>279</sup> Professor Hann's further statement on the use of blood product concentrates [PEN.015.0035] at 0037

<sup>280</sup> Professor Hann – Day 21, page 28

<sup>281</sup> Professor Hann's statement on the use of blood product concentrates [PEN.012.0203]

<sup>282</sup> Professor Hann – Day 31, pages 80–82

was the way ahead. When he took over, he shared the scepticism, common at the time, as to the efficacy and practicality of prophylaxis. He now considered that Dr Willoughby was right.<sup>283</sup>

**21.303** Professor Hann said that he and Dr Willoughby discussed the question of supplies from the USA, which had been affected by Hepatitis B.<sup>284</sup> Dr Willoughby's view was that the problem of Hepatitis B had largely been overcome. It was also Professor Hann's experience at that time that they were not seeing new cases. Dr Willoughby felt that in the very early 1980s NANB Hepatitis was a minor disorder, and that all products were susceptible to it. The evidence rehearsed in this chapter indicates that there was a body of professional opinion supporting that position. Professor Hann commented that the Royal Free Hospital in London (a major hepatitis centre) also thought NANB Hepatitis was a minor disorder at that time.<sup>285</sup>

**21.304** Professor Hann said that he and Dr Willoughby agreed that there needed to be a move within the NHS to self-sufficiency. Professor Hann would have preferred to be able to use NHS concentrate, but it was not possible then to use Scottish product exclusively: there were periods when they had to call in extra commercial products.<sup>286</sup> Whether that was a sustainable position is less easy to determine. When asked whether a clinician could have felt that there was not a reliable enough supply of Factor VIII coming through around 1979–80, Dr Foster of the PFC replied that he did not know how well informed clinicians were about the stock situation. From his own analysis there was not a sustained problem.<sup>287</sup>

**21.305** When Professor Hann took over, treatment policy was reassessed, and in some respects took a new direction. Very young and new patients were still treated in hospital. They would be offered cryoprecipitate treatment in the first instance if it was possible logistically to give it to them (that is, if their veins were adequate and they did not have any reactions). As a result there was a sustained but relatively low level use of cryoprecipitate in the period 1983–87, as shown in the Appendix at Table 21.4.

**21.306** Professor Hann said that cryoprecipitate treatment may have even been recommended as the first option for his patients in the difficult interim period in 1984 when the HTLV-III virus had been isolated, and some of the patients were found to have antibody to the virus upon testing.<sup>288</sup> When asked whether he would have offered a child who was already receiving Factor VIII concentrate in late 1983 the possibility of ceasing concentrate therapy and returning to cryoprecipitate, he said that he believed that was what they had in fact done at Yorkhill.<sup>289</sup> He was almost certain that in late 1983, when 'people like Peter Jones and others' were suggesting that children could be treated with cryoprecipitate, he did change some patients over to cryoprecipitate and continued others for longer than he would have done previously.<sup>290</sup> Some patients returned to cryoprecipitate treatment in 1984 for a period of time.<sup>291</sup> His oral evidence is supported by the numerical data. However, he stressed that it was not a matter of automatically switching every child over to cryoprecipitate. The decision had to be tailored to each individual patient.<sup>292</sup>

<sup>283</sup> Professor Hann – Day 21, page 28

<sup>284</sup> Ibid page 29

<sup>285</sup> Ibid page 29

<sup>286</sup> Ibid pages 27–30

<sup>287</sup> Dr Foster – Day 22, pages 129–130

<sup>288</sup> Professor Hann – Day 21, pages 68–69

<sup>289</sup> Professor Hann – Day 31, page 25

<sup>290</sup> Ibid page 27

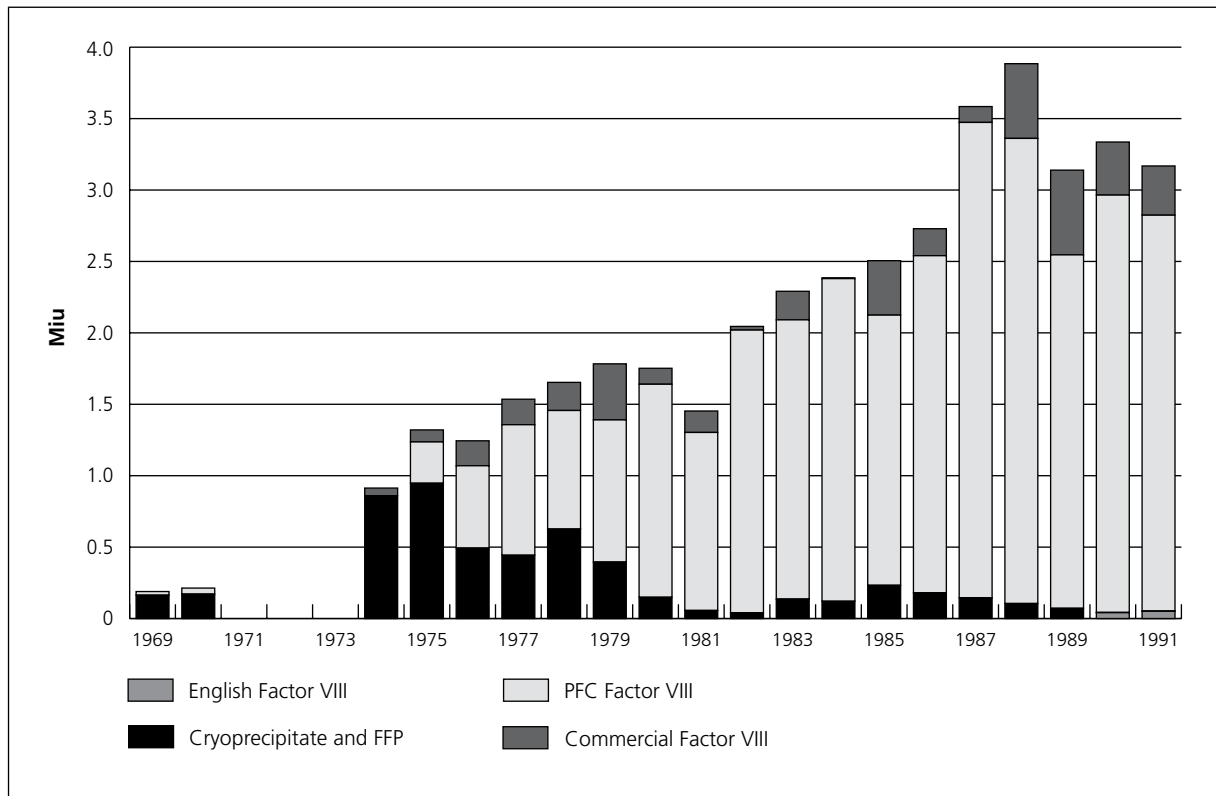
<sup>291</sup> Professor Hann – Day 21, page 68

<sup>292</sup> Professor Hann – Day 31, page 27

### Glasgow Royal Infirmary

**21.307** Following the same approach as above, data on Haemophilia A therapy at the GRI are summarised in the Appendix to this chapter at Table 21.5, and shown graphically in Figure 21.10. The Figure has been prepared on the same basis as in the case of Edinburgh and south east Scotland and Yorkhill.

**Figure 21.10: Glasgow Royal Infirmary Haemophilia A Therapy in Million International Units (Miu) – 1969–91**



**21.308** There are gaps in the data for 1971, 1972 and 1973, but these do not appear to be material to a general understanding of trends in product selection over the material part of the period covered.

**21.309** So far as it is possible to draw inferences about the early years, it appears that cryoprecipitate use peaked in 1975 and then fell progressively until 1982. There followed a slow upward trend until 1985, and thereafter a reduction in use until 1989. No cryoprecipitate was used in 1990 and 1991. Use of SNBTS Factor VIII concentrates began in 1975, more or less coinciding with the commissioning of the PFC at Liberton, and thereafter increased progressively until 1988. In the final three years of the period use fell and commercial products became a more significant factor. In this last respect there is a close parallel with Edinburgh and south east Scotland. Purity had become an issue and the commercial product had an added attraction.

**21.310** In contrast to Edinburgh and south east Scotland, the data show measurable usage of commercial products before 1980, reaching a peak of just over 28% of Factor VIII concentrate use in 1979. Between then and 1987 there is no discernible pattern in the use of commercial products, either in absolute terms or in relation to total concentrate use.

**21.311** The commercial products used varied. Human Factor VIII plasma products in the period to 1980 included Kryobulin, Hemofil, Profilate, Factorate and Humanate. Koate entered the picture in 1981 and 1982. Otherwise, from 1981 until 1984, Factorate, Humanate, and Hemofil appeared without discernible pattern. From 1985 onwards, Porcine Factor VIII was prescribed. Use of commercial human plasma products began again in 1988, and included Profilate, Kryobulin, Monoclata, and Haemate P. The detailed data in Table 21.5 include limited use of DDAVP in 1978, 1980, 1981 and more consistent use from 1985 to 1991.

**21.312** In view of the somewhat confused picture painted by the numerical data, it would have been helpful to have had a clear explanation of policy from the senior consultants in charge of patient care. Professor Forbes started to work with haemophilia patients in the GRI in 1965, initially under Professor Douglas, and then as Haemophilia Director. However, he candidly told the Inquiry that after forty years he found it quite difficult to remember the details of what he thought at any one time and that his memory was ‘not as good now as it was all those years ago’.<sup>293</sup> According to his recollection, the policy for treating bleeding, from an early date, was the use of pooled cryoprecipitate. Cryoprecipitate was preferred because, being locally harvested, it carried a lower risk of transmitting hepatitis than ‘concentrates which were made with indeterminate but huge numbers of patients’ plasma being pooled together’.<sup>294</sup> The policy continued for many years. Patients with mild disease received DDAVP, but with caution because of its long-term side-effects.

**21.313** Professor Forbes’ evidence on product choice was that he continued to use cryoprecipitate for both routine treatment in the centre and for distribution to people on home therapy. He said:

[I]n reality, we had to give them what we could and they had to accept that that was what was available. They had to be pretty intelligent to use it correctly and effectively and make it up themselves, and I think that that was a limiting factor.<sup>295</sup>

**21.314** Professor Forbes had reservations about the use of DDAVP.<sup>296</sup> It caused changes in blood pressure and fluid retention.<sup>297</sup> For patients at the GRI, he had made efforts to provide cryoprecipitate from small pools for mildly affected patients and those on home therapy.<sup>298</sup> However, he repeated that cryoprecipitate was used because it was available from the SNBTS. But, there was concern about the efficacy and safety of concentrates made in Scotland and so the preference was still for cryoprecipitate.<sup>299</sup>

**21.315** The supply position caused Professor Forbes concern. As described by him, SNBTS’s ability to service demand was in stark contrast to the picture painted by Mr Watt and Professor Ronald Girdwood. Professor Forbes thought that any suggestion that Scotland was virtually self-sufficient in Factor VIII was ‘cloud-cuckoo land’: he did not think Scotland was ever self-sufficient in quality Factor VIII at that time.<sup>300</sup> In his view self-sufficiency meant that:

<sup>293</sup> Professor Forbes’ statement on information given to patients [PEN.012.0411] at 0415

<sup>294</sup> Ibid [PEN.012.0411] at 0411

<sup>295</sup> Professor Forbes – Day 17, page 101

<sup>296</sup> Lowe et al, ‘DDAVP in Haemophilia’, *The Lancet*, 17 September 1977; 614–615 [PEN.015.0368]

<sup>297</sup> Professor Forbes – Day 17, page 114

<sup>298</sup> Ibid page 116

<sup>299</sup> Ibid page 105

<sup>300</sup> Ibid page 113



[A]t the drop of a hat, at any moment of time, if a patient required treatment, you could go to your people and say, 'We need to treat this patient, we need X, Y and Z,' that it would be available ....<sup>301</sup>

**21.316** However, it became clear that his requirement related to a combination of volume of supplies and quality. He said of the Factor VIII he wanted:

I mean stuff that you could rely on as to what it said on the bottle was actually in the bottle. So potent, effective therapy was the difficulty because there was such variation. So every time we gave a material, we measured it in the blood of the patient to ensure that there was enough to make them safe for whatever the procedure was. So if they were having major surgery, we would work out the dose required, we would give it and then we would check by a blood test after 20 minutes or so that we had achieved a haemostatic level of the Factor VIII or IX .... [If not] we would give another dose.<sup>302</sup>

**21.317** Professor Forbes confirmed that it was not a case of saying: 'The NHS Factor VIII isn't working, we had better get some commercial stuff'. Treatment would be continued with the NHS product.<sup>303</sup> He appeared to accept, subject to his reservations about consistency of Factor VIII efficiency, that there was enough product for routine treatment of patients in 1983. However, there was apprehension that there might be shortages if there had been a major car accident or major trauma, or a bleed into the brain.<sup>304</sup>

**21.318** Understandably, given the procurement role of the SNBTS at the GRI, Professor Forbes was not familiar with the supply position for Scotland as a whole. When he was shown Dr Donald Hopkins' letter to Dr Robert Crawford dated 4 December 1984<sup>305</sup> concerning the disposal of surplus SNBTS stock, he said he did not remember Dr Hopkins.<sup>306</sup> He did not know what the overall supply position was in Scotland relative to demand.

**21.319** In relation to the period discussed in this chapter, he said that he was not involved in procuring concentrates.<sup>307</sup> His department had no funds, and they 'used what was available'.<sup>308</sup> The system in Glasgow, as he described it, was that when clinicians 'wanted something to give', they had to approach Blood Transfusion, which then ordered it, and then it would depend on what deal they could make with the various companies.<sup>309</sup> The SNBTS had a unit embedded in the GRI, and it was the responsibility of the doctor in charge of that unit to decide whether to acquire commercial materials. Professor Forbes said that he had no idea how decisions on the purchase of commercial material were made.<sup>310</sup> As a clinician, he only knew whether he had commercial or NHS material available when it arrived in the ward and he was about to administer it.<sup>311</sup> On his evidence, if it is accepted as accurate, the SNBTS had, at least, a significant influence on the use of therapeutic materials. The prescribing clinician had no role in product choice. As Professor Forbes himself frankly admitted, it is unlikely that his recollection is completely reliable. In any

<sup>301</sup> Ibid page 123

<sup>302</sup> Ibid pages 131–132

<sup>303</sup> Ibid page 132

<sup>304</sup> Ibid pages 134–134

<sup>305</sup> Dr Hopkins' letter to Dr Crawford [SNB.007.4655]

<sup>306</sup> Professor Forbes – Day 17, pages 137–138

<sup>307</sup> Ibid page 22

<sup>308</sup> Ibid page 23

<sup>309</sup> Ibid pages 41–42 and 134

<sup>310</sup> Ibid pages 134–135

<sup>311</sup> Ibid pages 137

event, it is reasonably clear from UKHCDO data that use of commercial material in the GRI up to about 1984 involved a wide range of products from different manufacturers, at least consistent with sourcing according to market conditions rather than clinical assessment of the relative qualities of the products and the risks to patients.

**21.320** Due to the dimming of recollection with the passage of time, Professor Forbes' evidence cannot be accepted as a comprehensive, or sufficient, explanation of the position. It is clear that following the commissioning of the PFC at Liberton, the most significant therapeutic product prescribed was not cryoprecipitate but SNBTS Factor VIII concentrate. And his evidence does not explain the use of commercial concentrate, nor does it provide an explanation of the recorded use of DDAVP.

**21.321** Professor Lowe's evidence reflected more clearly the position in Figure 21.10. He told the Inquiry that factor concentrates had been introduced to the Glasgow Haemophilia Centre and increasingly used from the 1970s. However, there was a small amount of cryoprecipitate prescribed for patients with moderate severity Haemophilia A and von Willebrand's disease throughout the 1980s. This was because of the smaller blood donor pool and hence lower risk of hepatitis and HIV infection. The policy of the Directors at the time, as with many other haemophilia centres, was to keep cryoprecipitate and use it preferentially in patients who less frequently required treatment.<sup>312</sup>

**21.322** This policy continued until the UK Haemophilia Centre Directors guidelines on choice of blood products in May 1988 recommended that cryoprecipitate no longer be used for such treatment, unless the haemostatic efficacy of factor concentrates for treatment of von Willebrand's disease was in doubt.<sup>313</sup>

**21.323** Professor Lowe's recollection was that from about 1980 the Directors' policy was to treat patients with mild Haemophilia A preferentially with desmopressin (DDAVP), where appropriate and tolerated, or cryoprecipitate. Patients with mild Haemophilia B were treated preferentially with fresh frozen plasma.<sup>314</sup>

---

<sup>312</sup> Professor Lowe – Day 39, pages 164–165

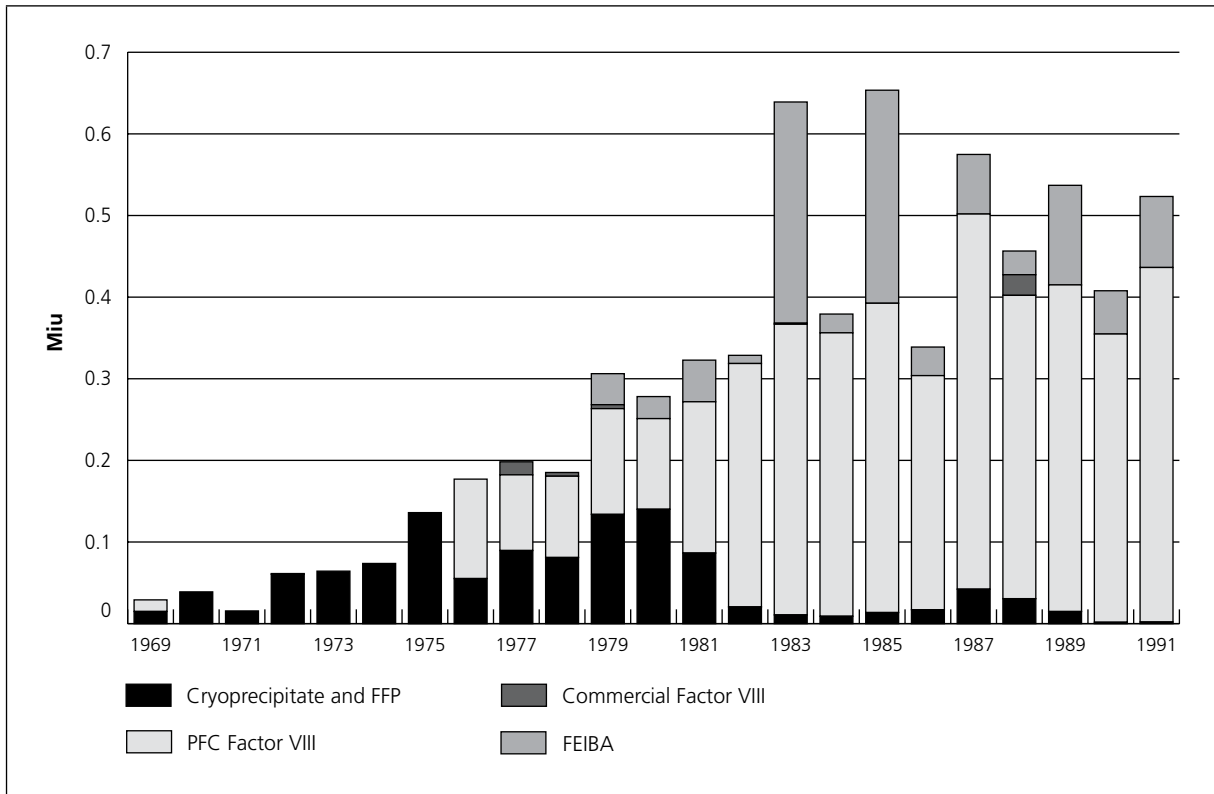
<sup>313</sup> Professor Lowe's statement on information given to patients [PEN.016.1250] at 1251

<sup>314</sup> Ibid [PEN.016.1250] at 1252

*Aberdeen*

**21.324** Numerical data for Aberdeen are set out in the Appendix to this chapter at Table 21.6. Graphically, the picture that emerges is shown in Figure 21.11.

**Figure 21.11: Aberdeen Haemophilia A Therapy in Million International Units (Miu) – 1969–91**

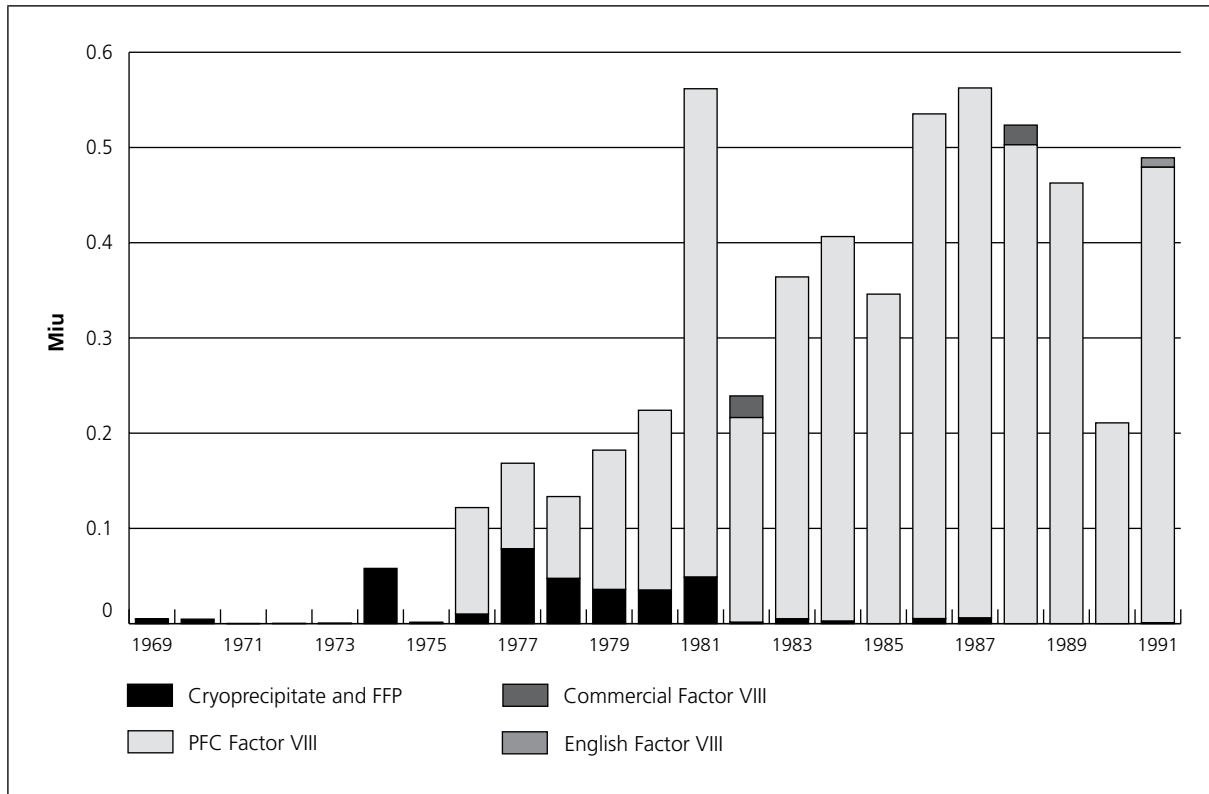


**21.325** The most noticeable feature of Figure 21.11 is the use of FEIBA for patients with inhibitors to Factor VIII concentrate, which provides a clear example of the adaptation of clinical practice to the perceived needs of specific patients. Otherwise, commercial product use was minimal and sporadic. In 1988 a relatively small quantity of Profilate was used, but there was no shift to greater use of commercial products generally such as occurred in Edinburgh and Glasgow. Cryoprecipitate use was inconsistent. It was initially displaced by use of SNBTS Factor VIII in 1976 after the PFC came on stream, but regained ground from then until 1980, after which use fell away until about 1985. For the next three years there was a small increase in cryoprecipitate use, but the PFC Factor VIII remained the dominant product throughout the period from 1981. Leaving aside the specific use of FEIBA, treatment policy at Aberdeen was clearly to use SNBTS products.

*Dundee*

**21.326** Numerical data for Dundee are set out in the Appendix to this chapter at Table 21.7. Graphically, the picture that emerges is shown in Figure 21.12.

**Figure 21.12: Dundee Haemophilia A Therapy in Million International Units (Miu) – 1969–91**

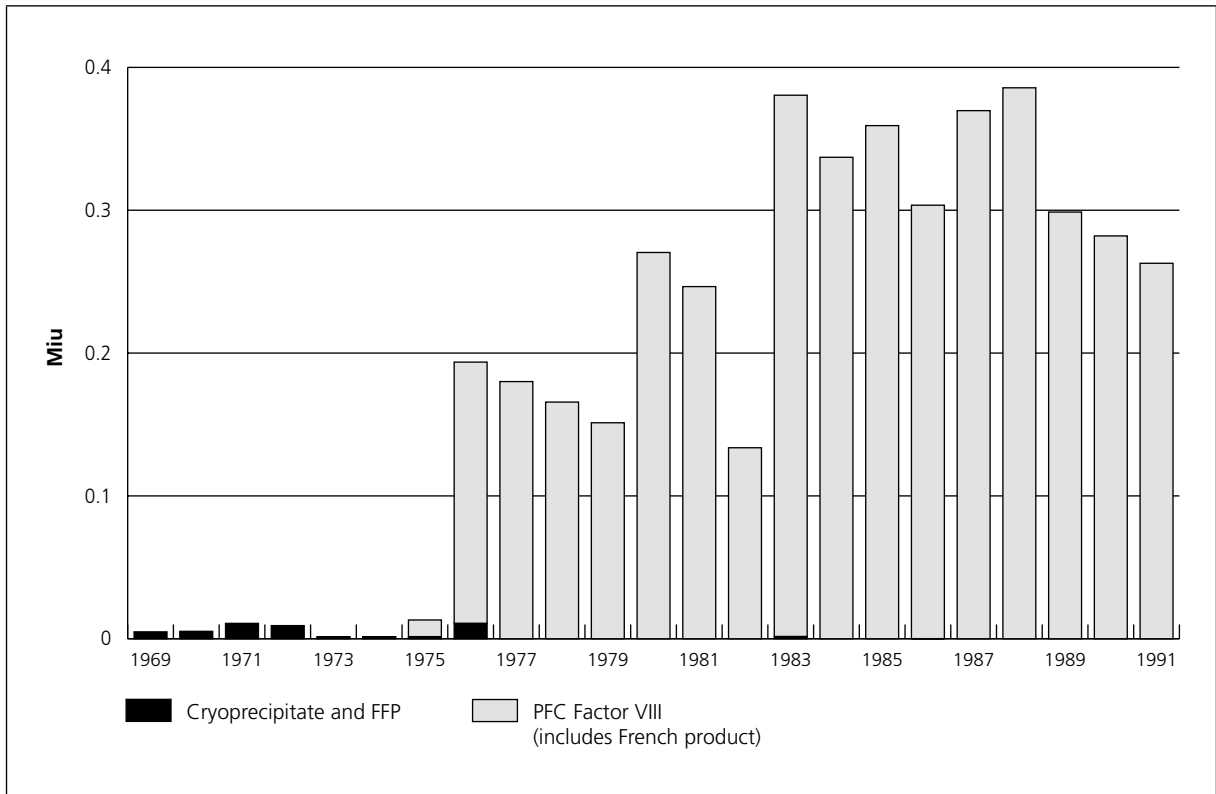


**21.327** Two small quantities of commercial material were purchased in 1982 (Porcine Factor VIII) and 1988 (Profilate). The 1988 transaction was a close parallel to Aberdeen's use of commercial human plasma Factor VIII in that year. A very small quantity of the BPL 8Y was used in 1991. Otherwise, treatment policy was consistently to use SNBTS products, predominantly Factor VIII concentrate after the PFC came on stream.

*Inverness*

**21.328** Numerical data for Inverness are set out in the Appendix to this chapter at Table 21.8. Graphically, the picture that emerges is shown in Figure 21.13.

**Figure 21.13: Inverness Haemophilia A Therapy in Million International Units (Miu) – 1969–91**



**21.329** Inverness used a tiny quantity of Hemofil in 1974. It is irrelevant to the pattern of use in the centre. The same comment can be made in relation to DDAVP. Small quantities were used from 1986 to 1991, but do not impact on the picture overall. From the commissioning of the PFC, Inverness used SNBTS Factor VIII almost exclusively.

**21.330** In relation to product choice and use, there is a clear distinction between the Glasgow and Edinburgh centres on the one hand and Aberdeen, Dundee and Inverness on the other. Practice in the three smaller centres involved far less use of commercial materials, and perhaps reflected most clearly the implementation of government, and SNBTS, policy that haemophilia treatment should be on a self-sufficient basis using domestic products other than in exceptional cases.

**21.331** Since various commercial products have been mentioned, it is perhaps worth noting their relative impacts on the UK market, as illustrated for 1980 and 1981:<sup>315</sup>

Manufacturer	Trade Name	International Units	
		1980	1981
Abbott	Profilate	1,649,000	1,909,000
Armour	Factorate	16,576,000	14,646,000
Cutter	Koate	4,935,000	3,823,000
Hyland	Hemofil	5,095,000	*5,554,000
Immuno	Kryobulin	5,377,000	7,377,000
Speywood	Humanate	615,000	1,561,000
Hyland	Interhem	502,000	
<b>TOTAL</b>		<b>34,749,000</b>	<b>34,870,000</b>

\*Includes Interhem

**21.332** Armour's Factorate was the most used product, with Hemofil, Kryobulin and Koate following. Relative to Scottish use, Abbott's Profilate might have been expected to have had a higher profile.

**21.333** The Inquiry has not investigated the issue of choice of product in England and Wales. That was not required by the Terms of Reference.

## Discussion

**21.334** Turning to the wider issues raised in respect of this period, it is clear that considerable advances had been made in the treatment of haemophilia. Patients' lives had been transformed by the new products which became widely available in the 1970s. In particular, the arrival of concentrates led to an overwhelming improvement in quality of life, especially for those with severe haemophilia.

**21.335** Although there was awareness that there were risks associated with concentrates, primarily the risk of contracting hepatitis, the natural history of hepatic disease was not well understood by 1981. As discussed in Chapter 15, *Knowledge of Viral Hepatitis 2 – 1975 to 1985*, there remained substantial deficits in knowledge of NANB Hepatitis and its natural history well into 1985. The seventh edition of Professor Sheila Sherlock's book *Diseases of the Liver and Biliary System* dated October 1985 noted that there was increasing concern 'in some quarters' about the potential seriousness of NANB Hepatitis. As at 1981, both clinicians and the haemophilia population in general considered that the life-enhancing benefits of concentrates far outweighed any perceived risks. As the 1970s progressed, more and more evidence had emerged reinforcing the risk of acquiring hepatitis, but with the exception of a few reported cases of serious illness and a very few fatal cases, hepatitis was not reported to be associated with serious outcomes.

**21.336** With the publications of Mannucci et al, and of the proceedings at the World Federation of Hemophilia and the International Society of Blood Transfusion symposium in Helsinki, the dilemma facing clinicians over the use of concentrates became more pronounced. Professor Forbes' evidence that the 'possible downside' of concentrate use was known, but the risk of death from bleeding was greater and drove clinicians to use the products is accepted. It was to the same effect as Dr Craske's views, reported in *The Lancet* of August 1975, relating to the balance of risk and benefit in the use of Hemofil.

<sup>315</sup> Department of Health table showing quantities of Factor VIII concentrate used in the UK, 1980 and 1981 [DHF.001.4517]

**21.337** From the point of view of Dr Craske and his colleagues in public health, reducing risk was a factor examined in their recommendations: use of commercial concentrates should be restricted to life-threatening situations and to major surgery. Until the end of the period of Dr Craske's surveys for the UKHCDO in 1982–83, their reports acknowledged the possibility of a non-B Hepatitis that was not Hepatitis A, but did not attempt to attribute specific risk to NANB Hepatitis, and as a result, Dr Winter noted, the recommendation to reserve commercial concentrates for severely affected haemophiliacs was based on irrelevant reasoning. A more cogent reason would have been that regularly treated patients with severe haemophilia would almost certainly have already acquired NANB Hepatitis, distinguishing them from new and infrequently treated patients. But that had not yet been realised. It was at the very end of this period that an association with NANB Hepatitis was specifically acknowledged. It would not be appropriate to conclude that Dr Craske's views would, or should, have carried particular weight at this point. Rather, they illustrate continuing confusion over the nature of the hepatitis risk that was only gradually being resolved.

**21.338** That confusion was apparent in the comments made in the 'World in Action' programme of 8 December 1975. The differences between Dr Maycock and Professor Zuckerman showed that professional opinion in the UK had not resolved a common position on the risks associated with large-pool factor concentrates. The ambition to remove risk by increasing manufacturing capacity in the public sector to self-sufficiency, in retrospect, illustrated the depth of misunderstanding of the risk of NANB Hepatitis transmission. Dr Winter's interpretation of the discussion in the programme is accepted: in retrospect it was about Hepatitis B. Although NANB Hepatitis had been postulated in 1974, it had not made the impact on professional thinking that would begin to be seen in the early 1980s.

**21.339** It is not appropriate to accept Dr Winter's evidence that the discussion 'should' have been about NANB Hepatitis in the circumstances, except in the sense that, with the benefit of hindsight, that was the real issue for patients. But it was not known to be the issue at the time. Professor Zuckerman could still talk of 'hepatitis or jaundice' being a particularly interesting infection as if the terms were synonymous. What is clear from the programme is that the clinical dilemma continued to be whether to accept the risk of serious morbidity and mortality associated with bleeding, or accept the risks associated with hepatitis, as they were understood at the time. Dr Winter's observations on the contribution of the patient who was on the point of discontinuing the use of Hemofil when he had a bleed in his elbow and sought immediate relief by using the preparation was eloquent of the problem. There was no settled view from haemophilia experts about the risk of hepatitis: the effects of haemophilia were only too clear to the patient.

**21.340** The 1975 programmes would have made an impression on any interested viewer. They clearly did affect the perception of clinicians. Professor Forbes' evidence of the reaction of haemophilia clinicians demonstrated that clearly. But it was the sensational aspect of the television programmes that struck home: the lines of people with alcohol, and other disadvantaged people, queuing to give blood. As Dr Winter noted, that was fundamentally irrelevant. The fact that they took alcohol did not prove their viral status. The technical discussion, for example the difference between Dr Maycock's and Professor Zuckerman's views, would not have added materially to the general understanding among clinicians of the fundamental nature of the problem of transmission of infection.

**21.341** Dr Craske's ongoing study of infection following infusion of commercial products is instructive. His report to the UKHCDO on 13 January 1977, comparing NHS and commercial Factor VIII, continued to focus on jaundice. Dr Biggs reported data returned from haemophilia centres on the incidence of jaundice. Professor Stewart's somewhat dismissive comments indicated that, for some haemophilia specialists, the risk of jaundice was something one simply had to live with.

**21.342** It was not until the early 1980s that there was a growing realisation that, while the risk of Hepatitis B was declining markedly due to constant improvements in screening blood donors for evidence of Hepatitis B infectivity, there was a new form of hepatitis (NANB Hepatitis). Little was known about the likely progression of this new illness, but by 1981 it was known to be very common among haemophilia patients treated with concentrates. As discussed in Chapter 15, *Knowledge of Viral Hepatitis 2 – 1975–1985*, it was not until 1984–85 that the natural history of NANB Hepatitis was beginning to be understood to involve a risk of serious long-term progressive liver disease with significant morbidity and mortality.

**21.343** Despite these acknowledged risks, there was no desire in the haemophilia community to revert to the pre-concentrate era. While cryoprecipitate was seen as less risky in terms of hepatitis transmission, there were too many disadvantages associated with its use. It was hoped that improved screening methods would lead to the eradication of hepatitis and other impurities in blood products. However, at the end of this period, about 1982–83, an unidentified virus was beginning to emerge that would transform the lives of the haemophilia population once again. This new virus, later identified as HIV, and the link with concentrates (particularly commercial in origin) was to have a devastating impact on the haemophilia population in the 1980s.

**21.344** Until that happened, haemophilia therapy continued to depend largely on concentrates, and the demand for the products increased.

**21.345** This chapter has touched on the preparation and supply of NHS blood and blood products, but has been concerned mainly with the second of the two relevant Terms of Reference noted at the beginning of the chapter:

8. To investigate the steps taken by those involved in, and those responsible for, the NHS in Scotland including NHS boards and SNBTS, their officers and employees and associated agencies, to prevent the provision of infected blood and blood products.

**21.346** There was considerable work done in the 1970s and early 1980s to identify and defer blood donations that were found to be infected with HBV and other viral conditions on routine testing with the best assays available from time to time. This is discussed in Chapter 25, *Screening of Donated Blood for Hepatitis B*. Steps taken to treat therapeutic products to eliminate or reduce the risk of transmission of viral infection are discussed in Chapter 23, *Viral Inactivation of Blood Products for Haemophilia Therapy up to 1985*. The technology developed and applied was targeted at the pathogens that were either known or postulated, with a degree of confidence, to be likely to be found in components of, and in products produced from, human blood. Nothing was done to prevent the provision of blood and blood products infected with the viruses that are of central importance in this Inquiry: NANB Hepatitis/HCV in the 1970s and early 1980s or, when it emerged, HTLV-III/HIV.



**21.347** Incidentally, technology developed to deal with known pathogens came to have significance in relation to identification of materials infected by one or other of these viruses or to inactivation of infection in blood products. However, there was nothing that could have been done to prevent the provision of blood and blood products infected with NANB Hepatitis in the period covered by this chapter. Firstly, and most importantly, there was no possibility of detection of the virus until it (or they) had been identified. Until HCV was partially isolated and characterised in 1988, it was speculated that there might be more than one pathogen causing hepatitis that was neither Hepatitis A nor Hepatitis B. HTLV-III/HIV was not known at all until 1982. Whole blood and the cellular components of blood for transfusion benefited from screening, but could not be treated to activate any virus in the materials.

**21.348** Moreover, both before and after the licensing of commercial Factor VIII for general prescription, the choice of therapeutic material was a matter of judgement for individual clinicians in relation to the needs of particular patients. Commercial products were administered in 1972, necessarily on a named patient basis, since they were not then licensed. After they were licensed, from 1983 onwards, clinicians were free to prescribe and use them more generally. Interference with clinical judgement at the point of treatment of the patient would have been considered to be a breach of the clinical autonomy of the practitioner.

**21.349** The NHS in Scotland could not have restricted the import and use of commercial products once they were licensed. Licensing was a function of the UK Government. NHS Boards were not in a position to make any contribution in this area.

**21.350** From 1974, the operational responsibility for the provision of human blood for transfusion and for the production of blood products had been delegated by the Secretary of State for Scotland to the CSA, subject always to such directions as the Secretary of State might give. As discussed in Chapter 17, *Blood and Blood Products Management*, the CSA did not exercise operational control over the delivery of the blood transfusion service, and regional and national managers had largely autonomous control of their respective operations. Blood transfusion directors asserted and were allowed a degree of operational autonomy comparable to that of clinicians.

**21.351** Scotland was in a particularly favourable position in respect that production capacity was sufficient in general to meet demand for NHS product. In the late 1970s, into early 1980s, demand outstripped supply briefly. But the continuing increase in demand for NHS products over the period was dramatic.

**21.352** In this period, all human plasma products, including cryoprecipitate, exposed haemophilia patients to the risk of transmission of NANB Hepatitis/Hepatitis C.

**21.353** So far as NHS products are concerned, they were perceived by most practitioners to be preferable to imported products, being prepared from local blood donations, and less likely to transmit infection. Promotion of their use was the obvious policy position to adopt over this period. That they turned out to be infective, though, at least in relation to HCV, less so than imported products, would only have been a basis for intervention if those responsible for the decision had been prepared to prohibit their use, and expose patients to the known risks of morbidity and mortality associated with haemophilia that had existed prior to 1973. That was never likely to happen, and would in any event have been strenuously resisted by patients and patient groups. The inexorable increase

in demand over this period shows the commitment of clinicians and patients alike to concentrate therapy.

**21.354** Looking to the factors that generated increasing demand for concentrates, home treatment and prophylaxis were clearly contributory factors, especially the first. Home treatment enabled people with haemophilia to lead a more normal life, but exposed patients to a greater amount of product than would have been used in purely reactive therapy. Exposure to commercial concentrate, where there was a lack of NHS product, led to greater exposure to transmission of viruses. The evidence as a whole demonstrated that home treatment was to the overwhelming advantage of the haemophilia population. It enabled the speedy and effective treatment of bleeds by the patients or their families who were trained in recognition of the symptoms of a bleed, and in the administration of therapy. That was preferable to the risks of inappropriate treatment in a hospital accident and emergency department with all the associated problems that involved, as described in the evidence.

**21.355** Could the NHS have intervened to prevent the introduction and expansion of home treatment? Again it would have involved an interference with clinical autonomy at the doctor-patient interface. It would not have been acceptable, and given the state of knowledge of the long-term risks associated with factor therapy at this time, it would have been wrong.

**21.356** Where prophylaxis was introduced, it might have exposed patients to substantially more product than on-demand treatment. But it prevented spontaneous bleeds, for example cerebral bleeds which used to be the most common cause of death for people with haemophilia, and it reduced joint damage and crippling, resulting in less pain in later life and a better quality of life for the patient.

**21.357** In this, as in most areas, it is superficially easy to ask, with the benefit of hindsight, whether all developments should have been held up until research had established that products and procedures were 'safe' in some absolute sense. However, safety is never absolute: it is always relative to some reference point in current knowledge. The manufacturers who promoted the use of early concentrates did not do so in the knowledge that they were 'unsafe'. They were conscious of the risks of 'hepatitis', as the risks were understood from time to time. But those risks were thought to be acceptable given the benefits of therapy. These subjects were discussed, researched and reported. In the final analysis, all concerned; manufacturers, haemophilia clinicians, patients, and the Haemophilia Society, wanted to carry on treatment with concentrate despite the risks rather than reverting to cryoprecipitate, because of the benefits they saw and experienced.

## Conclusions

- There was no evidence before the Inquiry that would support a finding that Scottish practitioners were influenced in their choice of therapeutic products by benefits provided by pharmaceutical companies.
- There was considerable work done in the 1970s and early 1980s to identify and defer blood infected with HBV and other viral conditions.
- Nothing could have been done to prevent the provision of blood and blood products infected with NANB Hepatitis in the 1970s and early 1980s or, when it emerged, HTLV-III/HIV. There was no possibility of detection of either virus until each had been identified (HIV in 1983–84 and HCV in 1988–89).
- Both before and after the licensing of commercial Factor VIII for general prescription, the choice of therapeutic material was a matter of clinical judgement. Commercial products were administered in 1972, necessarily on a named patient basis, since they were not licensed. After they were licensed, clinicians were free to prescribe and use them more generally. Interference with clinical judgement at the point of treatment of the patient would have been considered to be a breach of the clinical autonomy of the practitioner.
- The NHS in Scotland could not have restricted the import and use of commercial products once they were licensed. That was a function of the UK Government.
- There is no criticism that can legitimately be made of practice in relation to the use of factor concentrates over this period. Change was beginning. DDAVP had been recommended for mild haemophilia. Biopsy investigations had indicated a risk of more severe liver damage than had been anticipated. But the general body of medical opinion remained favourable to the continued use of concentrates. It would have been quite unrealistic for the NHS in Scotland to have promoted a different approach by the end of 1982.

## Appendix to Chapter 21

**Table 21.1: Consumption of Factor VIII concentrates, 1970–1990 (Millions of International Units)**

Year	All UK <sup>1</sup>			Scotland <sup>2</sup>			UK excl. Scotland <sup>3</sup>		
	NHS	Commercial	Total	NHS	Commercial	Total	NHS	Commercial	Total
1970	0.9	0.0	0.9	0.1	0.0	0.1	0.8	0.0	0.8
1971	3.1	0.0	3.1	0.1	0.0	0.1	3.0	0.0	3.0
1972	1.9	0.7	2.6	0.2	0.0	0.2	1.7	0.7	2.4
1973	2.5	0.8	3.3	0.2	0.0	0.2	2.3	0.8	3.1
1974	2.7	2.7	5.4	0.1	0.1	0.1	2.6	2.6	5.3
1975	3.1	5.1	8.2	0.4	0.1	0.5	2.7	5.0	7.7
1976	6.9	11.1	18.0	1.4	0.2	1.6	5.5	10.9	16.4
1977	12.9	15.0	27.9	1.7	0.3	2.0	11.2	14.7	25.9
1978	14.6	19.3	33.9	1.5	0.2	1.7	13.1	19.1	32.2
1979	15.1	26.2	41.3	1.8	0.8	2.5	13.3	25.4	38.8
1980	14.4	34.7	49.1	3.9	1.0	4.8	10.5	33.7	44.3
1981	22.5	35.5	58.0	3.5	1.2	4.7	19.0	34.3	53.3
1982	22.9	45.6	68.5	4.8	0.5	5.3	18.1	45.1	63.2
1983	30.0	36.2	66.2	5.9	0.4	6.3	24.1	35.8	59.9
1984	40.2	34.0	74.2	6.9	0.1	7.0	33.3	33.9	67.2
1985	23.1	50.9	74.0	5.7	0.4	6.1	17.4	50.5	67.9
1986	31.5	53.7	85.2	6.2	0.2	6.4	25.3	53.5	78.8
1987	26.0	59.2	85.2	8.5	0.1	8.6	17.5	59.1	76.6
1988	41.0	55.0	96.0	12.4	0.9	13.3	28.6	54.1	82.7
1989	65.5	36.5	102.0	7.1	1.2	8.3	58.4	35.3	93.7
1990	85.0	23.0	108.0	7.4	0.7	8.1	77.6	22.3	99.9

**Note 1:** UK data taken from Table 1 in the SNBTS paper *Self-sufficiency and the Supply of Blood Products in Scotland* [PEN.013.1125] at 1148. The paper states that the UKHCDO is the source of the data.

**Note 2:** Scottish data consolidated from Table 1 in the UKHCDO report *National Haemophilia Database: Bleeding disorder statistics for the Penrose Inquiry*, 2012 [PEN.019.0927] at 0935–55

**Note 3:** Data for the UK excluding Scotland were calculated by subtracting the Scottish figures from the UK figures.

**Table 21.2: Scottish use of Factor VIII replacement products 1969–1991 (International Units)**

Year	Cryoprecipitate and FFP	NHS Factor VIII concentrates	Commercial Factor VIII	FEIBA
1969	296,417	197,800	–	–
1970	348,074	115,810	–	–
1971	116,250	131,250	–	–
1972	253,476	222,350	–	–
1973	428,450	162,408	–	–
1974	1,601,797	83,148	54,012	–
1975	1,690,380	412,459	84,250	–
1976	1,267,125	1,432,107	174,774	–
1977	1,294,620	1,731,719	300,244	61,000
1978	1,403,280	1,475,578	224,269	128,500
1979	1,259,670	1,760,837	751,788	135,900
1980	1,538,725	3,867,751	958,441	171,000
1981	941,296	3,488,171	1,224,684	141,000
1982	681,880	4,754,658	541,426	188,000
1983	526,040	5,925,670	389,130	495,000
1984	304,046	6,889,163	138,010	100,000
1985	402,800	5,662,241	426,795	361,335
1986	293,228	6,153,435	207,390	489,600
1987	264,977	8,479,160	111,095	902,000
1988	202,549	12,442,246	868,665	424,650
1989	259,408	7,054,175	1,204,060	484,000
1990	11,184	7,429,473	717,093	585,000
1991	3599	7,289,270	461,731	529,000

**Note 1:** Data consolidated from Table 1 in the UKHCDO report *National Haemophilia Database: Bleeding disorder statistics for the Penrose Inquiry, 2012* [PEN.019.0927] at 0935–55

**Table 21.3: Edinburgh Haemophilia A Therapy (International Units)**

Year	Cryo	FFP	Cryo + FFP	PFC VIII <sup>1</sup>	English VIII	PFC + Eng VIII	Comm	FEIBA	Comm + FEIBA	DDAVP
1969		108,150	108,150	158,200		158,200				
1970	6350	121,666	128,016	73,850		73,850				
1971	76,800	13,020	89,820	131,250		131,250				
1972	179,050	4410	183,460	221,550		221,550				
1973	361,250	1120	362,370	162,400		162,400				
1974	608,700		608,700	83,070		83,070	500		500	
1975	604,380		604,380	111,840		111,840				
1976	697,760		697,760	439,344		439,344				
1977	640,640		640,640	355,976		355,976				
1978	647,325		647,325	272,589		272,589				
1979	694,190		694,190	201,486		201,486				
1980	1,212,470	650	1,213,120	1,644,750		1,644,750	164,000		164,000	
1981	720,160		720,160	840,130		840,130	442,018		442,018	
1982	612,000		612,000	1,612,800		1,612,800	7300	110,000	117,300	
1983	341,700		341,700	1,756,000		1,756,000	151,000	37,000	188,000	
1984	139,000		139,000	2,506,880		2,506,880	127,050	8000	135,050	6
1985	127,680		127,680	1,947,420		1,947,420	45,720	47,000	92,720	1
1986	44,930	6000	50,930	2,073,710		2,073,710	15,840	193,600	209,440	7
1987	42,560		42,560	2,842,810		2,842,810		87,000	87,000	11
1988	54,730		54,730	2,610,300	26,980	2,637,280	299,485	169,650	469,135	
1989	157,080		157,080	1,919,650		1,919,650	610,790	353,000	963,790	
1990				2,383,690	118,665	2,502,355	345,593	425,000	770,593	
1991				2,010,760	131,735	2,142,495	117,165	267,000	384,165	

**Note 1:** Includes 'French' product.

Table 21.4: Glasgow Yorkhill Haemophilia Therapy (International Units)

Year	Cryo	FFP	Cryo + FFP	PFC VIII <sup>1</sup>	English VIII	PFC + Eng VIII	Comm	FEIBA	Comm + FEIBA	DDAVP
1969										
1970										
1971										
1972										
1973										
1974										
1975										
1976										
1977	41,930	460	42,390	99,625		99,625	105,682		105,682	
1978	565		565	22,144		22,144	22,809		22,809	
1979	60		60	137,465		137,465	354,276		354,276	
1980	1305		1305	161,242		161,242	682,732		682,732	
1981	29,200		29,200	457,126		457,126	632,497		632,497	
1982	7050		7050	516,300		516,300	485,880		485,880	
1983	30,500		30,500	1,121,075		1,121,075	36,850		36,850	
1984	32,340		32,340	1,035,396		1,035,396	5460		5460	
1985	27,930	800	28,730	739,094		739,094				
1986	38,780		38,780	600,360		600,360	2720		2720	
1987	27,860	900	28,760	922,700		922,700				
1988	11,900	2	11,902	5,288,770		5,288,770				
1989	15,650	2	15,652	1,498,830		1,498,830				20
1990	7560	3	7563	1,133,610	25,840	1,159,450				
1991	10	564	574	1,161,330	27,100	1,188,430		31,000	31,000	

**Note 1:** Includes 'French' product.

**Table 21.5: Glasgow Royal Infirmary Haemophilia A Therapy (International Units)**

Year	Cryo	FFP	Cryo + FFP	PFC VIII <sup>1</sup>	English VIII	PFC + Eng VIII	Comm	FEIBA	Comm + FEIBA	DDAVP
1969	101,350	62,500	163,850	25,200		25,200				
1970	151,190	20,100	171,290	41,960		41,960				
1971										
1972										
1973										
1974	860,000		860,000				53,500		53,500	
1975	947,200	202	947,402	288,945		288,945	84,250		84,250	
1976	493,555		493,555	576,013		576,013	174,774		174,774	
1977	443,350		443,350	913,608		913,608	178,562	61,000	239,652	
1978	626,910		626,910	829,609		829,609	196,870	128,500	325,370	
1979	395,740		395,740	994,776		994,776	392,652	97,900	490,552	229
1980	147,750	1300	149,050	1,491,349		1,491,349	111,709	144,000	255,709	
1981	56,650	6	56,656	1,246,155		1,246,155	150,169	90,000	240,169	348
1982	40,950		40,950	1,978,658		1,978,658	25,496	68,000	93,496	538
1983	136,550		136,550	1,954,490		1,954,490	200,000	187,000	387,000	
1984	121,100	4	121,104	2,258,674		2,258,674	5500	69,000	74,500	
1985	223,990	8800	232,790	1,891,567		1,891,567	381,075	53,335	434,410	735
1986	175,800	5280	181,080	2,359,155		2,359,155	188,830	261,000	449,830	978
1987	142,439	3080	145,519	3,327,720		3,327,720	111,095	742,000	742,000	745
1988	103,640	1684	105,324	3,256,061		3,256,061	523,180	226,000	749,180	1400
1989	39,800	32,018	71,818	2,474,140		2,474,140	593,270	9000	602,270	1548
1990		1924	1924	2,880,750	40,961	2,921,711	371,500	107,000	478,500	1590
1991		22	22	2,722,085	50,900	2,772,985	344,566	144,000	488,566	1120

**Note 1:** Includes 'French' product.



Table 21.6: Aberdeen Haemophilia A Therapy (International Units)

Year	Cryo	FFP	Cryo + FFP	PFC VIII <sup>1</sup>	English VIII	PFC + Eng VIII	Comm	FEIBA	Comm + FEIBA	DDAVP
1969	4657	10,240	14,897	14,200		14,200				
1970	32,293	6600	38,893							
1971	15,540	2	15,542							
1972	50,750	9800	60,550	800		800				
1973	63,490	800	64,290							
1974	71,890	1820	73,710							
1975	134,750	1250	136,000							
1976	55,230		55,230	121,800		121,800				
1977	89,600		89,600	92,660		92,660	16,000		16,000	
1978	81,040		81,040	99,546		99,546	4590		4590	
1979	133,840		133,840	129,540		129,540	4860	38,000	42,860	
1980	140,130		140,130	111,050		111,050		27,000	27,000	
1981	86,480		86,480	185,320		185,320		51,000	51,000	
1982	20,510		20,510	298,180		298,180		10,000	10,000	
1983	10,710		10,710	356,085		356,085	1280	271,000	272,280	
1984	9030	12	9042	347,223		347,223		23,000	23,000	
1985	10,300	3300	13,600	378,920		378,920		261,000	261,000	
1986	17,080	8	17,088	286,760		286,760		35,000	35,000	
1987	42,210	8	42,218	459,600		459,600		73,000	73,000	
1988	30,590	3	30,593	371,600		371,600	25,300	29,000	54,300	
1989	14,840	18	14,858	400,130		400,130		122,000	122,000	
1990	1680	17	1697	353,120		353,120		53,000	53,000	
1991	2030	13	2043	434,280		434,280		87,000	87,000	

**Note 1:** Includes 'French' product.

**Table 21.7: Dundee Haemophilia Therapy (International Units)**

Year	Cryo	FFP	Cryo + FFP	PFC VIII	English VIII	PFC + Eng VIII	Comm	FEIBA	Comm + FEIBA	DDAVP
1969	3700	1000	4700	200		200				
1970	2385	2300	4685							
1971	114	4	118							
1972	263	8	271							
1973	551	22	573							
1974	50,400	7600	58,000							
1975	1086	38	1124	200						
1976	9860		9860	112,000		112,000				
1977	78,640		78,640	89,800		89,800				
1978	47,440		47,440	86,000		86,000				
1979	35,840		35,840	146,360		146,360				
1980	35,120		35,120	188,940		188,940				
1981	48,800		48,800	512,900		512,900				
1982	1370		1370	215,000		215,000	22,750		22,750	
1983	4240	800	5040	359,040		359,040				
1984	2560		2560	403,920		403,920				
1985				346,000		346,000				
1986	5280		5280	530,000		530,000				
1987	5920		5920	556,600		556,600				
1988				502,820		502,820	20,700		20,700	
1989				462,700		462,700				
1990				210,817		210,817				
1991	960		960	478,310	9,900	488,210				

**Table 21.8: Inverness Haemophilia A Therapy (International Units)**

Year	Cryo	FFP	Cryo + FFP	PFC VIII	English VIII	PFC + Eng VIII	Comm	FEIBA	Comm + FEIBA	DDAVP
1969	4820		4820							
1970	5190		5190							
1971	10,770		10,770							
1972	9195		9195							
1973	1217		1217	8		8				
1974	1387		1387	78		78	12		12	
1975	1474		1474	11,674		11,674				
1976	10,720		10,720	182,950		182,950				
1977				180,050		180,050				
1978				165,690		165,690				
1979				151,210		151,210				
1980				270,420		270,420				
1981				246,540		246,540				
1982				133,720		133,720				
1983	1540		1540	378,980		378,980				
1984				337,070		337,070				
1985				359,240		359,240				
1986	70		70	303,450		303,450				4
1987				369,730		369,730				24
1988				385,715		385,715				41
1989				298,725		298,725				108
1990				282,020		282,020				56
1991				262,870		262,870				24

**Note 1:** Includes 'French' product.



## CHAPTER 22

### HAEMOPHILIA THERAPY – USE OF BLOOD PRODUCTS 1985–1987

#### Introduction

**22.1** This chapter deals primarily with the treatment of patients with Haemophilia A following the introduction in Scotland in December 1984 of heat treatment of blood products.<sup>1</sup> The initial heat treatment protocol for Factor VIII was effective against HIV, but it was suspected, and later confirmed, that concentrates produced by the Protein Fractionation Centre (PFC) in Edinburgh and subjected to heat treatment continued to transmit Hepatitis C (HCV), then known as non-A non-B Hepatitis (NANB Hepatitis). That remained the case until the introduction of Z8, a heat-treated concentrate produced at the PFC and subjected to more rigorous heat treatment than its predecessor, NY. Z8 was issued to patients in Scotland from April 1987.<sup>2</sup>

**22.2** Difficult decisions in the treatment of patients with Haemophilia A therefore required to be made during the period 1985–87. For some patients in some situations, blood product therapy for haemophilia was unavoidable. But it was becoming increasingly clear that NANB Hepatitis was a potentially serious disease.<sup>3</sup> By this time, it had become clear that the use of Factor VIII therapy carrying a high risk of transmission of NANB Hepatitis was a decision to be taken only with the greatest care. This was especially so where the patient had never previously been treated with blood products and could, therefore, be assumed to be free from NANB Hepatitis. Virally inactivated Factor IX for the treatment of Haemophilia B patients was introduced in October 1985.<sup>4</sup> The period during which options on treatment presented particular problems for these patients was therefore shorter.

**22.3** Correspondence referred to in the Inquiry's Preliminary Report indicated that during the period 1 September 1985 to 30 June 1987 a total of 31 people in Scotland were treated for the first time with a blood product, either Factor VIII or Factor IX according to their index condition.<sup>5</sup> This information was provided for the purposes of a Scottish Executive Health Department (SEHD) Inquiry in 2000. The report of that inquiry stated that fewer than 10 of those people had tested HCV positive, although the status of a small number was unknown.<sup>6</sup> A further letter, dated 17 March 2000 (which was not available when the Preliminary Report was prepared) indicates that 29 patients were first treated between September 1985 and December 1987.<sup>7</sup> The Inquiry is not able to explain the reduction from 31 to 29, over a longer reference period, but it may be that there had been double counting in the earlier figure.<sup>8</sup> As indicated in Chapter 3, *Statistics*, this was a common problem arising from the registration of patients at more than one centre. Of the 29, six – all Haemophilia A patients – tested positive for HCV. The status of 14 patients (with Haemophilia A or B, von Willebrand's disease, or, in one case a Haemophilia B carrier) was not known. Most patients included in these figures will have been children when treated.<sup>9</sup>

<sup>1</sup> Chapter 23, *Viral Inactivation of Blood Products for Haemophilia Therapy up to 1985*, at paragraph 23.192.

<sup>2</sup> Chapter 24, *Viral Inactivation of Blood Products for Haemophilia Therapy 1985–1987*, paragraph 24.157.

<sup>3</sup> Chapters 15, *Knowledge of Viral Hepatitis 2 – 1975 to 1985*, and 16, *Knowledge of Viral Hepatitis 3 – 1986 Onwards*.

<sup>4</sup> Chapter 24, *Viral Inactivation of Blood Products for Haemophilia Therapy 1985–1987*, paragraph 24.67.

<sup>5</sup> Paragraph 9.326 of the Preliminary Report, drawing on information from the notes of a meeting held on 10 February 2000 [SGH.002.1597]

<sup>6</sup> Report of Scottish Executive Inquiry, 2000 [SGH.001.4414] at 4419. From [SGH.002.1597], the number testing positive appears to be eight.

<sup>7</sup> Letter from Dr Cachia to Dr Keel, 17 March 2000 [PEN.018.1483] at 1485

<sup>8</sup> The possibility of double counting was mentioned at the meeting on 10 February 2000 [SGH.002.1597] at 1597

<sup>9</sup> Professor Lowe – Day 54, page 60

**22.4** As referred to in paragraph 22.76, the Inquiry is directly aware of the circumstances of two such individuals. It does not have data for how many people might have been infected in the period December 1984 to September 1985. The SEHD chose September 1985 as the start date for the period of its investigation by reference to the point when the Blood Products Laboratory (BPL) in England was issuing a ‘hepatitis safe’ product, 8Y. The Inquiry selected December 1984 as the start of the period for its examination of this topic because that was when an ‘HIV safe’ product was available from the PFC in Edinburgh and the focus thereafter shifted back to the risk of transmitting NANB Hepatitis.<sup>10</sup>

**22.5** How treatment decisions were made during the relevant period, and the steps taken by clinicians to avoid the infection of patients with NANB Hepatitis, are matters examined in detail in this chapter.

### Hearings of evidence

**22.6** When hearings began in March 2011, this topic had not been designated as one to be considered at Oral Hearings of the Inquiry. On 4 May 2011, during the questioning of Professor Ludlam in relation to haemophilia treatment when AIDS was the principal risk of concentrate therapy, it became apparent that there was a gap in the topics insofar as this aspect was concerned.<sup>11</sup> A draft of a proposed additional topic was prepared and circulated amongst the Core Participants. The addition of the topic was formally confirmed by the Chairman of the Inquiry, and it was introduced and evidence was first led on Day 54.

**22.7** The topic was expressed as follows:

The use of blood product concentrates in Scotland in the period between the introduction of NHS heat-treated products in 1984 and the supply of NHS products sufficiently treated to inactivate Hepatitis C.<sup>12</sup>

### December 1984 guidance for haemophilia clinicians

**22.8** The Haemophilia Reference Centre Directors met at the BPL at Elstree on 10 December 1984. The meeting was chaired by Professor Bloom, at that time chairman of the UKHCDO. ‘Factor VIII Concentrates’ was one of the items discussed. It was agreed that treatment options would vary depending on whether or not the patient was HIV antibody-positive. The minutes record:

It was agreed that HT [heat treated] product should be given to all patients, if freely available, to include those found to be antibody +ve. In the case of antibody –ve patients, it was agreed that from now on, treatment must be with HT material.<sup>13</sup>

....

It was agreed that priority for NHS HT material would be given to children and past users of NHS material.<sup>14</sup>

---

<sup>10</sup> The emergence of an understanding of the risk of NANB Hepatitis from concentrate therapy in the 1970s is dealt with in Chapter 15, *Knowledge of Viral Hepatitis 2 – 1975–1985*.

<sup>11</sup> Day 19, pages 121–122

<sup>12</sup> Day 54, pages 9–10

<sup>13</sup> Note of the Haemophilia Reference Centre Directors Meeting, 10 December 1984 [SNF.001.3850] at 3853

<sup>14</sup> Ibid [SNF.001.3850] at 3858

....

The Chairman advised that he would issue guidelines following the meeting. In summary, the first choice would be HT material followed by the judgement of the individual clinician.<sup>15</sup>

**22.9** Professor Bloom prepared and sent guidelines, dated 14 December 1984 and entitled *Haemophilia Centre Directors Organisation AIDS Advisory Document*. The document listed the following options for treatment:

Options in probable decreasing order of safety from AIDS for Haemophilia A

1. Heated U.K. concentrate (note: still NANB hepatitis risk)
2. Single donor cryo. or FFP
3. Heated imported conc. (note: still NANB hepatitis risk)
4. Unheated U.K. conc.
5. Unheated imported conc – almost certain to be contaminated.

Note: Heated concentrates may still transmit hepatitis. Some of the distinctions e.g. between 3 and 4 are debatable and the long-term effects (e.g. immunogenicity) of using heated plasma proteins in this way are unknown....

RECOMMENDATIONS

1. Concentrate is still needed; bleeding is the commonest cause of disability and death.
2. Use DDAVP in mild Haemophilia and vWd<sup>16</sup> if possible.
3. For Haemophilia A needing blood products
  - (a) “Virgin” Patients those not previously exposed to concentrate, and children use cryo or heated NHS factor VIII (if available).
  - (b) Severe and Moderate haemophiliacs previously treated with factor VIII use heat treated NHS factor VIII, if available or heat treated US commercial.
4. Haemophilia B
  - (a) Mild Christmas Fresh frozen plasma if possible (otherwise NHS Factor IX).
  - (b) “Virgin” Patients and those not previously exposed to concentrate, use fresh frozen plasma (or NHS factor IX concentrate if essential)
  - (c) Severe and Moderate Christmas Disease previously exposed to factor IX concentrate continue to use NHS factor IX.<sup>17</sup>

**22.10** Professor Lowe and Professor Ludlam were asked about this guidance and its application in their respective haemophilia centres in the course of their oral evidence. Professor Ludlam was at the meeting on 10 December, whereas Glasgow was represented at the meeting by Dr Forbes.

<sup>15</sup> Ibid [SNF.001.3850] at 3859

<sup>16</sup> Von Willebrand's disease.

<sup>17</sup> *Haemophilia Centre Directors Organisation AIDS Advisory Document*, 14 December 1984 [SGF.001.2388] In evidence, Professor Ludlam confirmed that this document was 'pulled together' by Professor Bloom – Day 54, page 81

## *Glasgow*

**22.11** Professor Lowe told the Inquiry that treatment in Glasgow between the end of 1984 and 1986 reflected the guidance. He said:

[Practice in Glasgow was] very much in line with what you see there on the screen. The majority of our patients requiring factor concentrates were severe haemophiliacs. They had been treated for many years with Factor VIII concentrates. That was what they continued to have, and while patients could be told that the heat treatment was thought likely to reduce the risk of HIV, there was no evidence at the time that it would reduce the risk of non-A non-B Hepatitis. Hence, in patients who had not been previously exposed to concentrates, the desirability to try, as I have said, to limit the exposure to non-A non-B Hepatitis by considering the use of alternative products, cryoprecipitate or fresh-frozen plasma, according to individual circumstances.<sup>18</sup>

**22.12** He was pressed on what the choice would have been between cryoprecipitate and heated NHS concentrate, given that cryoprecipitate was not treated to inactivate HIV and NHS heated concentrate still carried a risk of NANB Hepatitis. He answered:

As I recall, the majority of our patients had the heated SNBTS Factor VIII concentrate. There were a small number of patients who had not previously received concentrate and for those, if one was particularly concerned about non-A non-B Hepatitis, then cryoprecipitate or FFP, for patients with Factor IX deficiency, might be preferable.<sup>19</sup>

**22.13** Professor Lowe said that Dr Forbes' policy had been very much to consider the individual patient. The introduction of screening of blood donations for HIV in October 1985 was an additional factor – cryoprecipitate was thereafter being made from donations which had been screened for HIV, improving its safety as a product. It was a period when the directors had to 'continuously weigh up what was happening'.<sup>20</sup>

**22.14** Greater detail was sought from Professor Lowe as to the type of patients who posed particular dilemmas at that time. He felt that the group of patients who would not have been on heated Factor VIII at that time was very small in number and would have been dealt with by Dr Forbes. He struggled to remember individual instances of this dilemma, and it is not possible to be confident that his evidence of discussions reflects only recollection, free from an element of reconstruction after the event. Subject to that, he thought that the sort of conversation which would have taken place with infrequently treated patients who had moderately severe haemophilia would have been along the following lines:

"Well, you know, there is a choice. You can have a product which, while heat-treated, the concentrate, it's coming from thousands of donors and there is no guarantee that you will not get an episode of non-A non-B Hepatitis, which you don't want."

---

<sup>18</sup> Professor Lowe – Day 54, page 17

<sup>19</sup> Ibid page 18

<sup>20</sup> Ibid page 19



He added:

And particularly after the introduction of HIV testing of blood donors, cryoprecipitate, you know, while it could still have a small risk of HIV, had a very good safety compared to concentrate, a reduced risk of getting hepatitis.<sup>21</sup>

**22.15** With von Willebrand's patients, there was an additional reason to prefer cryoprecipitate. If Factor VIII concentrate was used, the deficient von Willebrand Factor was not being replaced. Haemostasis was easier to achieve with cryoprecipitate than with concentrate.

**22.16** Professor Lowe was then asked to apply his mind to the sort of choices that had to be made with patients whose haemophilia was mild. He alluded to the involvement in decision-making of the patients themselves: [I]t was very much part of the unit's policy to recognise that there was a risk of hepatitis and to share that with the patients'.<sup>22</sup> For a patient with mild haemophilia, the first choice would be to use desmopressin (DDAVP).<sup>23</sup> He could not remember any patients with mild haemophilia or von Willebrand's disease who had to have a blood product during the 1985–87 period. Even for the patient with mild haemophilia having a bleed, desmopressin was usually effective, because the transient increase in Factor VIII was usually enough to stop the bleed.<sup>24</sup> Sometimes even the physiological response to bleeding, whereby the levels of Factor VIII rise naturally, was enough to deal with the problem in a person with mild haemophilia.<sup>25</sup> But, Professor Lowe explained in later questioning, in a patient with haemophilia desmopressin is generally less effective in response to bleeding which has already started than it is in preventing bleeding.<sup>26</sup> With a joint or muscle bleed, concentrate therapy was 'much more likely' to be required.<sup>27</sup>

**22.17** At that time, if a patient with mild haemophilia was having a major bleed, it would be necessary to discuss with him the use of concentrates and the risk of hepatitis. And even if cryoprecipitate were to be used, it would have been necessary to tell the patient that large doses over a period of days would also carry a risk of infection with NANB Hepatitis.<sup>28</sup> An average adult dose would use material from 20 donors.<sup>29</sup>

**22.18** Professor Lowe was then asked about the 'steer' which might have been given to such a patient by medical staff. After some deliberation, he answered that if patients had asked what he personally would do in their situation, he would have told them he would opt for treatment with cryoprecipitate from 20 donors who were HIV tested.<sup>30</sup>

<sup>21</sup> Ibid page 22

<sup>22</sup> Ibid page 24

<sup>23</sup> In later questioning, Professor Lowe agreed that desmopressin becomes less effective after about 48 to 72 hours of use, and that it has some drawbacks with children in particular, principally fluid retention. See Day 54, pages 67–68.

<sup>24</sup> Professor Lowe – Day 54, pages 25–26. Further discussion of the mechanisms involved in the use of desmopressin can be found in Professor Lowe's evidence at Day 54, pages 70–73.

<sup>25</sup> Professor Lowe – Day 54, page 26

<sup>26</sup> Ibid page 72

<sup>27</sup> Ibid page 73

<sup>28</sup> Ibid page 27. Professor Ludlam made the same point (see Day 54, pages 132–6): treatment with cryoprecipitate still carried a risk of NANB Hepatitis. Estimates given in evidence of the scale of the risk varied – plainly, this depended on the incidence of the virus in the donor population at the time. If the incidence was 0.4%, as it was found to be by Minor et al in their examination of donor samples ('Antibody to Hepatitis C virus in plasma pools', *The Lancet*, 21 July 1990 [SGF.001.1380]) then exposing a person to 250 donations in his life would be expected to cause infection. Professor Ludlam was more pessimistic, saying that an adult treated with cryoprecipitate for five days would 'almost certainly' contract NANB Hepatitis. See also Dr Colvin – Day 55, page 139. The incidence of Hepatitis C in the donor population is discussed more fully in Chapter 3, *Statistics*.

<sup>29</sup> Professor Ludlam – Day 54, page 136

<sup>30</sup> Professor Lowe – Day 54, page 30

**22.19** Considering the issue more generally, Professor Lowe agreed that there was a general desire among haemophilia treaters to avoid the use of concentrates at that time. The reasons for that were the awareness that initial heat treatment was not effective against NANB Hepatitis, which was ‘more or less inevitable if you got concentrate’ and the growing realisation that NANB Hepatitis was not, as had previously been thought, a ‘relatively benign disease’.<sup>31</sup> In answer to later questioning, he agreed that the dose likely to be required was also a factor because, if the patient were to be having daily cryoprecipitate for two weeks, the advantages of cryoprecipitate over concentrates would vanish because of the patient’s being exposed to several hundred donors.<sup>32</sup> For that reason, there was ‘more of an equipoise for a small number of patients between cryoprecipitate and concentrate’.<sup>33</sup>

**22.20** As far as Factor IX was concerned, it was decided in Glasgow in April 1985 to use commercial heat-treated product until the NHS heat-treated product became available in the autumn.

**22.21** There is no record of the English product, 8Y, being used in Glasgow over the period 1985–1987, and Professor Lowe did not recall any such use.<sup>34</sup> In response to more general questions about knowledge at the time of the development of 8Y, Professor Lowe had no memory of hearing informally about the advances in England,<sup>35</sup> or of anyone proposing that Glasgow could attempt to obtain a small supply of 8Y to treat particular patients.<sup>36</sup> By way of explanation for his unfamiliarity with the then current position in England, Professor Lowe said that, even once he had been appointed as a consultant, Dr Forbes had made it clear that he was running the haemophilia unit and Professor Lowe was his assistant. Professor Lowe was developing services in relation to thrombosis, rather than haemophilia.<sup>37</sup> He was anxious, however, to correct any impression that there was a lack of communication between himself and Dr Forbes.<sup>38</sup>

### *Edinburgh*

**22.22** Professor Ludlam agreed that in relation to the period under examination, it was fair to say that therapeutic policy was ‘guided by a desire to avoid the use of blood products unless there was no alternative’.<sup>39</sup> In his statement to the Inquiry, Professor Ludlam had said:

When [the first heat-treated product] NY 68 degree/2 hour, was introduced in December 1984 ... it was widely acknowledged that it was very likely to transmit non-A non-B hepatitis.<sup>40</sup>

**22.23** Later in his statement, Professor Ludlam informed the Inquiry that, during this period:

[I]n the majority of patients, the sole aim was to prevent HIV transmission and this was accomplished by using heat-treated concentrates, even although it

---

<sup>31</sup> Ibid page 33

<sup>32</sup> Ibid pages 64–65

<sup>33</sup> Ibid page 66

<sup>34</sup> Ibid pages 40–41. UKHCDO data indicate that 8Y was first used in Glasgow Royal Infirmary and in Yorkhill in 1990.

<sup>35</sup> Ibid page 44

<sup>36</sup> Ibid page 46

<sup>37</sup> Ibid page 47

<sup>38</sup> Ibid pages 56–57

<sup>39</sup> Ibid page 74

<sup>40</sup> Professor Ludlam’s statement on the use of blood product concentrates between 1984 and 1987 [PEN.017.1790]

was thought likely that they transmitted hepatitis viruses. The policy adopted in Scotland was as set out in the 14th December 1984 UKHCDO Circular by Professor Bloom.<sup>41</sup>

**22.24** As far as cryoprecipitate was concerned:

Cryoprecipitate was a non heated product, prepared from individual donors, which could transmit HIV and hepatitis viruses. Once the lifetime patient exposure to cryoprecipitate reached approximately 100 donors (about 5 infusions in an adult) the risk of non-A non-B hepatitis approached 100%.

Until October 1985, donors were not tested for anti-HIV. After this date there was uncertainty about its efficacy to exclude all donations infectious for HIV. This was because there was uncertainty about the sensitivity of the anti-HIV test to detect all antibody positive donations. Furthermore there were potentially donors, recently infected with HIV, who were viraemic, but in whom the anti-HIV antibody had not yet arisen, and whose donation would therefore be infectious but would not be detected by the anti-HIV test. This is the so called 'window period' and can last up to about 6 months after primary infection with HIV. Later techniques were developed to detect HIV in the 'window period', in the absence of antibody, (NAT (nucleic acid testing)) and these are now in current use for screening donations).

During the period 1984–1987, if only a single, or very occasional, treatment with a blood product was required, it could be argued that cryoprecipitate was safer, with respect to non-A non-B hepatitis, than heat-treated NHS concentrate. The disadvantage of cryoprecipitate, however, was that it was not heat-treated and therefore could transmit HIV.<sup>42</sup>

**22.25** Thus, treatment policy in Edinburgh during the period under investigation for patients with Haemophilia A or von Willebrand's disease who were probably not infected with NANB Hepatitis was as follows:

- Children with severe or moderate haemophilia would be treated with cryoprecipitate or heat-treated Factor VIII.
- For those with mild haemophilia and von Willebrand's disease, the options were: to manage without the use of a blood product; to use DDAVP where possible; to use cryoprecipitate occasionally for treatment of Haemophilia A when only small amounts of treatment were necessary; or to use heat-treated Factor VIII.
- The heat-treated concentrate used would have been the PFC-issued NY, heat-treated at 68°C for 24 hours, apart from after August 1986, when a small supply of 8Y existed in Scotland and was available for patients not previously exposed to the virus who presented with a major bleed.<sup>43</sup>

<sup>41</sup> Ibid [PEN.017.1790] at 1792

<sup>42</sup> Ibid [PEN.017.1790] at 1793

<sup>43</sup> Summarised from Professor Ludlam's statement on the use of blood product concentrates between 1984 and 1987 [PEN.017.1790] at 1794–5

**22.26** For patients with Haemophilia B, the options were fresh frozen plasma or unheated NHS Factor IX, until October 1985, when product heated at 80°C for 72 hours became available in Scotland.<sup>44</sup>

**22.27** In oral evidence, Professor Ludlam agreed that the incidence of NANB Hepatitis from unheated concentrates was understood at that time to be very, very high.<sup>45</sup> Specific information regarding the incidence in haemophilia patients in Edinburgh in 1989, shortly after HCV tests were developed, was available to the Inquiry. This was in the form of a letter sent by Professor Ludlam et al to *The Lancet*. Sera from 61 patients with Haemophilia A or B or von Willebrand's disease had been tested for antibody to HCV. Of the 48 who had received non-heated concentrates (before 1985), 41 were seropositive by this early anti-HCV test. It was not clear at the time why all 48 were not seropositive. The negative cases may have been or included individuals who had cleared the virus and, over time, had become anti-HCV negative or, given that it was an early test, they may have been HCV positive at the time but not identified by the test. Of the remaining 13, seven had received only heat treated concentrates and all were seronegative. Six who had received only cryoprecipitate or red cells were also negative.<sup>46</sup>

**22.28** Professor Ludlam's awareness at that time of the severity of NANB Hepatitis was also explored. First, he was asked about the article entitled 'Progressive liver disease in haemophilia: an understated problem?' by Dr Hay et al in *The Lancet* of 29 June 1985.<sup>47</sup> The article was familiar to Professor Ludlam and he thought it would have been so at the time of its publication. He considered that the aspect which had not been previously appreciated up to that point was that the disease was progressive.<sup>48</sup>

**22.29** Next, Professor Ludlam was shown an article from *Blood*, published in August 1985, entitled 'A study of liver biopsies and liver disease among hemophiliacs'.<sup>49</sup> The study had involved 155 patients with haemophilia, some of whom had received a lifetime exposure to more than 100,000 units of concentrate. The incidence of cirrhosis found was 15%, with chronic active hepatitis affecting 7%. The article recognised the possibility of insidious progression to cirrhosis. Professor Ludlam remembered noticing it at the time.<sup>50</sup>

**22.30** A further letter on this topic (this time from Dr Schimpf) appeared in *The Lancet* of 8 February 1986, reporting results from the haemophilia centre in Heidelberg. The author agreed with Dr Hay and his colleagues that liver disease in haemophilia was an understated problem.<sup>51</sup> Professor Ludlam described Dr Schimpf as 'a very distinguished haemophilia treater'.<sup>52</sup> He was sure he would have seen the letter.<sup>53</sup>

**22.31** In the light of this material, Professor Ludlam offered his view that it was around that period that it 'became clear that it [liver disease in haemophilia] was potentially serious and potentially progressive'.<sup>54</sup>

<sup>44</sup> Professor Ludlam's statement on the use of blood product concentrates between 1984 and 1987 [PEN.017.1790] at 1795

<sup>45</sup> Professor Ludlam – Day 54, page 82

<sup>46</sup> Ludlam et al, 'Antibodies to Hepatitis C virus in haemophilia', *The Lancet*, 2 September, 1989; 560–1 [LIT.001.3859]

<sup>47</sup> Hay et al, 'Progressive liver disease in haemophilia: an understated problem?', *The Lancet*, 29 June 1985; 1495–7 [LIT.001.0335] This article, which reported finding progressive liver disease in 17 of 79 patients tested (these being patients selected for their exposure to blood products) is considered at Chapter 15, *Knowledge of Viral Hepatitis 2 – 1975–1985*.

<sup>48</sup> Professor Ludlam – Day 54, pages 85–86

<sup>49</sup> Aledort et al, 'A study of liver biopsies and liver disease among hemophiliacs', *Blood*, 1985; 66:367–72 [LIT.001.0505]

<sup>50</sup> Professor Ludlam – Day 54, page 88

<sup>51</sup> Schimpf, 'Liver disease in haemophilia', *The Lancet*, 8 February, 1986; 232 [LIT.001.0341] at 0342

<sup>52</sup> Professor Ludlam – Day 54, page 92

<sup>53</sup> Ibid page 94

<sup>54</sup> Ibid page 94

*The London Hospital*

**22.32** Dr Colvin assisted the Inquiry by giving evidence both in relation to his own practice at the London Hospital, one of four centres in London, over the period examined, and also by endeavouring to put himself in the position of a haemophilia clinician in Scotland.

**22.33** In his evidence, Dr Colvin was asked about the role of cryoprecipitate at that time. Initially, he expressed considerable reservations about the therapeutic potential of cryoprecipitate during the period under examination. He was referred to a study, published in *Clinical and Laboratory Haematology* in 1987, in which he had reported on six patients, not previously exposed to concentrates, who were treated with cryoprecipitate between October 1982 and July 1984.<sup>55</sup> No patient had shown signs of NANB Hepatitis. The report suggested that, following the introduction of screening of donated blood for anti-HIV in October 1985, the use of cryoprecipitate in selected cases should be reconsidered. Notwithstanding these published views, Dr Colvin felt that by the time of publication, ‘the world had moved on, and I think by that time we had really given up using cryoprecipitate’.<sup>56</sup> In expressing these views, he highlighted the interval between the study and the date of publication of the article. He considered that the paper revealed the uncertainty of the period, and the range of options which were examined.

**22.34** On his second day of giving evidence on this topic, however, Dr Colvin slightly refined his position on the use of cryoprecipitate:

I suspect that by 1986, despite my publication in 1987, I would have thought twice about using cryoprecipitate. But I think it would not have been an unreasonable point to have made, [that the safety of cryoprecipitate had been improved by HIV screening of donors] and the fact that I allowed my paper to be published in 1987 implies that I thought even at that time it was a reasonable approach to the problem. But you would have to take every case on its merits. As I implied in my previous answer, one had to factor such a lot of different issues into the equation before you made a decision, and the decision you made wasn’t necessarily the right decision and it was perfectly possible for another physician to make a reasonable different decision.<sup>57</sup>

In other words, therefore, there was a period – a ‘brief window’<sup>58</sup> – after the introduction of donor screening for HIV when cryoprecipitate could have been a possible treatment for some patients if one were worried about the safety of the available concentrate.<sup>59</sup>

**22.35** On his first appearance on this topic, when asked how he would have treated patients had he been in Scotland during this period, Dr Colvin referred to the possibility of either postponing elective procedures to avoid the use of blood products or using desmopressin.<sup>60</sup> Where treatment was necessary:

<sup>55</sup> Colvin et al, ‘A prospective study of cryoprecipitate administration: absence of evidence of virus infection’, *Clinical and Laboratory Haematology*, 1987, 9:13–15. [LIT.001.0640]

<sup>56</sup> Dr Colvin – Day 55, pages 136–7.

<sup>57</sup> Dr Colvin – Day 74, page 106

<sup>58</sup> Ibid page 105

<sup>59</sup> Professor Howard Thomas was referred in evidence to an article he co-authored with haemophilia clinicians: Kernoff, PBA et al, ‘High Risk of non-A non-B hepatitis after a first exposure to volunteer or commercial clotting factor concentrates: effects of prophylactic immune serum globulin’, *British Journal of Haematology*, 1985; 60:469 [LIT.001.0800]. The article was submitted in 1984. In the conclusions, reference is made to patients with mild bleeding disorders now being ‘more appropriately treated’ with cryoprecipitate or desmopressin than with concentrates. See Professor Thomas – Day 52, pages 87–106. See also his further comments on cryoprecipitate at Day 52, page 156.

<sup>60</sup> Dr Colvin – Day 55, pages 148–9

[I]t was extremely difficult to know what to do. But I think that for very small usage in adults, where you were going to really have quite a small number of units and then not use any more, for instance for very mild haemophilia, where you couldn't use DDAVP, [cryoprecipitate] was an option. I think that for very small children, where tiny volumes of cryoprecipitate would achieve haemostasis, it was also an option but it was an option with diminishing benefits as the number of units went up.

Q. Yes. And I suppose the other consideration that struck me is that in this period, even with a child who has severe haemophilia, you could reason that a better product might be going to come along, so you are not talking about trying to assess how much cryoprecipitate this child will require for the next ten or 20 years. It might be for quite a short period?

A. That is exactly [what] my reasoning was in carrying on with cryoprecipitate until 8Y became available for the children.<sup>61</sup>

**22.36** Dr Colvin referred again to the many uncertainties prevailing during this period. It was really only possible to 'do what seemed a good idea at the time'.<sup>62</sup>

I still feel that any decision made to use 8Y or the Scottish equivalent at that point was based on a kind of informed intuition. I certainly would have liked to have said at the time that I was convinced that one product was better than another. I think we were all extremely relieved when it became apparent that 8Y and the Factor IX equivalent in due course actually were safe. It was a piece of – I was going to say good luck; it wasn't good luck exactly but I think we were all extremely relieved that in retrospect this was the case. But I think there is huge danger of using the retrospectoscope to say that one should have taken the particular view because it later turned out that that was the answer.<sup>63</sup>

**22.37** Had he been in Scotland, would he have tried, as Professor Ludlam did, to obtain a supply of the English product?<sup>64</sup> Dr Colvin thought it more likely that his course of action would have been to wait and see in relation to developments in England.<sup>65</sup>

**22.38** On the second occasion on which he gave evidence on this topic, Dr Colvin was again asked about what he did during the relevant period and what he would have done had he been practising in Scotland. He replied:

I have suggested that I would have used heat-treated commercial Factor VIII concentrate where essential, especially for more significant bleeding episodes or major surgery, where the use of substantial quantities of concentrate was anticipated. So what we had really was a policy of trying to look after those who had been least treated and trying to look after, really, children. So until the spring/summer of 1985, I was still trying to use cryoprecipitate for the children but I then changed over to 8Y really as soon as it became available, and I think probably around the time of this letter [to haemophilia directors dated 24 July

---

<sup>61</sup> Ibid pages 151–2

<sup>62</sup> Ibid page 156

<sup>63</sup> Ibid page 157

<sup>64</sup> Professor Ludlam's request for 8Y from England is narrated below at paragraph 22.54

<sup>65</sup> Dr Colvin – Day 55, page 158

1985<sup>66</sup>]. As far as adults were concerned, particularly, I am afraid, people who had been given a lot of treatment in the past, or who were due to have major surgery which would require a lot of concentrate to be given, then it was very often the case that we had to consider using commercial heat-treated concentrate because, as I think was made clear around that time, the provision of 8Y was only sufficient for a proportion of the patients under our care.<sup>67</sup>

**22.39** For any individual adult patient, who had not previously received concentrates but required treatment, there would be questions as to how much was likely to be used. Dr Colvin would have wanted to avoid using too much 8Y for any one individual. But if only a small amount was going to be used, then it would have been 8Y: 'that was what was available to us and we thought that was the best concentrate to use at the time'.<sup>68</sup> In addition, such a patient was actually a valuable resource as far as new products were concerned, so Dr Colvin would have wanted to try to enter him in a trial if possible.<sup>69</sup>

**22.40** In the last part of his testimony, Dr Colvin reminded the Inquiry that:

[I]t wasn't easy to know what the right answer was, and the responsible physicians acting within the spectrum of appropriateness sometimes came to different conclusions.<sup>70</sup>

## 8Y

### *Emerging information about safety*

**22.41** As previously noted, there appears to have been no use of the English heat-treated Factor VIII product, 8Y, in Glasgow.<sup>71</sup> But it was used in Edinburgh. It is therefore necessary to consider the background to the use of English product to treat patients in Scotland.

**22.42** 8Y was treated at 80°C for 72 hours.<sup>72</sup> It was issued routinely for the treatment of patients with haemophilia in England with effect from September 1985. The Inquiry was interested to ascertain when clinicians in Scotland became aware of this product, and what view they took of it.

**22.43** In his statement, Professor Ludlam pointed out that:

The viral safety, with respect to transmission of non-A non-B hepatitis, of the BPL product, treated at 80 degrees/72 hours, introduced in England in September 1985 was unknown at that time. It was not until mid 1986 that evidence started to be reported to suggest that it might be a 'hepatitis reduced' concentrate.<sup>73</sup>

**22.44** In evidence, he reminded the Inquiry that, although 8Y was of particular benefit to patients who had not previously been treated with concentrates, in that it prevented their being infected with NANB Hepatitis, the priority in England in 1985 was to protect all haemophilia patients from HIV.<sup>74</sup>

<sup>66</sup> Information Sheet, *Dried Factor VIII Concentrate: High-Purity, Heat Treated*, issued to English and Welsh Haemophilia Directors and Regional Transfusion Directors by Blood Products Laboratory, 24 July 1985 [DHF.003.0476]

<sup>67</sup> Dr Colvin – Day 74, page 89

<sup>68</sup> Ibid page 90

<sup>69</sup> Ibid page 92

<sup>70</sup> Ibid page 103

<sup>71</sup> See paragraph 22.21 above

<sup>72</sup> The technical background to the achievement of this heating protocol in England is dealt with in Chapter 24, *Viral Inactivation of Blood Products for Haemophilia Therapy 1985–1987*

<sup>73</sup> Professor Ludlam's statement on the use of blood product concentrates between 1984 and 1987 [PEN.017.1790] at 1791

<sup>74</sup> Professor Ludlam – Day 54, page 99

**22.45** In relation to the view which clinicians had at that time of the safety of 8Y, Professor Ludlam recalled that there was no certainty at all that dry heat treatment to 80°C would be effective in respect of removing NANB Hepatitis transmission risk, and there was a lot of international scepticism about dry heat treatment at any temperature being effective.<sup>75</sup>

**22.46** The contemporaneous material was reviewed with Professor Ludlam in evidence. At PFC on 17 March 1986, a meeting took place between fractionators based in Scotland and England. In paragraph 5 of the minutes of the meeting relating to viral inactivation, it is recorded that:

Dr Smith outlined clinical trial results of the 8Y F VIII product so far. While results cannot be considered conclusive at this stage, he indicated that no cases of virus infection have occurred (attributable to 8Y material) after 12 months' experience of 8Y in virgin haemophiliacs.<sup>76</sup>

Professor Ludlam pointed out certain flaws in this information, but was willing to accept that these might be questions of the weight this information should bear.<sup>77</sup>

**22.47** Turning to events in England, Professor Ludlam was shown the minutes of a meeting of the Central Blood Laboratories Authority (CBLA), Central Committee for Research and Development in Blood Transfusion on 9 July 1985.<sup>78</sup> The minutes referred to a trial, then ongoing, in which patients thought to be susceptible to NANB Hepatitis (because they had either never previously had concentrate or had not had it for a long time) were given 8Y. Several of them had already passed the point at which the first evidence of NANB Hepatitis transmission would have been expected. That information is also contained in an information sheet dated 24 July 1985, issued by BPL and distributed to all haemophilia directors and regional transfusion directors in England and Wales.<sup>79</sup> The sheet explains that the product has been heated at 80°C for 72 hours to reduce the risk of viral infection, and that 'further assurance is sought over freedom from risk of viral transmission'.

**22.48** In the light of this material, Professor Ludlam was asked if, in 1985, he was hearing 'news from England'. Although he would not have received the information sheet, he told the Inquiry that he was aware the studies were going on, and pointed out the difficulty in recruiting patients for such an exercise. Whilst he found it difficult to recall conversations or other sources of information, he put the date of his knowledge – a 'general feeling' – about 8Y at 1986.<sup>80</sup> He also reiterated that there was 'a lot of scepticism' about how effective dry heat treatments would be.<sup>81</sup>

**22.49** He was later asked if Dr McClelland had reported to him 'encouraging' signs regarding the English product that were mentioned at a subsequent meeting of the CBLA Central Committee for Research and Development in Blood Transfusion on 19 December 1985.<sup>82</sup> Professor Ludlam thought not.

<sup>75</sup> Ibid page 100

<sup>76</sup> Note of a meeting held at PFC on March 17 1986 [SNB.007.5664] at 5666. Dr Smith gave extensive evidence about the technological progress in developing 8Y and testing its effectiveness which is discussed elsewhere.

<sup>77</sup> Professor Ludlam – Day 54, page 102

<sup>78</sup> Minutes of the sixth meeting of the Central Committee for Research and Development in Blood Transfusion, 9 July 1985 [PEN.016.1142]. This meeting did not have representation from Scotland.

<sup>79</sup> Information Sheet, *Dried Factor VIII Concentrate: High-Purity, Heat Treated*, issued to English and Welsh Haemophilia Directors and Regional Transfusion Directors by Blood Products Laboratory, 24 July 1985 [DHF.003.0476]

<sup>80</sup> Professor Ludlam – Day 54, pages 106–107

<sup>81</sup> Ibid page 108

<sup>82</sup> Professor Ludlam – Day 55, pages 96–98



**22.50** It was also suggested to Professor Ludlam that there was a much more local source of information about 8Y. In January 1986, Dr Perry wrote a report for the regular joint meeting of SNBTS directors and the haemophilia directors.<sup>83</sup> In it, he recorded that the BPL was now issuing their product heated at 80°C for 72 hours and that ‘preliminary clinical data’ indicated that this material was ‘non-infective with respect to HTLV III, NANB and Hepatitis B’.<sup>84</sup> The meeting was held on 5 March 1986; in fact Professor Ludlam sent apologies and, in evidence, he was not clear about whether or not he would have received the background papers.<sup>85</sup>

**22.51** At a meeting of Haemophilia Reference Centre Directors on 22 September 1986, Dr Rizza presented the directors with a paper on the study into the effectiveness of the heat treatment of 8Y (and its equivalent for Haemophilia B, 9A).<sup>86</sup> The analysis was restricted to results in those patients who had no previous exposure to concentrates, although some had received cryoprecipitate. Fortnightly measurements had taken place to detect raised liver enzymes and the trial had also involved exposure to multiple batches, to create greater exposure in the patients. None of the patients had recorded an ALT or AST measurement above 2.5 times the upper limit of normal. Dr Smith acknowledged in his report that the data were inconclusive due to some gaps in follow-up, but might nonetheless further encourage haemophilia directors to use 8Y and 9A in previously untreated patients. A statistician had calculated that the number of negative cases found could still be consistent with an infectivity rate of up to 14%; that was plainly better than for unheated concentrates. This pilot study was to be followed by a more formal prospective controlled trial with a stricter protocol.<sup>87</sup>

**22.52** As with the information presented at the meeting at PFC,<sup>88</sup> Professor Ludlam pointed out weaknesses in the data. But he agreed that the information was ‘reassuring’.<sup>89</sup>

**22.53** This report was also reviewed with Dr Colvin. He pointed out that the numbers of patients were very small. Although no infection was found in the patients treated, infection might have been apparent had a larger number of patients been involved. He also pointed out that some of those who were tested could previously have had NANB Hepatitis and cleared the virus, therefore if they had been infected by 8Y, that infection would not have been evident.<sup>90</sup> He was not, however, critical of the use of patients who had had some previous exposure to cryoprecipitate: ‘the use of patients who were not truly untreated was a risk worth taking to get the data that one needed to be reasonably confident that a particular product was safe’.<sup>91</sup> There had been false dawns before – heat-treated products had previously been demonstrated to continue to transmit both NANB Hepatitis and HIV, so all those involved were understandably cautious about how safe

<sup>83</sup> PFC Report for SHS Haemophilia/SNBTS Directors Meeting (March 1986) [SNB.001.5469]

<sup>84</sup> Ibid [SNB.001.5469] at 5472

<sup>85</sup> Professor Ludlam – Day 54, page 110

<sup>86</sup> The Inquiry has a copy of a paper *Surveillance of previously untreated patients for possible virus transmission by BPL Factor VIII and Factor IX concentrates, 8Y and 9A: Interim Report* [SNF.001.1123], but the paper refers to information being summarised by Dr Jim Smith on 30 September 1986 – some revision of, or addition to, the paper must therefore have taken place between 22 and 30 September. The information quoted in paragraph 22.51 is drawn from the paper.

<sup>87</sup> A fuller report, giving results in relation to 32 patients, was published as ‘Effect of Dry-Heating of Coagulation Factor Concentrates at 80 c for 72 Hours on Transmission of Non-A, Non-B Hepatitis’, *The Lancet*, October 8 1988; 814–816 [LIT.001.0330]. This was discussed by Dr Colvin in his report for this topic, [PEN.017.1674] and in evidence at Day 55, Page 145. Even this study did not fulfil the protocol for such research laid down by the International Society on Thrombosis and Haemostasis (ISTH) – Dr Colvin – Day 74, page 93.

<sup>88</sup> See paragraph 22.46 above.

<sup>89</sup> Professor Ludlam – Day 54, page 116

<sup>90</sup> Dr Colvin – Day 55, page 143

<sup>91</sup> Ibid page 144

any new product might actually prove to be.<sup>92</sup> Even as late as 1988, in an article dealing with a number of different studies which had been carried out into treated products, Mannucci and Colombo felt able to say only that Factor VIII concentrates treated at 80°C were ‘presumed innocent’.<sup>93</sup>

### *Supply of 8Y to Edinburgh*

**22.54** Despite reservations, Professor Ludlam appears to have had about the information emerging in 1985 and 1986 regarding 8Y, he nevertheless took steps to obtain some for patients. On 27 June 1986, Dr Boulton, deputy director of the Edinburgh and South East Scotland Regional Blood Transfusion Service, wrote to Dr Cash about the development of heat-treated products in Scotland. In his letter, he related a conversation he had had with Professor Ludlam about trials of more severely heated product prepared in Scotland. 8Y had been mentioned:

Apparently a few weeks ago he was asking Brian McClelland if VIIIY could be made available in the event of a “virgin” haemophiliac being presented.<sup>94</sup>

**22.55** Professor Ludlam thought that the background to this must have been that someone had passed on the latest information about 8Y. It probably then came up in conversation with Dr McClelland that 8Y was a better product than the Scottish heat-treated product insofar as the prevention of NANB Hepatitis was concerned.<sup>95</sup> He was asked why, given the limitations on the information then available about 8Y, he was still interested in obtaining some. For him it was an issue of comparative risk. It was highly likely that all SNBTS concentrate then available, heated at the time at 68°C for 24 hours, would transmit hepatitis. The evidence from the 8Y studies was that it appeared to be less likely to transmit non-A non-B Hepatitis. It was a matter of degree. 8Y would be an improvement on what was currently available in Scotland. It might not be hepatitis-free but it might be less infective.

**22.56** Another letter from Dr Boulton dated 27 June 1986 was also examined in evidence with Professor Ludlam. This time, Dr Boulton was writing to Dr Perry at PFC.<sup>96</sup> His letter included the following passage:

A young haemophiliac who previously had minimal therapy with factor VIII received an infusion of the current heat-treated product a month ago. He now shows signs of liver enzyme rises indicating non-A non-B hepatitis. Christopher [Ludlam] is a bit ruthless with his own staff about this because he feels that this patient should have received VIIIY or an equivalent product. However, the patient is apparently quite well clinically.<sup>97</sup>

**22.57** The Inquiry was interested to explore with Professor Ludlam whether the episode referred to in Dr Boulton’s letter had been the impetus for his attempt to obtain a supply of 8Y.

<sup>92</sup> Ibid pages 144–45; Dr Colvin’s report on the use of blood product concentrates between 1984 and 1987 [PEN.017.1674]

<sup>93</sup> Mannucci and Colombo, ‘Virucidal Treatment of Clotting Factor Concentrates’, *The Lancet*, October 1 1988; 782–785 [LIT.001.0456]

<sup>94</sup> Dr Boulton’s letter of 27 June 1985 to Dr Cash [SNB.007.5869]

<sup>95</sup> Professor Ludlam – Day 54, page 119

<sup>96</sup> Dr Boulton’s letter of 17 June 1986 to Dr Perry [SNB.007.5871]

<sup>97</sup> It appears that the patient was transfused in May 1986.

**22.58** The word used by Dr Boulton to describe Professor Ludlam’s feelings at the time (‘ruthful’) was unusual. Professor Ludlam described himself as having been sad that his team had not had 8Y to give to the patient at the time. He did not disagree with Dr Boulton’s articulation of these sentiments.<sup>98</sup> It was put to Professor Ludlam that this incident had the effect of sharpening his focus on obtaining some 8Y. He answered:

To be honest, I’m not certain which way round it occurred. I think it was in my discussions with the blood transfusion colleagues after it had happened, that the real potential, possible extra safety of 8Y was being highlighted in my mind.<sup>99</sup>

**22.59** He emphasised to the Inquiry the preciousness of 8Y in England; for the first time, clinicians there had a heat-treated NHS product, after having been desperate for one in the first part of 1985. Every bottle was valued and he was not sure that he would be able to have any, should he make such a request.<sup>100</sup> He concluded:

So I’m sorry, I can’t remember exactly how the sequence of thoughts went. But certainly this sad episode of a patient susceptible to non-A non-B [who] had acquired non-A non-B ... highlighted the issue.<sup>101</sup>

**22.60** He was then asked whether, if he personally had been looking after the patient concerned and had had a supply of 8Y, he would have used it. Professor Ludlam thought that, in these circumstances, he would have been ‘very tempted’ to use it.<sup>102</sup>

**22.61** The evidence concerning the dissemination of guidance to more junior staff about the treatment of patients and about the circumstances in which blood products should be used is discussed more fully in paragraphs 22.71 to 22.86 below.

**22.62** As far as the obtaining of 8Y in 1986 is concerned, the Inquiry followed the trail of correspondence culminating in the sending to Edinburgh of a small stock of 8Y in August 1986. Dr Perry replied to Dr Boulton on 2 July 1986. The PFC was ‘poised to introduce yet another FVIII product which will be heat treated at 80°/72hours and should therefore be comparable to 8Y’. As soon as this product was available, virgin patients (previously untreated patients, sometimes referred to as ‘PUPs’) would be able to gain access to it.<sup>103</sup> On 4 July, Dr Boulton wrote to Dr Perry,<sup>104</sup> asking him to confirm that Dr Boulton’s notes of their telephone conversation the day before<sup>105</sup> were accurate. By letter dated 7 July, Dr Perry confirmed they were ‘about right’. He added:

While there will be no PFC product virucidally comparable to 8Y until September ‘86, after that time it would be my intention to supply the Phase III product [the 80°/72 hours product, virucidally equivalent to 8Y] to “virgins” since we hope to demonstrate by that time that it is virucidally equivalent thus removing the need to go South. However, in the immediate future (July–September ‘86), we could probably get supplies of 8Y for special cases. It would of course be preferable if these were obtained and supplied through PFC.<sup>106</sup>

<sup>98</sup> Professor Ludlam – Day 54, page 121

<sup>99</sup> Ibid pages 129–130. See also Day 55, page 104, where Professor Ludlam accepted that this incident ‘must have been part of the discussion’.

<sup>100</sup> Professor Ludlam – Day 54, page 130. See also Day 55, page 112.

<sup>101</sup> Ibid page 130–31

<sup>102</sup> Ibid page 131

<sup>103</sup> Dr Perry’s letter of 2 July 1986 to Dr Boulton of [SNB.007.5909]

<sup>104</sup> Dr Boulton’s letter of 4 July 1986 to Dr Perry [SNB.007.5910]

<sup>105</sup> Dr Boulton’s notes [SNB.007.5911] The notes are shown in typed form in the Preliminary Report at paragraph 11.315.

<sup>106</sup> Dr Perry’s letter of 7 July 1986 to Dr Boulton [SNB.007.5913]

**22.63** On 7 July, Dr Boulton wrote to Dr Perry again, apologising for ‘pestering’ him. Dr Ludlam had written to Dr McClelland asking if it would be possible to obtain some of the BPL products for use ‘if a previously untreated haemophilic presented for replacement therapy’. Dr Ludlam was asking for 500 vials. Dr Boulton felt this was a large quantity. He wanted to know if it might be possible for Dr Perry to obtain perhaps 50 vials. This would be enough to cover an initial injection and, if necessary, more could be sought urgently from Oxford.<sup>107</sup> Accordingly, on 10 July, Dr Perry wrote to Mr Norman Pettet at the BPL, relaying the request for 50 vials.<sup>108</sup>

**22.64** On 24 July, Mr Pettet replied. He said that he had tried to telephone Dr Perry the previous week. With Dr Lane’s agreement, he had spoken to Dr Jim Smith, who had ‘a novel proposal’ for Dr Perry: ‘perhaps Scotland would like to participate in our trial of Factor VIII Y!’. Dr Perry and the haemophilia directors involved would have to agree, and the patients would have to meet the criteria. But in case there were some patients who did not strictly meet the criteria, now or in future, Mr Pettet had put aside some 8Y for immediate despatch to PFC (or any other destination) if required. He could arrange for the product to be sent to PFC at that point, unless arrangements for cover had already been made with Dr Smith.<sup>109</sup> But on the same day, Dr Perry wrote to Dr Boulton. He had now confirmed that BPL were happy to supply 50 vials to PFC ‘on the understanding that, in the event that the material is used in suitable virgin patients, appropriate serial samples would be taken to contribute to their overall infectivity study’. Dr Perry thought this arrangement was reasonable; he would pass the product to Dr Boulton as soon as possible and he would be grateful if Dr Boulton could inform Dr Ludlam of the arrangement.<sup>110</sup> Also on 24 July, Dr Perry wrote to Dr Smith at BPL, confirming the arrangement made by telephone and asking for a supply of 50 vials of 8Y as a contingency. This material would be issued on condition that BPL’s clinical trial protocol was observed.<sup>111</sup> On 28 July, Dr Perry confirmed matters to Mr Pettet.<sup>112</sup>

**22.65** On 1 August, Dr Smith wrote to Dr Perry, sending 50 vials of 8Y and some copies of the clinical protocol.<sup>113</sup> He referred in his letter to the use of the 8Y to protect ‘Category 1 patients’ – Dr Smith explained that these will have been previously untreated patients, though he was not able to remember the precise definition of such patients.<sup>114</sup> On 5 August Dr Perry wrote to Dr Boulton to inform him that the supply of 8Y had arrived and that 20 vials had been sent to the transfusion centre at the Royal Infirmary in Edinburgh.<sup>115</sup> On 7 August, Dr Perry wrote to Dr Boulton again, advising him that two batches of Factor VIII heated at 80°C for 72 hours had been manufactured and that PFC were on target to begin trials of this product at the end of August or beginning of September.<sup>116</sup>

**22.66** Professor Ludlam gave evidence about his actual use of the 8Y thus obtained. This was a precious commodity: Professor Ludlam thought he would have told his own staff about the product, but they would not have been free to use it – they would have been expected to seek permission from him.<sup>117</sup>

<sup>107</sup> Dr Boulton’s letter of 7 July 1986 to Dr Perry [SNB.007.5914]

<sup>108</sup> Dr Perry’s letter of 10 July 1986 to Mr Pettet [SNB.006.0336]

<sup>109</sup> Mr Pettet’s letter of 24 July 1986 to Dr Perry [SNB.007.5980]

<sup>110</sup> Dr Perry’s letter of 24 July to Dr Boulton [SNB.007.5982]

<sup>111</sup> Dr Perry’s letter of 24 July to Dr Smith [SNB.007.5984]

<sup>112</sup> Dr Perry’s letter of 28 July 1986 to Mr Pettet [SNB.007.5986]

<sup>113</sup> Dr Smith’s letter of 1 August 1986 to Dr Perry [SNB.007.5990]; Delivery note [SNB.007.5991]; Instructions for use [SNB.007.5992]

<sup>114</sup> Dr Smith – Day 60, page 121

<sup>115</sup> Dr Perry’s letter of 5 August 1986 to Dr Boulton [SNB.007.6024]

<sup>116</sup> Dr Perry’s letter of 7 August 1986 to Dr Boulton [SNB.007.6048]

<sup>117</sup> Professor Ludlam – Day 55, page 65

**22.67** Of the 50 vials, Professor Ludlam used 20 vials for a patient with an allergic reaction to PFC NY concentrate. He subsequently obtained some more 8Y from Newcastle. He could not remember if this was because the other 30 vials had been used up.<sup>118</sup> Professor Ludlam referred to himself as having breached the understanding on which the 8Y had been given, in that he used it not for a previously untreated patient but for a patient with an allergy to PFC product.<sup>119</sup> He also acknowledged that being allowed to have any at all was outwith the normal arrangements for the supply of products by the BPL:

[E]ach English region had an allocation of 8Y, depending on how much plasma it supplied to BPL. As Scotland didn't supply any plasma to BPL, it had, in a sense, no right of access to 8Y. So it was a concession that had to come out of somebody else's supply, one of the English health authority's allocation.<sup>120</sup>

**22.68** It can be seen from the circular letter dated 24 July 1985 that the supply of 8Y to centres in England was tightly controlled, in view of the scarcity of the product. The circular provides:

It is recognised that, until the new production unit at Elstree is completed, output of 8Y will meet about one third of current demand for concentrate and for this reason, attempts have been made to define those patients likely to benefit most from the security inherent in 8Y.

Therefore, Haemophilia Centre Directors are being asked to compile lists of their patients considered 'at risk' and most Centres have complied. It is the considered view at BPL that, where possible, liaison between the Haemophilia Services and the BTS should aim at directing Factor 8Y to these patients, using the existing framework of distribution and supply.<sup>121</sup>

**22.69** On his second day of giving evidence on this topic, Professor Ludlam was asked why no request for a supply of 8Y for previously untreated patients in Scotland was made before the summer of 1986. He suggested that such a question needed to be put to someone from the Blood Transfusion Service. As indicated above, he had been pressing Dr McClelland on supplies of 8Y, and Dr Perry thought that the PFC would have been the appropriate intermediary. In responding to subsequent questioning, he observed that, rather than his request being obviously the right thing to have done at the time, it might have transpired that he had 'rather jumped the gun' as the trial was still ongoing and the product might have turned out not to be materially better.<sup>122</sup>

### *Telling other clinicians in Scotland*

**22.70** Professor Ludlam was also asked whether this stock of 8Y was for the whole of Scotland.

Q. Just one last matter, professor. When this supply of 8Y was obtained in the summer of 1986, was it for Edinburgh patients or was it for everybody in Scotland?

---

<sup>118</sup> Ibid pages 141–2 and pages 119–120

<sup>119</sup> Ibid page 120

<sup>120</sup> Ibid page 121

<sup>121</sup> Information Sheet, *Dried Factor VIII Concentrate: High-Purity, Heat Treated*, issued to English and Welsh Haemophilia Directors and Regional Transfusion Directors by Blood Products Laboratory, 24 July 1985 [DHF.003.0476]

<sup>122</sup> Professor Ludlam – Day 55, page 109

A. Well, as I think is clear, I requested it and it was held primarily at the protein fractionation centre and therefore it was available for anyone who wished to apply to use it.

Q. Yes. And Dr Perry didn't send you all 50 vials?

A. He sent me 20, I think.

Q. But as matters turned out, I think you used the whole 50 vials. Did you ever mention to any of your colleagues in Scotland that that stock existed?

A. I assume that would be a responsibility for Dr Perry. He had a new product available for patients.

Q. Right. Is that a "no". Do you have any memory of ever saying in a conversation, "Oh, there is a stock of 8Y at PFC?"

A. I'm sorry, I can't remember.<sup>123</sup>

**22.71** In light of this evidence, Dr Perry was also asked about the securing of this stock of 8Y, and whether there was an arrangement that this 8Y was available on a more general basis for patients in Scotland? He replied that colleagues at the BPL:

[W]ere prepared and able to supply small quantities of product for specific clinical situations, and the specific clinical situation was a previously untreated patient, and their positive response to our request demonstrated the principle that that was viable. I think if that had been then extended to an arrangement where BPL were being asked to supply product for all sorts of other reasons, an 8Y product, then I think they would have resisted that, for the reasons that I have described. So my clear understanding at the time was that this small supply of product was for very specific requirements.<sup>124</sup>

**22.72** Dr Perry was asked whose responsibility it was to inform clinicians in other parts of Scotland that this small supply of 8Y was available. He replied:

A. There were basically two options, and, of course, with hindsight, the best outcome would have been that either myself or Dr Ludlam, as chairman of the Scottish haemophilia centres directors study group – either of us could have more widely notified the other four haemophilia centre directors that this product was available and, to the best of my knowledge, that didn't occur.

Q. Can you give us any explanation or indication as to why that may not have occurred?

A. I have attempted to give you the explanation why I didn't take that particular position, because I didn't think it was a responsibility. Again, against this backdrop of being quite clear to make sure that, as a manufacturer, we were not exceeding our brief, I thought it was not the responsibility of SNBTS or indeed the PFC director, the manufacturer, to make wider notification of this. This was a specific facilitating arrangement that we carried out on behalf of Professor Ludlam.<sup>125</sup>

---

<sup>123</sup> Ibid pages 63–64

<sup>124</sup> Dr Perry – Day 74, page 51

<sup>125</sup> Ibid pages 53–54

**22.73** Dr Perry was asked if he could have sent a circular advising of the stock of 8Y. He agreed that that could have been done.

I think, with hindsight, I would certainly agree that that would have been an appropriate thing to do but I would still suggest that a more appropriate thing to do would have been for the haemophilia centre directors themselves to have – in the knowledge that this was available – we had established the principle with Professor Ludlam – then there was a possibility that they too could have communicated amongst themselves.<sup>126</sup>

He continued:

But I think I'm trying not to suggest that we could not have had a role to play here, and I think with hindsight I would agree: if I had my time again, I think I could have quite simply ... written to other haemophilia centre directors – actually, it would have been to regional transfusion directors as well, who were responsible for supply of the product – and made them available [aware]. It's quite possible – I have absolutely no evidence that this took place, but through various informal channels and communications I would have mentioned that this actually happened but I have no evidence for that.<sup>127</sup>

**22.74** In view of Dr Perry's reference to the Scottish Haemophilia Centres Directors' Study Group, the Inquiry has examined whether the directors were meeting as a group at this time. According to Professor Ludlam, the Scottish directors met as a group from about 1985.<sup>128</sup> In any event, they will have encountered each other regularly at meetings, and knew each other's identity and contact details. Information about the obtaining of a small supply of 8Y could have been disseminated among them by Professor Ludlam.

**22.75** There also arises the question of how hospitals in Scotland which did not have haemophilia centres but which might find themselves dealing with a person with haemophilia in an emergency would know that there was a supply of safer product for such patients in Edinburgh. This is further referred to below at paragraph 22.98 in the context of 'horizontal dissemination' of guidance.

### **Dissemination of guidance**

**22.76** The Inquiry was contacted by two people with haemophilia who contracted Hepatitis C from blood products during the period 1985–87. One of these individuals was treated in Edinburgh, not by Professor Ludlam personally but by a junior clinician, at night. The other person was treated in a remote part of Scotland. The Inquiry explored in evidence the issues of how guidance was given by senior clinicians to more junior staff ('vertical dissemination') and, given that people with previously undiagnosed haemophilia might present at any hospital at any time, how guidance was distributed around Scotland ('horizontal dissemination').

---

<sup>126</sup> Ibid page 56

<sup>127</sup> Ibid page 57

<sup>128</sup> Professor Ludlam – Day 18, page 7. Compare, however, other evidence set out at paragraph 22.87.

### *Vertical dissemination*

**22.77** Professor Ludlam was asked what steps he, as a haemophilia centre director, had taken to ensure distribution of guidance on treatment during the relevant period to members of staff who might be encountering patients with haemophilia. In particular, he was asked about the guidance document prepared by Professor Bloom after the meeting on 10 December 1984.<sup>129</sup>

**22.78** In response, Professor Ludlam indicated that he thought that what was in the guidance document represented practice in the Edinburgh centre at the time. The team was small: Professor Ludlam, a lecturer, a registrar and a haemophilia sister, and policies were ‘generally accepted and well-known within the team’. He could not remember whether there were written policies, locally produced, at that time.<sup>130</sup>

**22.79** Professor Ludlam confirmed that, during the period under investigation, the patients whose treatment raised the most difficult issues were those individuals with little or no previous exposure to blood products. He thought it would be ‘quite clear’ that such patients should be discussed at a senior level. At one extreme, if a baby without previous exposure came in with a life-threatening bleed, a major intracranial bleed, then his judgement would have been that that child required concentrate, because of speed of administration and known level of Factor VIII in the therapy.<sup>131</sup> He would almost certainly have been contacted.<sup>132</sup> As far as new staff were concerned, Professor Ludlam pointed to the continuity offered by the haemophilia sister, and the lecturer, whose post was a more permanent one.<sup>133</sup>

**22.80** Professor Ludlam also told the Inquiry about weekly meetings:

We had weekly educational meetings, at which we would discuss our internal arrangements, our internal policies, we would have outside speakers. I seem to recall a speaker from the blood transfusion coming to talk about developments in clotting factor concentrates.<sup>134</sup>

These meetings took place at 8.30 am on Fridays.

**22.81** The Inquiry was interested to probe further how medical staff would know that particular patients – the 1% who were not regular patients at the Centre – posed difficult questions as far as treatment of bleeding was concerned. Professor Ludlam’s answer to this was that such individuals would obviously stand out. They would not have case notes. If that was because they were visiting Edinburgh they might have haemophilia cards, or they might be able to explain themselves what their normal treatment was.<sup>135</sup> Junior staff were always free to come straight to Professor Ludlam if they needed advice about a patient.<sup>136</sup> As far as those staff who might think they did not require advice were concerned, Professor Ludlam answered that he very quickly got an impression of the level of competence and understanding of a new member of staff. If over-confidence was a problem, he would speak to them. He always said to new staff to contact him if they had

---

<sup>129</sup> See paragraphs 22.8 to 22.9 above.

<sup>130</sup> Professor Ludlam – Day 55, page 47

<sup>131</sup> *Ibid* page 49

<sup>132</sup> *Ibid* page 50–51

<sup>133</sup> *Ibid* page 51

<sup>134</sup> *Ibid* page 53

<sup>135</sup> *Ibid* page 55

<sup>136</sup> *Ibid* pages 55–56. See also page 87.



a query. He endeavoured to give staff as much responsibility as he could and as much as they felt comfortable with, whilst also equipping them with an understanding of the sort of areas and topics that he liked to be informed about.

**22.82** Professor Ludlam's evidence on the matter of dissemination within the department ended with the following exchange:

Q. Professor Ludlam, because this is an Inquiry, I think I have to probe just a little bit further and put to you that the sort of scenario we have been discussing – that is the patient with mild haemophilia who needs treatment, who has had no or minimal previous exposure to concentrates, needing treatment, where there is a continuing risk of hepatitis, which is a very significant adverse consequence and the treatment decision is a very difficult dilemma – that whole package is something that called for specification, so a written document or an advance instruction from you communicated to all staff. Looking back, even just in retrospect, what's your response to that?

A. Well, it could give rise to the wrong therapy. Let me caricature. A patient with mild haemophilia is involved in a road traffic accident, comes into hospital unconscious, may have an intracranial bleed. The recipe, the guidance says give DDAVP for mild haemophilia. That would be totally inappropriate for many reasons I could go into, if you wanted to.

Q. I was wondering perhaps about a simpler response. What if the guidance said in block capitals "phone me"? Would that not help?

A. That is, in a sense, what the guidance was. Here is an unusual situation.

Q. But you didn't see the need for making that kind of provision in advance, as it were, for putting down in writing, so there wasn't debate, what you expected the response to be?

A. I expected people to get in touch with me if it was not clear how they should proceed with the medical care of patients. That applied not just to mild haemophilia. I looked after patients with leukaemia and lymphoma and a whole range of conditions, and if one of my staff had some doubt about how to proceed, then they asked me.<sup>137</sup>

**22.83** It was not clear that this explanation dealt with the full range of possibilities giving rise to a need for the intervention of a more senior colleague. More junior staff might not be aware that the situation confronting them raised a problematic issue. They might think, wrongly, that it was clear how the patient should be treated. However, it is highly improbable that any form of general guidance could exclude the possibility of incorrect clinical judgement.

**22.84** The question of what would happen if such a patient presented in the casualty department of the hospital was also covered with Professor Ludlam. He explained that if haemophilia was suspected, a clotting screen would be performed. If the results revealed mild haemophilia, then staff from the haematology department would go to see the patient themselves. That situation was very unusual.<sup>138</sup> Of course, if the patient had been investigated before, then the patient himself might be able to inform medical staff

---

<sup>137</sup> Ibid pages 58–60

<sup>138</sup> Ibid page 69

about any clotting problems. But with such investigations, wider questions might arise in borderline cases about whether or not a particular individual should be ‘labelled’ as having a clotting disorder, because of the implications such a diagnosis might have for other areas of his life, such as life insurance.<sup>139</sup>

**22.85** Professor Ludlam was asked to consider what would have happened during the relevant period if a patient who was bleeding arrived in casualty and also informed staff of some sort of history of bleeding easily. His answer was that a clotting screen would have been performed – the threshold for such an investigation was very low.<sup>140</sup> As far as the mechanics of requesting and arranging a clotting test were concerned, Professor Ludlam explained the interaction between casualty and the haematology departments as follows:

The system was that clotting tests came – we get a lot of requests for clotting tests from Accident & Emergency and if one turned up with an unexpected abnormality, as might occur in haemophilia, then that result was reported back to the person who requested it, and our duty registrar was informed and our duty registrar would then use his judgement as to whether or not to follow it up, and certainly if there was a question of a screening test potentially identifying a patient with haemophilia, then he would make sure the Factor VIII and Factor IX levels to start with were measured, and he would go and liaise with the doctor in the Accident & Emergency department.<sup>141</sup>

**22.86** Insofar as the decision about administering any blood products was concerned, Professor Ludlam would expect to have heard himself if a new patient with haemophilia was in casualty – although plainly circumstances might dictate otherwise if, for example, he was unavailable.<sup>142</sup> At first, Professor Ludlam thought that there was no written guidance issued to the casualty department by his department during the period being examined but, on reflection, he recalled that every two or three years, the haematology department met with the casualty department and updated a guidance sheet as to how staff in casualty should respond to a person who presented with haemophilia, or potential haemophilia.<sup>143</sup>

### *Horizontal dissemination*

**22.87** The Haemophilia Centre in Edinburgh was the reference centre for the centres in the east of Scotland, namely Dundee, Aberdeen and Inverness.<sup>144</sup> As reference centres, Edinburgh and Glasgow were part of ‘a UK arrangement for overseeing haemophilia treatment’.<sup>145</sup> In view of this, Professor Ludlam was asked what steps he had taken during this period to give guidance to those treating patients with haemophilia in those other centres. In response, he explained that, prior to the setting up of the Factor VIII working party in 1988:

[T]he centres were much more independent, standalone centres and there was not a great deal of interplay between them. Occasionally I would get a phone call about a difficult patient or something that was causing a difficulty or a problem, but there weren’t regular meetings like there are now, where we meet every two or three months.

<sup>139</sup> Ibid page 71

<sup>140</sup> Ibid pages 73–74

<sup>141</sup> Ibid Page 75. See also pages 78 and 79, for evidence to similar effect.

<sup>142</sup> Ibid page 76. See also pages 82–85.

<sup>143</sup> Ibid page 86.

<sup>144</sup> Professor Ludlam – Day 18, page 3

<sup>145</sup> Ibid page 62

Q. Right. You did use the word “overseeing” but it seems, from what you are now saying, as though, at least in the mid 1980s, it was more of a reactive role. So if somebody phoned you up for advice, you would be happy to provide it?

A. Yes, I think it evolved from being very separate, individual centres until the mid-1980s and, as a result of the development of all these new products and the need to test them, for one reason, brought us together to collaborate more.<sup>146</sup>

**22.88** The guidance document, prepared by Professor Bloom in December 1984, would have been sent to the other east of Scotland centres by the UKHCDO, from Oxford.<sup>147</sup>

**22.89** The Inquiry was interested in how physicians in other hospitals who might have to treat a patient presenting with haemophilia for the first time would have been aware of the most recent guidance. Professor Ludlam suggested that such clinicians would either use their best judgement, or telephone a haemophilia centre known to them.<sup>148</sup>

**22.90** There did not seem to be any system for sending guidance from the UKHCDO to hospitals around the country which were not haemophilia centres but which might suddenly have to deal with a patient who had haemophilia and who was in the midst of a bleed. Professor Ludlam suggested that, had a small child presented to a hospital in the Highlands with a bleed thought to be haemophilia, transfer to Inverness or Glasgow would be ‘the sort of usual [response]’.<sup>149</sup> He thought that, at the time which was being discussed, it would have been possible to get a small child to Inverness or Glasgow within 12 hours. He agreed that physicians in remote locations might not be aware of the most recent guidance on haemophilia, particularly with the centralisation of care which was already happening in the 1980s.<sup>150</sup>

**22.91** It was also put to Professor Ludlam that no-one in Scotland appears to have had the responsibility to change the 1984 guidance as different options became available or as the relative merits of the different products changed. Professor Ludlam thought this was ‘fair comment’, although he also pointed out that this was ‘a very, very confusing period’.<sup>151</sup> As far as general guidance for hospitals all over Scotland was concerned, Professor Ludlam was asked who would have been responsible for providing such advice:

Q. [W]e are thinking about this difficult period and if it were to be thought that it would have been a good idea for somebody to try to make sure that all hospitals in Scotland had some assistance with the current thinking on how to deal with patients with haemophilia presenting for the first time, say, or patients with mild haemophilia who hadn’t had previous exposure to concentrates, the patients who present the particular dilemmas. If it had been thought that it would be a good idea for all the hospitals in Scotland to know what the thinking was, whose job would it have been to make sure that that sort of information is sent round?

A. Well, I suppose it’s a medical policy decision. It perhaps should come from the chief medical officer.<sup>152</sup>

---

<sup>146</sup> Professor Ludlam – Day 54, page 146. See 22.74 regarding the question of when the Scottish directors began meeting as a group.

<sup>147</sup> Professor Ludlam – Day 54, pages 146–147

<sup>148</sup> Ibid page 148

<sup>149</sup> Ibid page 152

<sup>150</sup> Ibid page 153

<sup>151</sup> Professor Ludlam – Day 55, page 111

<sup>152</sup> Ibid page 62

**22.92** Later, when Professor Ludlam was pressed about this, and it was put to him that these were matters of individual clinical judgement, he highlighted the fact that, from time to time, circulars are produced by the health departments to alert physicians to particular situations, for example in the context of infectious diseases. It was suggested to him that there would be limits to what such guidance could offer:

Q. So if you are thinking of guidance from the chief medical officer, for example, I take it you are not thinking that the chief medical officer will say, "In this instance, use cryoprecipitate; in this instance, use Factor VIII concentrate," or are you anticipating that that sort of level of detail would be prescribed from government?

A. It would be very helpful if the chief medical officers would give that advice.<sup>153</sup>

**22.93** It was suggested to Professor Ludlam both that any such guidance would have to have been obtained by the Chief Medical Officer (CMO) from the haemophilia directors anyway, and that there was in existence the guidance document from December 1984. He maintained his position that more guidance from others on therapeutic policy, would have been helpful. Haemophilia doctors felt that the problem was being 'left at our door'. For them to have had some guidance and 'potentially to address some of the issues that we have been thinking about between England and Scotland by ... the chief medical officers ... might have been helpful'.<sup>154</sup>

**22.94** With these comments having been made by Professor Ludlam, those representing the Scottish Government sought and were granted permission to lodge a response from Dr Iain Macdonald, former chief medical officer for Scotland.<sup>155</sup>

**22.95** Dr Macdonald dissented from Professor Ludlam's view as to what was public policy and what was medical policy. In his opinion, it was the responsibility of the medical profession to evolve treatment policies. This was what the Reference Centre Directors were doing in 1984.

**22.96** Dr Macdonald acknowledged that there was a degree of sensitivity about the boundary between public and medical policies. Decisions about issues on which a CMO should write to his medical colleagues in the NHS lay in this sensitive area. There were circumstances in which it was established and accepted practice for CMOs to write to NHS colleagues. There were two broad categories in which this was normally done. These were: the prevention or limitation of the spread of infectious diseases, and the early detection of disease by screening populations at risk.

**22.97** Concerning Professor Ludlam's proposition that a CMO letter outlining clinical matters would have been helpful, Dr Macdonald concluded:

I have to say that if this had been put to me as CMO, I believe that I would have concluded that the introduction of a government department into an essentially clinical matter being handled by UKHCDO would not have been helpful and probably not acceptable. I would therefore have felt bound to decline.<sup>156</sup>

---

<sup>153</sup> Ibid page 126

<sup>154</sup> Ibid pages 126–8

<sup>155</sup> CMO Letters – Comment by Dr Iain S Macdonald [PEN.018.0620], referred to at Day 74 page 109.

<sup>156</sup> CMO Letters – Comment by Dr Iain S Macdonald [PEN.018.0620] at 0622

It therefore appears that the provision of guidance on how to treat a person with haemophilia presenting in an emergency was not seen within the Scottish Home and Health Department (SHHD) as a government responsibility.

**22.98** At the time, it might have been understood that haemophilia centres were willing to provide advice to any clinician in Scotland treating a patient with haemophilia. However, it is not clear how non-specialist clinicians would have become aware of guidance issued by the specialist organisation, the UKHCDO, to assist in dealing with a particular problem or how they would have known that a better product might be available in Edinburgh for previously untreated patients.<sup>157</sup> The latter observation also applies to the period after December 1986, when Scottish product more rigorously heated (at 75°C for 72 hours) was released by PFC for clinical trials; it is not clear that hospitals which were not haemophilia centres, or even those which were but which were not involved in the trial, were informed of the availability of this product.<sup>158</sup>

## Discussion

**22.99** The period covered by this chapter was, on any view, challenging for those concerned with the treatment of patients with coagulation deficiencies. The ‘golden interval’, when the introduction and development of factor concentrates appeared to have been an ‘enormous quantum leap’ in therapy, had come to an end with the ‘years of viral contamination problems’.<sup>159</sup> Transmission of HIV, and the consequences of infection with that virus, and growing appreciation of the risks associated with NANB Hepatitis were dominant issues in the middle years of the 1980s. In the light of later experience and research, it seems clear that the development of heat-treated factor products, introduced in Scotland in December 1984, provided effective protection against the risk of transmission of HIV by PFC’s standard concentrates. It would not, however, be clear for some time to clinicians and others dealing with patients that that was the case. In the meantime, increasing understanding of the natural history of NANB Hepatitis was reflected in growing concerns about the use of those concentrates in routine therapy.

**22.100** In attempting to capture the atmosphere of the period, it is necessary to bear in mind that different groups of medical experts and scientists would have different perceptions of risk and benefit from the use of therapeutic products. In addition, government and regulatory agencies, whether involved centrally or at the periphery of developing thought, would reflect, in their response to emerging knowledge, the understanding of their roles at the time. The clinical independence of the practitioner would have been accorded a higher priority than would be conceivable after the formation of the Scottish Intercollegiate Guidelines Network (SIGN) in 1993.<sup>160</sup> There is a need for caution against an assumption that, in the period with which this chapter is concerned, there were simple and uncontroversial answers to questions about the appropriate therapy to adopt, generally or in particular circumstances. The situation was altogether more complex; there were and are no easy answers.

---

<sup>157</sup> Professor Ludlam – Day 55, page 107

<sup>158</sup> See Chapter 24, *Viral Inactivation of Blood Products for Haemophilia Therapy 1985–1987*, at paragraphs 24.132 to 24.137 for details of these events.

<sup>159</sup> Dr Winter – Day 15, page 73

<sup>160</sup> See paragraph 22.116 for further details.

**22.101** A number of issues were focused in questions to be explored in evidence. The first question dealt with the period between the production and introduction of BPL's product 8Y and the development of PFC's product Z8, and was expressed in these terms:

Given that, with effect from Autumn 1985, the Factor VIII concentrate 8Y, produced in England, was more severely heated than the Scottish product, could a supply of 8Y have been obtained to be held for the treatment of any Scottish patients with haemophilia who had received little or no previous exposure to concentrates and who required treatment before the equivalent Scottish product was available?<sup>161</sup>

It is therefore necessary to examine the position concerning the availability of 8Y for Scottish patients.

### *Supply of 8Y for Scotland*

**22.102** The cross-border supply of therapeutic products for routine use for any class or classes of patients raises issues about the general relationships between Scottish fractionators and the SNBTS on the one hand and English fractionators and the NBTS on the other that are materially different from the transfer of materials for specific or limited use. When an official request was made for a limited supply of 8Y, arrangements were made, subject to conditions. Professor Ludlam was also able to obtain some 8Y from Newcastle, he thought probably on a personal approach to the haemophilia director there.<sup>162</sup> In one sense these two events show that, in absolute terms, it was possible to obtain some supplies of 8Y for use in Scotland.

**22.103** The arrangements for the official supply were made after discussion in England. It is significant that in his letter dated 24 July, Mr Pettet records that he has 'spoken to Dr Lane' about the request. It was not treated as a matter of incidental interest.

**22.104** The position generally was that the SNBTS and the PFC had responsibility for meeting the needs of the NHS in Scotland, and the NBTS and the BPL had responsibility for the needs of the service in England and Wales. How that came about is discussed in Chapter 19, *Production of Blood Products – Facilities*. Distribution of therapeutic products in England and Wales was managed on a basis that recognised that the BPL could not satisfy all domestic demand: the regions received the BPL products in proportion to their provision of raw materials. The shortage was particularly significant in the case of 8Y, at least until production facilities could be expanded. Initially, it was expected that output would meet about one third of current demand for concentrate. The arrangements (apart from the special needs of clinical trials to provide information for product licensing purposes) were that Factor 8Y would be issued through Regional Blood Transfusion Centres, unless special provisions existed by agreement for product to be sent direct to the Haemophilia Centre. Allocations to the BTS were to observe the pro rata requirements for distributions agreed between the BPL and the BTS.<sup>163</sup>

<sup>161</sup> List of issues proposed by Inquiry Counsel, 10 February 2012 [PEN.019.0843] at 0854

<sup>162</sup> Professor Ludlam – Day 55, page 120. The Inquiry subsequently learned that this supply appears to have been arranged via Dr Boulton – see letter of 24 August 1987, [PEN.019.1535]. The letter indicates that Dr Boulton was exploring the possibility of obtaining a regular supply of 8Y from England.

<sup>163</sup> Information Sheet, *Dried Factor VIII Concentrate: High-Purity, Heat Treated*, issued to English and Welsh Haemophilia Directors and Regional Transfusion Directors by Blood Products Laboratory, 24 July 1985 [DHF.003.0476]

**22.105** Haemophilia Centre Directors were asked to identify patients ‘at risk’ (patients who were HTLV III antibody negative and who had no history of hepatitis) as potential recipients of the new product. On 15 August 1985 a DHSS circular explained that output of heat treated product (8Y) at the BPL had been increased to the maximum level possible in the current plant.<sup>164</sup> The letter was circulated in England, Wales and Northern Ireland, but not Scotland.<sup>165</sup>

**22.106** Information about the new product was not available uniformly in Scotland. Dr Foster did not know of the information sheet distributed in July.<sup>166</sup> He knew that BPL started issuing 8Y routinely in September 1985 and not before, but he did not know the stage reached in developments at April 1985.<sup>167</sup> In contrast, Dr McClelland who was a member of the Central Committee for Research and Development in Blood Transfusion, and Dr Forrester who attended as representative of the SHHD had information provided at the Committee’s meeting in 19 December 1985 that Dr Rizza had been trialling the product for about nine months.<sup>168</sup> But it was not suggested that either communicated relevant information to Dr Foster. Dr Foster had his own source of information in Dr Smith, but that related to the scientific and development aspects of the product and not to its availability. For other information he depended on Dr Perry. The impression from this evidence was that Scottish officials received information on a casual basis about the new product. They were not involved, as Scottish officials, in the development and distribution of the product, which was consistent with the territorial division of responsibility, and with DHSS policy related to the distribution of 8Y.

**22.107** There is no evidence that the BPL could have provided a significant supply of 8Y to Scotland for the treatment of previously untreated patients (PUPs) in the period 1985–87, or in any event could have done so without detriment to the interests of English and Welsh patients. Given that 8Y was the only HIV-safe NHS Factor VIII concentrate available from the BPL, routine supplies could only have been made at the expense of English and Welsh patients. The reasonable inference from the arrangements made for distribution of what was a scarce resource is that no such supply could or would have been forthcoming. Dr Smith’s expedient of providing a small quantity as an extension of the trial of the product in England and Wales, and the sequence of steps taken before the request was granted, indicate that the actual supply was an exceptional event. For his part, Professor Cash would not have sought any 8Y. He would not have wanted to take a scarce resource from England and Wales where there were severe difficulties.<sup>169</sup> He thought the haemophilia clinicians might have taken a different view and that they might have considered that there should be an approach to England to obtain some.<sup>170</sup> But the basis for that opinion of the haemophilia directors was not clear.

**22.108** The question is hypothetical: the issue was never tested. But the restrictive conditions on the official supply of the 50 vials, and the further arrangement to obtain supplies from Newcastle, added to the official position of the DHSS on actual supplies, indicate that, on balance, a request by the SNBTS or by individual haemophilia clinicians for a share of the BPL product would not have been successful. Whether some kind of barter or exchange could

<sup>164</sup> DHSS circular [DHF.002.5543]

<sup>165</sup> DHSS internal minute, 15 August 1985 [DHF.002.5542]

<sup>166</sup> Dr Foster – Day 56, pages 50–51

<sup>167</sup> Legal advice to the BPL at that time was to avoid sharing information with the PFC, for intellectual property reasons. Dr Smith – Day 60, pages 62–63.

<sup>168</sup> Minutes of Central Committee for Research and Development in Blood Transfusion, 19 December 1985 [PEN.016.1152]

<sup>169</sup> Professor Cash – Day 157, pages 153–5

<sup>170</sup> Ibid page 156

have been negotiated that might have offered comfort to NBTS Directors adds another layer of speculation. The SHHD or even Scottish Office Ministers might have been asked to intervene with UK counterparts. Possibilities can always be advanced, but it is not possible to conclude that a practicable arrangement could have been arrived at.

**22.109** That is not quite the end of the matter, however, because of the small supply of 8Y (50 vials) which was obtained for Scottish patients in the summer of 1986. As narrated, this was at the behest of Professor Ludlam and the product was not used outwith Edinburgh. Moreover, it appears to have taken place in response to the realisation that a previously untreated patient had contracted NANB Hepatitis from treatment in Edinburgh in May 1986. That this small supply occurred does not demonstrate that a larger quantity could have been obtained. Indeed had the procurement of 8Y been publicised to other haemophilia directors in Scotland, growth in requests for more ad hoc supplies might have been met with refusal. But it is unfortunate that neither the existence of a small stock of product in Edinburgh nor the possibility of obtaining some from England for any previously untreated patient presenting for care seems to have been drawn to the attention of physicians in other areas of the country. Having regard to the way in which arrangements to obtain and store that supply were made, it would have been for the SNBTS, probably through the PFC, with its remit for all of Scotland, to direct attention to this therapeutic option. As Dr Perry himself recognised, he could have written to other Haemophilia Centre Directors and to Regional Transfusion Directors to tell them about the product. It might also have been expected that Professor Ludlam would share information about the supply of 8Y with other haemophilia directors in Scotland.

**22.110** Two other questions were formulated which, in the light of the evidence, are, strictly speaking, superseded. They were (1) whether, if a supply of 8Y could have been obtained for the treatment of Scottish patients with haemophilia who had received little or no previous exposure to concentrates and who required treatment before the equivalent Scottish product was available (other than the small ad hoc supply procured by Dr Perry in the summer of 1986) such a supply should have been procured, and (2) when and by whom should such a supply have been obtained?<sup>171</sup>

**22.111** If it had been possible to conclude that a general supply of 8Y could have been made available, should such a supply have been organised? In the abstract, it certainly appears desirable that a supply of product which seemed likely to offer a greater measure of safety to patients should be achieved. But in practice, the second question, which addresses the mechanics of organising that supply, is more important.

**22.112** There are a number of practical issues that would have arisen if there had been an attempt to convert the hypothesis into reality. Obtaining a national supply would not have been a task for Dr Ludlam: his attention was focused on providing for the needs of patients in or attached to the Edinburgh centre. It appears that it would not have been thought to be within the responsibility of the SHHD or the CMO because they did not interfere in clinical matters. It might have been considered to be within the remit of the SNBTS to procure a supply for Scotland, although it is not clear by whom such an initiative could have been taken. On one view, it would not have been Dr Perry's responsibility to make the request: his sphere of responsibility was the production of NHS concentrates for patients in Scotland. On the other hand, he did envisage that the PFC would have been an appropriate channel for requesting material.

---

<sup>171</sup> List of issues proposed by Inquiry Counsel, 10 February 2012 [PEN.019.0843] at 0854



**22.113** For England and Wales, the DHSS had a role in questions of supply: it appears clearly to have been their decision that restricted the general availability of 8Y to England, Wales and Northern Ireland, and targeting of particularly vulnerable patients was an aspect of that decision. Only the SHHD could have played a role in securing an adjustment of that policy for the benefit of similar vulnerable patients in Scotland.

### *Guidance for treatment of patients*

**22.114** The next question that arose was whether, in the absence of a supply of 8Y to treat patients with little or no previous exposure to concentrates, the general approaches to blood product therapy for haemophilia in Scotland in the period 1985 to 1987 were reasonable.<sup>172</sup>

**22.115** Patient core participants have submitted that there was a failure to make provision for a sophisticated system to identify those who might be previously untreated patients with coagulation issues should they present for medical care (apparently at any level, general practitioner, health centre, or hospital).<sup>173</sup> The general care of patients who have or may have coagulation defects, is not within the Terms of Reference. There was, however, no evidence of a general issue that could have been dealt with systematically. There was no evidence that it would have been practicable to treat every patient who was not already receiving care as a haemophilia patient as potentially suffering from a coagulation defect.

**22.116** Turning to more general questions of what ought to have been available by way of guidance, the objective of SIGN shows that in relation to clinical practice there was soon to be recognised a need for general guidelines. The objective of the organisation is:

The Scottish Intercollegiate Guidelines Network (SIGN) was formed in 1993. Our objective is to improve the quality of health care for patients in Scotland by reducing variation in practice and outcome, through the development and dissemination of national clinical guidelines containing recommendations for effective practice based on current evidence.<sup>174</sup>

**22.117** It is clear that such guidelines are not perceived to threaten and do not threaten clinical independence. Indeed, the initiative for the formation of SIGN came from the Scottish Medical Royal Colleges.<sup>175</sup>

**22.118** At this point, the dilemma confronting haemophilia clinicians continued to be whether to use concentrates although they knew that concentrates exposed the patient to risk of transmission of hepatitis viruses. As knowledge of the natural history of NANB Hepatitis developed, the balance in perception of risk/benefit inevitably changed. On one side of the equation, the natural history of haemophilia remained as it always was: the risk of bleeding that could extend to fatal bleeding into the gut or brain, and, short of that, could lead to the development of disabling disease of the joints, among other consequences. Haemophilia remained a serious and often life-threatening condition requiring treatment.

<sup>172</sup> List of issues proposed by Inquiry Counsel, 10 February 2012 [PEN.019.0843] at 0854

<sup>173</sup> Patient interest core participants: Submissions for the C3A Topic [PEN.019.0657] at 0657–59

<sup>174</sup> Health Improvement Scotland (2013), <http://www.sign.ac.uk/about/introduction.html> Last accessed 13 May 2013.

<sup>175</sup> McAlister G, The Scottish Intercollegiate Guidelines Network (SIGN), *Guidelines in Practice*, Vol 4, No 10. [http://www.equidelines.co.uk/equidelinesmain/gjp/vol\\_4/oct\\_01/macalister\\_sign\\_oct01.htm](http://www.equidelines.co.uk/equidelinesmain/gjp/vol_4/oct_01/macalister_sign_oct01.htm) last accessed 17 June 2014.

**22.119** Against that background, it would be reasonable to suggest that the clinician would use the least damaging product that was available to him or her for effective treatment of the particular manifestation of the underlying disease that the patient was experiencing at the time.

**22.120** That appears, generally, to have been the approach reflected in the guidelines, dated 14 December 1984, prepared by Professor Bloom and sent to Regional Directors: *Haemophilia Centre Directors Organisation AIDS Advisory Document*.<sup>176</sup> Although expressed primarily as guidance related to AIDS, then the most significant threat envisaged, it was more general in its approach. Available therapeutic materials were listed in order of safety, and the risk of NANB Hepatitis was specifically mentioned. The UKHCDO view was expressed that bleeding was the commonest cause of disability and death, and that concentrate was still needed. The use of DDAVP was recommended in appropriate cases. And where concentrates were needed, advice was tendered as to the priorities to be observed.

**22.121** It was reasonable for haemophilia clinicians to follow this guidance in practice. Professor Lowe said that the advice was followed in Glasgow. Professor Ludlam based his practice in Edinburgh on the advice. So far as that advice was followed, it provided a reasonable underpinning of clinical practice in Scotland. The evidence of Professor Ludlam and of Professor Lowe that the policy of their respective centres was to follow the UKHCDO advice is accepted.

**22.122** However, that led inevitably to a question whether the arrangements for the dissemination of general guidance to clinicians regarding haemophilia treatment during this period were satisfactory.

**22.123** In some respects this is the more fundamental question. There may be little point in a small number of senior clinical consultants knowing a system, including any guidelines incorporated in it, if (a) their associates and subordinates and (b) clinicians outwith a narrow core of specialists (of which those senior clinical consultants are the characteristic members) do not know of the guidance and are not equipped to follow it.

**22.124** There has to be a mechanism within a system of practice that ensures, so far as reasonably practicable, that guidance is disseminated as required to inform all practitioners likely to be called on to minister to patients' needs, and that ensures appropriate compliance with what is regarded as best practice from time to time. No system can anticipate, far less resolve, all of the issues that may arise in clinical practice. As Professor Ludlam observed, an over-prescriptive system that stipulated for the use of DDAVP in treating a mildly affected haemophilia patient would be counter-productive in the case of a patient who had had a serious road traffic accident. Emergencies will always demand ad hoc decisions adapted to patients' needs. A clinician faced with a patient in extreme pain may prescribe treatment that would normally be contrary to recommended practice if satisfied that the course is necessary to secure the patient's safety, for example, and nothing else is available. However, in this as in other circumstances, elaboration of exceptions tends to underline the need for the basic rule.

---

<sup>176</sup> *Haemophilia Centre Directors Organisation AIDS Advisory Document*, 14 December 1984 [SGF.001.2388]

**22.125** Two questions arise: were there basic guidelines, and who was responsible for disseminating them? Looking at the needs of Scotland as a whole, there clearly were not basic guidelines for general application. The UKHCDO guidelines prepared by Professor Bloom were addressed to a particular group of recipients who could be expected to understand the complex background and to be familiar with the issues implicit in the advice given. They were not designed for, and would have been less easily understood by, a general practitioner holding an occasional clinic in a remote cottage hospital. In one of the two instances of which the Inquiry has notice, an island hospital held a supply of PFC factor concentrate. Other outlying units might well have held such therapeutic materials. The need for guidance seems obvious – even if only to alert non-specialist physicians to the dilemmas arising in therapeutic decisions at this time, and the need to take advice.

**22.126** The need for guidance extends beyond directions on reconstituting or otherwise preparing therapeutic materials for use. Taking a patient’s informed consent to the use of therapy requires that the clinician is equipped with information on the risk/benefit balance of the use of the particular product, and both understands and has the advice necessary to communicate relevant issues to the patient.

**22.127** These issues were probably not peculiar to haemophilia – they must have been relevant to other chronic conditions as well. The needs of small local hospitals or GPs in remote areas had to be considered and they should have been kept ‘in the loop’ of thinking. On the evidence available to the Inquiry, there was no such guidance.

**22.128** This was a period in which there was increasing understanding that it was almost certain that patients treated for the first time with factor concentrates, or with little previous exposure, would be exposed to NANB Hepatitis infection on first receiving an infusion of any concentrate other than those most severely heat treated. There was a clear need for central direction and advice on the approach properly to be adopted to the use of available products and the implications for patients of their use.<sup>177</sup>

**22.129** By today’s standards, the arrangements appear very vague. Relying heavily on observations by Professor Thomas, the patient interest core participants have submitted:

The evidence available to the Inquiry suggests ... that little formal structure existed to ensure that important information and opinions about the risks of transmission of NANB hepatitis to uninfected patients, the known severity of the disease, what treatment options were available and how treatment decisions might be affected by this information was conveyed clearly and efficiently to anyone other than the most senior staff at Scottish haemophilia reference centre[s] (ie Edinburgh and Glasgow). In particular there would seem to be little evidence of formal efforts being made to communicate any such information to junior staff or to hospitals where such treatment decisions may have to be made outwith these main centres.<sup>178</sup>

**22.130** The vertical dissemination of information within hospitals is discussed below. Otherwise, the submission is generally well founded. It is not appropriate to place as much reliance on the evidence of Professor Thomas in this regard as is set out in the patient core participants’ argumentation in support of the submission: he was not and is not a

---

<sup>177</sup> Patient interest core participants: Submissions for the C3A Topic [PEN.019.0657] at 0663–64

<sup>178</sup> Ibid [PEN.019.0657] at 0670–71

haemophilia clinician and this was not his field.<sup>179</sup> But these points do not detract from the general validity of the submission.

**22.131** There was no guidance from central government agencies, from the SHHD or the CMO. Irrespective of whether departmental involvement in the content of such guidance would have been appropriate,<sup>180</sup> it is unsatisfactory that the only facilities equipped with guidance were haemophilia centres, which had the material distributed by the UKHCDO. Patients with haemophilia needing emergency treatment could present at any casualty department in the country. Representatives of the SHHD were involved as members of or as in attendance at meetings of representatives of clinicians, scientists and medical members of the SNBTS. If it were accepted that it was inappropriate for them to participate in or guide discussion,<sup>181</sup> they nevertheless remained a conduit for the communication of information to government and had a distinct role in advising on the financing of research and development across a broad front. It would have been for the SHHD to arrange for the distribution of guidance to the NHS in Scotland as a whole. There was already a precedent for government involvement in delivery of haemophilia care in England and Wales in the shape of a DHSS Circular Family Practitioner Notice addressed to general medical and dental practitioners in January 1976, concerning revised arrangements for the care of persons suffering from haemophilia and related conditions.<sup>182</sup> According to that Notice, the functions of haemophilia centres included giving advice to general practitioners about the emergency treatment of haemophilia patients on their list. This Notice was appended to a DHSS Health Circular dated February 1976, addressed to Regional Health Authorities and Family Practitioner Committees for action, and to Area Health Authorities and Boards of Governors for information.<sup>183</sup> Whilst the Notice does not appear to have been formally circulated in Scotland, it was referred to and appears to have reflected the arrangements for haemophilia care in Scotland as well as in England and Wales.<sup>184</sup> It was, in any event, an indication of what was thought appropriate for a central government department to do in the field of haemophilia care. Although the 1976 document was a Circular and not a CMO letter, it did specify what sort of care was to be provided by a haemophilia centre and by a reference centre. Moreover, the need for a haemophilia centre to provide guidance to general practitioners on the emergency care of patients with haemophilia was specifically referred to. It did not mention providing guidance to ‘local’ hospitals, which might also be required to provide emergency care and, in that regard, may have been incomplete. But it illustrates a desire on the part of central government to establish and maintain a coherent system for the provision of care for people with haemophilia.

**22.132** In another context, the Inquiry has noted the intervention of Dr Yellowlees, CMO, England and Wales, in May 1975 in a debate over the collection of blood donations in prisons, a matter otherwise considered to be within the responsibility of Regional Transfusion Directors.<sup>185</sup>

<sup>179</sup> Professor Thomas’s evidence at Day 52, pages 155–163 is general and rather second hand.

<sup>180</sup> The appropriateness of involvement was disputed by the Scottish Government in its closing submissions [PEN.019.0274] at 0278 and 0335

<sup>181</sup> As was submitted by the Scottish Government in its closing submissions PEN.019.0274 at 0278 and 0335

<sup>182</sup> Family Practitioner Notice FPN 105 (HC(76)4) *Organisation of Haemophilia Centres* January 1976 [DHF.002.4280]

<sup>183</sup> Health Circular HC(76)4 *Arrangements for the care of persons suffering from haemophilia and related conditions*, and accompanying memorandum February 1976 [DHF.001.2747] and [DHF.002.4280]

<sup>184</sup> See references for example in minutes of meeting of Reference Centre Directors on 1 March 1982 [LOT.003.2907] at 2908 and in minutes of joint meeting of Haemophilia Centre Directors, SNBTS Directors and SOHHD on 12 May 1994 [LOT.003.1908] at 1913

<sup>185</sup> See Chapter 26, *Donor Selection – Higher Risk Donors*, paragraphs 26.79 to 26.80

**22.133** Efficient and effective provision for the care of vulnerable populations such as those with coagulation deficiencies is not a matter that should depend on narrow definitions of departmental or agency competency or their individual remits: responsibility rests ultimately with government as a whole. Ministers control budgets, subject to Parliamentary oversight. Whoever proposes, Ministers dispose in the funding of work in the national health sector. As a practical matter, the overall shape of the service, as distinct from clinical care of a particular patient, is the responsibility of central government departments and associated agencies. That responsibility shifts among departments and agencies as circumstances demand: there are few immutable principles that dictate current competencies and provide insuperable barriers to the resolution of issues affecting public health. Nor should there be. Any doubts about the competency of the health departments to issue guidance in this particular area would have been resolved had a challenge arisen.

**22.134** The second aspect of this question relates to vertical dissemination of advice and instruction. It arises on the hypothesis that a particular hospital or other operating division of the service has available sources of advice and information at some, typically senior, level, and the question focuses on the approach adopted to the dissemination of that information and advice down through the particular organisation or part of the organisation concerned with immediate patient care.

**22.135** The patient interest core participants submitted in this regard that:

- Minimally treated patients included those who had received treatment in the past for their bleeding disorder, but not with factor concentrates or with large volumes of cryoprecipitate.
- The treatment of virgin and minimally treated patients over this period merited special consideration by treating doctors on the basis that (a) the state of knowledge was such that it was highly likely if not certain that they would be infected with a potentially lethal disease if treated with the then available Scottish factor VIII concentrate (NY) and (b) it was probable that such patients would not yet be infected with that disease.
- The then available Scottish factor VIII concentrate should not have been given to virgin or minimally treated patients over this period unless it was unavoidable.
- The priority in the treatment of bleeding episodes in such patients should have been to try to achieve haemostasis with other treatments which carried less of a risk of transmission of NANB hepatitis, such as DDAVP (for mild patients) or cryoprecipitate or alternative products sourced outside Scotland before resorting to the use of SNBTS factor VIII concentrate.<sup>186</sup>

**22.136** The third point is well made, against the background of the narrative in the first and second points, since it appears to recognise the need for clinical judgement. The fourth point is over-prescriptive and inappropriate. It is not for this Inquiry, nor would it have been appropriate for any general guidance, to dictate an order of treatment relating to the patient's underlying coagulation deficiency without regard to the circumstances requiring medical attention. Professor Ludlam's evidence relating to the use of DDAVP to treat a patient with a mild coagulation disorder following severe trauma, already referred

---

<sup>186</sup> Patient interest core participants: Submissions for the C3A Topic [PEN.019.0657] at 0678

to, illustrates that conclusively. However appropriate for routine purposes, DDAVP would be wholly inappropriate for a patient who was bleeding severely after a road traffic accident.

**22.137** Professor Ludlam gave evidence about the arrangements in his department in Edinburgh. For present purposes this is but one example, and as such illustrates what could happen during the material period.

**22.138** It is, however, difficult to derive a clear picture of the situation in Edinburgh at that time. Professor Ludlam's evidence frequently consisted of informed speculation about what would have been the position or must have been the position, without direct recollection of events as they happened. This perhaps followed necessarily from the passage of time and the lack of contemporaneous records and forms that might have been in use. The unsatisfactory nature of the evidence can best be illustrated by his change in position relating to written guidance to casualty staff on handling patients with haemophilia or potential haemophilia. He clearly had thought about his evidence after the first occasion on which he spoke of this subject, and, with the benefit of that, he changed position. It can be accepted that his revised evidence is reliable. But it does not resolve all difficulty. According to his revised evidence, there was a meeting every two to three years between haematology and casualty officers to update the guidance sheet issued from haematology. At any one time, therefore, almost three years might have elapsed since the guidance was last updated. During the period with which this chapter is concerned, the emphasis on seeking advice from the haemophilia clinicians or the haematology department generally would have been expected to have changed. The need to involve specialists to ensure an appropriate selection and use of coagulants would have required greater emphasis.

**22.139** Within his department, Professor Ludlam conducted weekly tutorial sessions. That was an appropriate course of action. But it might best have been supported by notes for reference in the course of clinical practice. Reliable recollection of what is said at such sessions cannot be assumed generally, and certainly cannot be assumed in the context of an anxious response to the needs of a patient who might be in extreme need of immediate therapy. More precise protocols, including a requirement to refer issues to senior colleagues for definitive advice, would have been desirable. Without written guidance, there was inevitably a risk that junior staff, who might be satisfied that they knew the correct course of action, might act in a way that was inconsistent with the views of more senior colleagues.<sup>187</sup>

**22.140** As observed by the patient interest core participants,<sup>188</sup> it is implicit in Professor Ludlam's evidence that it would have been beneficial (for him) to have had guidance from the CMO or government department, and that it would have been at least as beneficial for clear guidance to have been provided in turn for more junior members of his department.

**22.141** The patient interest core participants have made a specific submission in these terms:

[I]nadequate steps were taken in light of the infection of a virgin patient in May 1986 in Edinburgh with NANB hepatitis to avoid a re-occurrence of this infection in similar patients around Scotland.<sup>189</sup>

---

<sup>187</sup> It is odd that there was no update of UKHCDO guidance between December 1984 and May 1988. But that would not bear on the need in Scotland to reflect in guidance changing knowledge of the effectiveness and relative infectivity of products.

<sup>188</sup> Patient interest core participants: Submissions for the C3A Topic [PEN.019.0657] at 0679

<sup>189</sup> Ibid [PEN.019.0657] at 0689

**22.142** As previously observed, the Inquiry had notice of two cases of transmission of NANB hepatitis to previously untreated patients in the relevant period, 1 September 1985 to 30 June 1987. There was no evidence available to the Inquiry of transmission of infection other than in the two known cases. It is not within the Inquiry's Terms of Reference to investigate specific cases other than as required to illustrate or inform general discussion. But the circumstances in which these patients were treated (one at night, without the involvement of the most senior haemophilia clinicians and the other in a remote part of Scotland) are precisely the sort of situations in which the need for up-to-date written guidance on the risks of NANB Hepatitis and the relative risks and benefits of the therapeutic products available was most pressing.

## **Conclusions**

### *Availability of 8Y*

**22.143** The distribution of 8Y in England, Wales and Northern Ireland was strictly controlled under agreements between the BPL and the NBTS that provided for distribution of finished products pro rata to regions' supplies to the BPL of raw materials for fractionation.

**22.144** It cannot be concluded on the evidence available that a barter or other arrangement could have been negotiated that might have procured a supply of 8Y for use in Scotland in exchange for reciprocal supplies of PFC products.

**22.145** For these reasons, it is highly unlikely that regular supplies of 8Y would have been made available for use in Scotland.

**22.146** It is the case, however, that BPL 8Y appears to have been available for use in Scotland on request in very limited quantities in exceptional circumstances at least from the middle of 1986.

**22.147** A request for 8Y to treat a Scottish patient with haemophilia who had received little or no previous exposure to concentrates and who required treatment before the equivalent Scottish product was available was likely to have been successful if treated as part of the field trial of the product or if made ad hoc to satisfy particular and specific requirements of the patient's management acceptable to the BPL and the NBTS.

**22.148** Once the arrangement for limited supplies of 8Y had been made in the summer of 1986 at the initiative of Professor Ludlam, no steps were taken to inform medical practitioners, in particular haemophilia treaters, that supplies of BPL 8Y might be procured even on a limited basis. There was accordingly a failure to provide information that could have informed clinicians of the possibility of obtaining access to the product in appropriate circumstances.

**22.149** In addition, no steps were taken to draw to the attention of physicians outwith Edinburgh the fact that there was already a small stock of 8Y held there.

### *Blood product therapy in Scotland: 1985–87*

**22.150** UKHCDO's guidelines, dated 14 December 1984 and distributed as the 'Haemophilia Centre Directors Organisation AIDS Advisory Document', provided reasonable guidance for haemophilia clinicians to follow in practice in this period.

**22.151** Those guidelines were distributed to Haemophilia Centre Directors. They were followed in Glasgow and Edinburgh, and probably at other Regional Haemophilia Centres with haemophilia directors.

**22.152** There is, however, no evidence of the distribution of any guidance to practitioners in hospitals in Scotland which did not have haemophilia centres, who might find themselves dealing with a person with haemophilia in an emergency, on the use of blood products in coagulation disorder therapy.

**22.153** It would have been the responsibility of the SHHD to have arranged for the provision of appropriate guidelines, probably in consultation with the UKHCDO and the Scottish haemophilia clinicians.

**22.154** There is no substance in the suggestion that the issue of such guidelines by the SHHD would have infringed clinical independence in the management of individual patients.

**22.155** Although guidelines for the service as a whole were less common in the period 1985–87 than they subsequently became, the principle of departmental guidance concerning the system of care for patients with haemophilia was established by 1976.

**22.156** Guidance within institutions was a matter for the senior clinician in charge of haemophilia care and patient management.

**22.157** Such guidance, in writing, was necessary, and it was necessary for it to be amended and updated as information available about therapeutic products, their effectiveness and likely side-effects changed with developing knowledge of the diseases to be treated.

**22.158** Scottish Haemophilia Directors had no administrative authority to impose an obligation on each other or on clinicians in charge of haemophilia care in general hospital units to follow any such written guidance.



## CHAPTER 23

### VIRAL INACTIVATION OF BLOOD PRODUCTS FOR HAEMOPHILIA THERAPY UP TO 1985

#### Introduction

**23.1** It had been known, internationally, since the mid-1940s that transfusion of blood and blood products carried a risk of transmission of infectious agents.<sup>1</sup> Identification of the agents giving rise to risk, and understanding of the natural history of infections resulting from transmission developed over time. The general nature of the risk was understood by fractionators when coagulation factor concentrates were developed in their modern form in the early 1970s.

**23.2** This chapter examines the efforts of the Protein Fractionation Centre (PFC) in Edinburgh, in the period up to 1985, to inactivate viruses (initially hepatitis viruses and later HIV) which were present in its Factor VIII and Factor IX concentrates in this period. It describes how scientific, technical and practical difficulties in bulk production of Factor VIII and Factor IX concentrates were overcome, enabling the PFC to introduce heat-treated Factor VIII concentrate in December 1984 that was effective in controlling transmission of HIV, with more stringent heat-treating protocols developed thereafter, and heat-treated Factor IX concentrate – HT-DEFIX – in May 1985. Inactivation of the Hepatitis C virus is discussed in Chapter 24, *Viral Inactivation of Blood Products for Haemophilia Therapy 1985–1987*.

**23.3** Superficially, the problems related to viral contamination of blood and its derivatives and viral inactivation of blood products can be expressed simply. Blood (and specifically blood plasma) can be a vector for human viruses, and can result in blood products manufactured from such plasma also being infective.<sup>2</sup> The aim behind viral inactivation is to remove or destroy such viruses – using heat, chemicals, radiation, or a combination of these – and so to make blood products safe for human use.

**23.4** However, inactivating viruses in blood products proved to be extremely complex, scientifically, technically and on a practical level. Blood is chemically complex, as are the viruses it harbours. Technical issues can and did arise in ensuring that the active element in a blood product (for example Factor VIII) was not also destroyed or damaged along with any virus. The inactivation of viruses can also increase the cost of a product – making it economically unattractive – and can impact negatively on the resultant yield.<sup>3</sup> These factors can affect the likelihood that demand for a given product can be met. In addition, where a virus has yet to be identified, it can be difficult to establish with certainty that a given inactivation process has been successful. As discussed in this chapter, the PFC was confronted by these and other practical issues when attempting to inactivate non-A, non-B (NANB) Hepatitis and HIV in the period up to 1985.

---

<sup>1</sup> Maunsell, 'Transmission of hepatitis during blood transfusion', *British Medical Journal*, 1 December 1945; 783 [LIT.001.0246]

<sup>2</sup> As explained elsewhere in this Report, the risk of infectivity rises where large plasma pools are used as the source material for a given blood product.

<sup>3</sup> In the case of Factor VIII, the amount of Factor VIII activity recovered from a given quantity of frozen plasma.

## Historical background

### *Albumin*

**23.5.** The Cohn fractionation process was a key step in the manufacture of human blood products. An important goal behind Cohn's research was to develop a product which could act as a substitute for human plasma in the treatment of wartime casualties.<sup>4</sup> Albumin provided the solution. It was crucial that albumin for military use remained stable ('undenatured' in technical terms) under battlefield conditions. According to John Edsall, who was involved in Cohn's original research:

We knew that the albumin would be sent all over the world, including regions of intense heat such as the north African desert or the southwest Pacific. It had to remain undenatured by exposure to heat for months, indeed for years, if it was to serve its purpose.<sup>5</sup>

**23.6** Human plasma proteins tend to become damaged and lose effectiveness when temperatures are raised, and this presented a practical problem. As outlined in Dr Peter Foster's paper on heat treatment:

Human proteins in their natural state exist at body temperature and are prone to damage at raised temperatures. Proteins removed from their natural environment may be even more susceptible to heat induced damage, either from heat directly or from an increase in the activity of substances, such as enzymes, which can degrade proteins. Heat causes proteins to denature and become insoluble (e.g. cooked vs. uncooked egg white) and can occur at modest temperatures, well below the boiling point of water, with different proteins differing in their ability to withstand heat.<sup>6</sup>

**23.7** Research into techniques for improving the ability of albumin to withstand heat led to the discovery by Dr J Murray Luck in 1944 that the addition of chemicals known as 'stabilisers' could enhance albumin's thermal stability with the result that it could be heated for a longer period at a higher temperature before breaking down.<sup>7</sup> Further research focused on destroying bacterial contaminants. This work showed that pasteurisation (heating in solution) was possible and an albumin product which was pasteurised for 10 hours at 60°C was introduced in the USA from June 1945.<sup>8</sup> While albumin was the principal application of pasteurisation, other proteins, Antithrombin 3 and Factor XIII were also pasteurised with appropriate stabilisers.<sup>9</sup> Pasteurisation as a process was not specific to these applications in the pharmaceutical industry. It was established technology in the food industry where it was necessary to reduce or remove microbiological contaminants (for example in milk).<sup>10</sup>

---

<sup>4</sup> SNBTS Briefing Paper on the Development of Heat Treatment of Coagulation Factors [PEN.013.1309] at 1319

<sup>5</sup> Edsall, 'Stabilization of serum albumin to heat, and inactivation of the hepatitis virus', *Vox Sanguinis*, 1984; 46:338–340 [SNB.008.5701]

<sup>6</sup> SNBTS Briefing Paper on the Development of Heat Treatment of Coagulation Factors [PEN.013.1309] at 1319

<sup>7</sup> Edsall, 'Stabilization of serum albumin to heat, and inactivation of the hepatitis virus', *Vox Sanguinis*, 1984; 46:338–340 [SNB.008.5701]

<sup>8</sup> Dr Foster – Day 41, page 60

<sup>9</sup> Dr Smith – Day 59, pages 47–49

<sup>10</sup> Dr Perry's statement on viral inactivation to 1985 [PEN.012.1759] at 1763–64

**23.8** Awareness that hepatitis could be transmitted by transfusions of blood plasma was, in Dr Foster's view, the reason for Dr Edwin J Cohn recommending studies to assess whether 'serum hepatitis' (blood-borne hepatitis) could be transmitted by albumin which had been pasteurised for 10 hours at 60°C (or whether other heating conditions were needed).<sup>11</sup> These studies involved treating patients with heat-treated albumin which had been spiked with, or derived from, plasma which was known to be infected with hepatitis. The results suggested that pasteurised albumin did not transmit blood-borne hepatitis virus(es).

**23.9** Further studies in the 1970s, following the discovery of the Hepatitis B virus, demonstrated, firstly, that the Cohn fractionation process itself physically removed most of the Hepatitis B virus from albumin before pasteurisation. Albumin was produced from Fraction V, the final stage in the fractionation process. Virus in the source plasma was removed differentially at the successive stages of the process, reducing the virus load before the application of heat. Secondly, it was discovered that pasteurisation alone was insufficient to destroy the Hepatitis B virus. It was the combination of fractionation and pasteurisation which was effective in inactivating the Hepatitis B virus in the albumin solution.<sup>12</sup>

**23.10** By the 1970s the combination of cold ethanol fractionation and pasteurisation for 10 hours at 60°C was thought to be effective in inactivating hepatitis in albumin. There had been only one documented example of a Hepatitis B outbreak connected to the production of albumin and this was shown to have related to the incorrect bulk pasteurisation of the product, Plasma Protein Fraction (PPF), rather than to any inherent defect in the established heating protocol.<sup>13</sup> PPF was albumin of slightly reduced purity. Given its apparent safety, pasteurisation for 10 hours at 60°C became the recommended procedure for the treatment of albumin.<sup>14</sup>

**23.11** By the time the Hepatitis C virus (HCV) had been identified in May 1988, it was recognised that the most promising approach to the reduction of transfusion-associated disease was the combination of biophysical removal and biochemical inactivation of virus.<sup>15</sup> The characterisation of the Hepatitis C virus was incomplete, however, and it was not possible to culture the virus. But enough was known to enable the identification of viruses sufficiently similar in structure for experimental purposes. It became possible to carry out experiments which tested the degree to which the Cohn fractionation procedure and pasteurisation physically removed and/or inactivated Hepatitis C in various blood products using similar 'model' viruses as proxies for Hepatitis C.<sup>16</sup> The procedure followed was to spike product with virus and to test by assay the degree to which the virus had been removed by fractionation or destroyed by heat treatment (so-called 'validation studies').<sup>17</sup> These studies had various strands, but the key conclusions were as follows:

<sup>11</sup> SNBTS Briefing Paper on the Development of Heat Treatment of Coagulation Factors [PEN.013.1309] at 1319 and Dr Foster – Day 41, page 63

<sup>12</sup> SNBTS Briefing Paper on the Development of Heat Treatment of Coagulation Factors [PEN.013.1309] at 1320

<sup>13</sup> Professor van Aken's report on Stable Plasma Protein Solution and the transmission of HCV [PEN.001.0306] at 0307; Professor van Aken – Day 2, pages 47–49; SNBTS Briefing Paper on the Development of Heat Treatment of Coagulation Factors [PEN.013.1309] at 1321

<sup>14</sup> Dr Foster – Day 41, pages 64–65 and SNBTS Briefing Paper on the Development of Heat Treatment of Coagulation Factors [PEN.013.1309] at 1321

<sup>15</sup> Alter et al, 'Photochemical decontamination of blood components containing hepatitis B and non-A, non-B virus', *The Lancet*, 24/31 December 1988; 1446–50 [LIT.001.3984]; Chapter 16, *Knowledge of Viral Hepatitis 3 – 1986 Onwards*

<sup>16</sup> See Professor van Aken – Day 2, pages 29–33 for a discussion of culturing and the use of model viruses.

<sup>17</sup> For more information on virus spiking and Hepatitis C see Professor van Aken's report on Stable Plasma Protein Solution and the transmission of HCV [PEN.001.0306] at 0307

- The Cohn fractionation process did not lead to the Hepatitis C in the original plasma being spread evenly among the resulting protein fractions. Most Hepatitis C was to be found in cryoprecipitate. The least amount was found in the fractions from which albumin is derived.<sup>18</sup>
- Pasteurising albumin for 10 hours at 60°C inactivated Hepatitis C and HIV to a level which could be considered safe.<sup>19</sup>

**23.12** Work on heat-treating albumin highlighted the vulnerability of human plasma proteins to damage when temperatures are raised, but also demonstrated that chemical stabilisers could be used to protect proteins from the effects of heat. In addition, it was demonstrated that the effectiveness of fractionation, with or without viral inactivation, to remove or eliminate virus infection could be tested by validation studies using model viruses. These factors came to be of general relevance as research into viral inactivation of blood products progressed.

### *Factor concentrates*

**23.13** Although using chemical stabilisers to pasteurise albumin for 10 hours at 60°C was regarded as successful in inactivating the hepatitis virus, it was widely understood that this approach could not simply be replicated for coagulation factors.<sup>20</sup> Dr Foster's views on the position reached at the beginning of the 1980s are summarised briefly at the end of Chapter 20, *Haemophilia Therapy – The Period up to the Early 1980s*. It is necessary to discuss them in greater detail. The coagulation factors are more 'heat labile' than albumin. They are more easily destroyed or damaged by heat.<sup>21</sup> Finding chemical stabilisers capable of protecting factor concentrates against heat sufficient to inactivate viruses was not straightforward.

**23.14** As noted in Chapter 20, *Haemophilia Therapy – The Period up to the Early 1980s*, among other reasons, Dr Foster's views were influenced by early SNBTS research that had provided evidence to support the generally accepted view that Factor VIII was temperature sensitive.<sup>22</sup> Collaboration with Dr Alan Johnson, New York University, during the 1970s, included development of the PFC's intermediate purity Factor VIII concentrate. One aspect of this research related to the filtration of the final solution to remove impurities. A very fine membrane filter (0.22 micrometre) was used, with the solution at a temperature of 20°C. This was found to lead to a loss of Factor VIII activity. Dr Johnson suggested raising the temperature of the solution to increase solubility and speed up filtration. The manufacturing process was changed: the temperature at filtration was raised from 20°C to 30°C. There was an even greater loss of activity. According to Dr Foster:

These observations confirmed that factor VIII activity could be destroyed by even a modest increase in temperature and it seemed inconceivable that factor VIII could be heat treated at a temperature high enough to eliminate the risk of hepatitis transmission.<sup>23</sup>

<sup>18</sup> Professor van Aken – Day 2, pages 35–39; Yei S et al, 'Partitioning of hepatitis C virus during Cohn-Oncely fractionation of plasma', *Transfusion*, 1992; 32/9 [LIT.001.3218] at 3221

<sup>19</sup> Professor van Aken – Day 2, pages 44–45

<sup>20</sup> See above at 23.7

<sup>21</sup> Dr Foster – Day 41, pages 64–65; SNBTS Briefing Paper on the Development of Heat Treatment of Coagulation Factors [PEN.013.1309] at 1321

<sup>22</sup> Dr Foster – Day 41, pages 87–89; SNBTS Briefing Paper on the Development of Heat Treatment of Coagulation Factors [PEN.013.1309] at 1339–40

<sup>23</sup> SNBTS Briefing Paper on the Development of Heat Treatment of Coagulation Factors [PEN.013.1309] at 1340

**23.15** In his witness statement Dr James Smith expanded on this point. Factor VIII is a much larger molecule than albumin, a relatively small protein. Because of its size and complexity, Factor VIII is possibly the worst candidate among coagulation factors for heat treatment. Factor VIII activity requires that the entire molecule retain its structure intact. Bonds in the molecule are easily broken by heat. Enzymes in plasma also destroy activity. Calcium, on which the integrity of the molecule depends, is readily removed by some of the solutions used in processing. Processing had to be as fast and cold as possible. It did not come naturally to a fractionator, used to handling Factor VIII with extreme sensitivity ('with kid gloves' in Dr Smith's words), to place a dry preparation into an oven at 80°C or to place a solution in a water bath at 60°C. Dr Smith added:

Unlike albumin, there is no fortunate short-cut to protecting Factor VIII (and most other plasma proteins) against heat. They need to be protected by high concentrations of salts, amino acids or sugars, at far higher than physiologically-tolerable concentrations. These protectants then have to be removed in later stages which can be quite demanding and likely to lose yield. It transpires that for Factor VIII, the preferred protectants are sugars and glycine, which at the high concentrations used make a sticky solution, difficult to work with at large scale. Even after pasteurisation, the common methods for recovering a small amount of protein from a large volume of viscous liquid were challenged to the limit in the early 1980s. In addition, these post-heating manipulations must be done in an expensive, controlled environment to avoid recontamination; there is no question of pasteurising in the final container.<sup>24</sup>

**23.16** Dr Smith said that fractionators resisted almost viscerally the application of high temperature to Factor VIII.<sup>25</sup> It is important to emphasise the implications of some of the points made. Protectants were essential in the course of heat treatment, but at concentrations that required their separation from the Factor VIII proteins after heating. It was not possible, therefore, to pasteurise the final freeze-dried Factor VIII product in vial. If freeze-dried Factor VIII was to be heat-treated to inactivate virus contamination, it would require significantly different technology from pasteurisation.

#### *Other obstacles to early progress with virus inactivation of factor concentrates*

**23.17** In addition to the challenges of heat treatment, in the period up to 1980 various other obstacles lay in the path of successfully inactivating viruses in factor concentrates.<sup>26</sup> There was a lack of common understanding of the problem of virus transmission. Dr Smith drew a distinction between haemophilia clinicians and patients on the one hand and fractionators on the other in this period.<sup>27</sup> Whether or not his assessment of the position was correct or fair, he had a clear perception that those concerned with the manufacture of therapeutic products had a distinctive appreciation of the risks of transmission of virus infection. As he saw it, there was little pressure from clinicians and patients to take viral hepatitis seriously in this period. The view that NANB Hepatitis could have severe long-term consequences was not widely held. (As discussed in Chapter 15, *Knowledge of Viral Hepatitis 2 – 1975 to 1985*, the risk of progression to serious disease was not generally

<sup>24</sup> Dr Smith's statement on viral inactivation to 1985 [PEN.012.1551] at 1568–69

<sup>25</sup> Dr Smith's statement on viral inactivation to 1985 [PEN.012.1551] at 1567

<sup>26</sup> For these and other obstacles identified, see: Dr Smith's statement on viral inactivation to 1985 [PEN.012.1551] at 1567; SNBTS Briefing Paper on the Development of Heat Treatment of Coagulation Factors [PEN.013.1309] at 1323–24; and Professor van Aken's statement on the introduction of dry heat treatment of Factor VIII concentrate [PEN.012.1932] at 1932

<sup>27</sup> Dr Smith's statement on viral inactivation to 1985 [PEN.012.1551] at 1554

appreciated until the second half of 1985.) By 1980, the risk of Hepatitis B transmission was thought to have been tamed by donation testing, and it was expected that a vaccine would soon be available. He said that it took AIDS to get the attention of the majority of haemophilia treaters and patients on to blood-borne viruses.

**23.18** When the SNBTS and Haemophilia Directors met on 30 January 1981 (for the first time since 1977) the topic of virus inactivation was not mentioned.<sup>28</sup> By that point, it was known to Professor John Cash and PFC scientists that Behringwerke AG had claimed that it had succeeded in pasteurising Factor VIII, though information on the company's work had yet to be published in any scientific journal that was widely available.<sup>29</sup> So far as the record shows, the information was not shared with the transfusionists and haemophilia specialists present on 30 January 1981.

**23.19** Fractionators were, in Dr Smith's view, much more concerned about NANB Hepatitis than other specialists: in his words, they could see their entire industry going down the tubes unless they did something about the threat.<sup>30</sup> The agent of transmission of NANB Hepatitis was a very recalcitrant virus, with no convincing markers until the end of the decade. There were very few tools, especially for proving whether any attempt at inactivation had succeeded. Scientists were also misled by persistent claims that there might be more than one NANB Hepatitis virus.

**23.20** Having regard to the evidence of Dr Smith and Dr Foster (and of Professor Willem van Aken at paragraphs 23.220 to 23.227 below), the obstacles to technological progress which they would have perceived in about 1980 were:

- NANB Hepatitis was widely perceived to be a mild, transient illness with only very rare serious sequelae.<sup>31</sup>
- It was widely believed that NANB Hepatitis was transmitted by voluntary blood donations much less frequently than by plasma from paid donors, which was the predominant component in the large pool products of commercial fractionators.<sup>32</sup>
- There was no credible marker or screening test for NANB Hepatitis, at the stage of donation or in the course of manufacture.
- At the time, understanding of the nature and structure of the Factor VIII molecule and related proteins was limited.<sup>33</sup>
- There was a lack of knowledge of the agent responsible for NANB Hepatitis and the lack of a marker for NANB Hepatitis precluded spiking and validation studies to test the efficacy of a given viral inactivation procedure.<sup>34</sup>
- The only way to confirm infectivity in a concentrate was to inject it into three previously untreated chimpanzees, an endangered species. The chimpanzee model was ultimately unreliable in predicting whether a heat-treated product was potentially free from NANB Hepatitis.<sup>35</sup>

<sup>28</sup> Minutes of meeting [SNB.001.5055]

<sup>29</sup> See paragraph 23.33 below

<sup>30</sup> Dr Smith – Day 59, page 25

<sup>31</sup> Dr Smith's statement on viral inactivation to 1985 [PEN.012.1551] at 1567

<sup>32</sup> Ibid [PEN.012.1551] at 1567

<sup>33</sup> Dr Foster – Day 41, pages 102–103

<sup>34</sup> Note that HIV had yet to become a concern for fractionators at this point in time.

<sup>35</sup> Dr Smith's statement on viral inactivation to 1985 [PEN.012.1551] at 1567; Dr Foster – Day 41, pages 72–75; See Kasper et al, 'Recent evolution of clotting factor concentrates for hemophilia A and B', *Transfusion*, 1993; 33:422–434 [SGH.002.1947] at 1950

- It was thought by some that there were two variants of NANB Hepatitis virus whose properties differed in important ways.
- It was thought that heat-treating Factor VIII could potentially alter its structure and lead to the formation of so-called 'neo-antigens' in patients' immune systems – that is the creation of antibodies to Factor VIII which would prevent further infusions of Factor VIII from being effective.<sup>36</sup>
- There was a concern that heat-treating Factor IX could lead to increased thrombotic reactions in patients – that is the formation of blood clots.<sup>37</sup>
- It was obvious that effective pasteurisation would be at a cost in Factor VIII yield, the amount of Factor VIII activity recovered from a given quantity of frozen plasma.<sup>38</sup> That was an obstacle for a public service struggling to reach or to maintain self-sufficiency.
- There was a need to balance possible decreases in yield against an increasing demand for factor concentrates.<sup>39</sup>

**23.21** For Dr Smith, these concerns had a real and practical significance. In April 1981, he was responsible for designing the coagulation section of the, then proposed, new BPL fractionation facility for England and Wales.<sup>40</sup> In his field, it was beginning to be realised generally that NANB Hepatitis was a more serious problem for recipients of plasma products than hitherto appreciated. He was of the view that this was undermining broader perceptions, among patients and expert groups, of the safety of large-pool fractionation. There was no solution to the risk of transmission for large-scale production. The production of small-pool Factor VIII and Factor IX concentrates was uneconomical. Nevertheless, he planned for sufficient small-pool concentrates to be produced either aseptically or under tight environmental control, to protect infants and other previously untreated patients from NANB Hepatitis, until a solution was 'arrived at by someone'. He was buying time 'until the cavalry appeared'.

**23.22** The scheme would have reduced the statistical risk for the most vulnerable.<sup>41</sup> Dr Smith said:

[B]y that time I was the person in the dock – or the driving seat, depending how you care to put it – who was responsible for having contingency planning and it would seem to me in 1981 that we might not be arriving at a solution to non-A non-B Hepatitis by the time we wished to move into the new building.<sup>42</sup>

With all his experience and expertise, he did not foresee a solution to the problem of virus inactivation at that time.

**23.23** Although research was undertaken from the mid-1940s until around the 1970s with the aim of inactivating the agent responsible for the transmission of serum (blood-transmitted) hepatitis, the evidence available to the Inquiry, and noted briefly at the end of

<sup>36</sup> Professor van Aken – Day 47, pages 12–15. These antibodies are otherwise referred to as 'inhibitors'.

<sup>37</sup> For details see Kasper et al, 'Recent evolution of clotting factor concentrates for hemophilia A and B', *Transfusion*, 1993; 33:422–434 [SGH.002.1947] at 1948; Professor van Aken–Day 47, pages 23–24

<sup>38</sup> Dr Smith's statement on viral inactivation to 1985 [PEN.012.1551] at 1567; Dr Smith – Day 59, pages 28–29; Dr Foster – Day 41, page 71

<sup>39</sup> Dr Foster – Day 41, page 71; Dr Smith – Day 59, pages 28–29

<sup>40</sup> Dr Smith's statement on viral inactivation to 1985 [PEN.012.1551] at 1556–57

<sup>41</sup> Dr Smith – Day 59, page 67

<sup>42</sup> Dr Smith – Day 59, pages 63–64

Chapter 20, *Haemophilia Therapy – The Period up to the Early 1980s*, indicates that none of the methods used were effective in eliminating infectivity without causing unacceptable damage to the product in question. The methods included: (i) the application of heat; (ii) the addition of chemicals; and (iii) the application of different forms of radiation.<sup>43</sup> Research was also undertaken in the 1970s into the physical filtering of viruses in the production process. None of these methods was used in the routine manufacture of human plasma products.<sup>44</sup> There had been a measure of success in eliminating the risk of transmission of Hepatitis B, until the mid-1970s thought to be responsible for most blood-borne hepatitis, by effective screening of donors, not by treating blood and blood products.

### **Commercial research**

**23.24** By the end of the 1970s/early 1980s, however, potentially promising research was being undertaken by commercial companies. As regards Factor VIII, the research was primarily focused on either heating the product in solution (pasteurisation) or dry-heating of the product as a freeze-dried powder. Pasteurisation had the perceived advantage that – being water-based – it was likely to be more effective at destroying viruses, but equally it was more likely to damage blood proteins. As outlined by Dr Smith during his oral evidence:

Virtually all biological, chemical reactions operate with the assistance of – through the medium of water. The water which you would think is simply a background material, holding the things together, is in fact a player in virtually all the reactions. Turning to the reactions which tend to inactivate proteins or denature them, these are heavily dependent on how much water is there. In a dry-heated product you are down to less than 1 per cent of water. In a pasteurisation situation it is all water essentially. Therefore, the ... potential damage to your protein is much more severe in the aqueous pasteurisation context than it is in the dry heating context. Equally, of course, the damage you are doing to viruses, you hope, is much more severe.<sup>45</sup>

**23.25** The use of stabilisers to protect the protein was essential. However, the choice of stabiliser was crucial since:

[I]n pasteurisation, in trying to protect your protein from what you know will be a damaging experience, you add too much of the wrong kind of stabilisers, you always fear that you have also, in doing so, failed to inactivate so much of the virus; you have protected the virus as well as the protein.<sup>46</sup>

**23.26** It was also, to a large degree, a matter of trial and error:

It's largely empirical. There are certain classes of substance which have been used more than others: salts, amino acids, sugars, at very high concentration ... you would start with certain things, and only then, having exhausted those and all the conditions under which you might apply them, you would start to turn to rather more exotic protectants.<sup>47</sup>

<sup>43</sup> Dr Foster – Day 41, pages 65–66; For more details see SNBTS Briefing Paper on the Development of Heat Treatment of Coagulation Factors [PEN.013.1309] at 1321

<sup>44</sup> Dr Foster – Day 41, page 66; SNBTS Briefing Paper on the Development of Heat Treatment of Coagulation Factors [PEN.013.1309] at 1322

<sup>45</sup> Dr Smith – Day 59, pages 31–32

<sup>46</sup> Dr Smith – Day 59, page 32

<sup>47</sup> Dr Smith – Day 59, page 32



**23.27** In contrast to pasteurisation, where a product had been freeze-dried in powder form, the lack of water and the presence of a vacuum would, in principle, make it more difficult to direct heat to the core of the powder.<sup>48</sup>

**23.28** Commercial research led to the release of a wide range of commercial heat-treated Factor VIII and Factor IX products in the USA (from 1983). Appendix 1 to this chapter tabulates the products together with the dates of licensing in the USA.<sup>49</sup> Commercial heat-treated products were not licensed by the UK Medicines Control Agency for release in the UK until February 1985.<sup>50</sup> Some products were not available in the UK. Behring's product, Haemate P, was available in small quantities from 1980 in Germany and some other places.<sup>51</sup> It was not licensed in the UK and was not available here at any time.<sup>52</sup>

**23.29** These products, which were difficult to develop, were not widely used.<sup>53</sup> Each additional step in the manufacturing process carried a yield penalty. With the exception of pasteurisation, they were not effective in destroying the agent(s) responsible for NANB Hepatitis. Initial chimpanzee studies of Hemofil T suggested that it was effective in preventing transmission of NANB Hepatitis but not Hepatitis B. In human recipients, the opposite outcome was reported.<sup>54</sup> The animal model was not reliable.

**23.30** As the tables in Appendix 1 to this chapter show, licences for heat-treated factor concentrates began to be issued in the USA in March 1983. Some at least of the procedures that were developed were protected by patents, and, in the nature of things, prior publication of the inventive steps in the processes developed was unlikely, and, to the extent that it happened at all, even more unlikely to be comprehensive. As far as the SNBTS is concerned, its first heat-treated Factor VIII product (heated to 68°C for two hours) was released in December 1984.<sup>55</sup>

## Research at the Protein Fractionation Centre: progress in the early 1980s

### 1980

**23.31** From the perspective of the PFC, there appear to have been few notable developments in the field of viral inactivation of factor concentrates early in 1980. Dr Brian McClelland attended a meeting of the Medical Research Council Working Party on Post-Transfusion Hepatitis on 14 February 1980.<sup>56</sup> However, as regards hepatitis the discussion recorded was limited to: (i) work by the German company Biotest (not Bayer as noted in the minutes of this meeting<sup>57</sup>) into using  $\beta$ -propiolactone together with ultraviolet radiation to inactivate hepatitis (this work did not ultimately lead to a successful product) and (ii) the polyelectrolyte process developed by Dr Johnson mentioned at the end of Chapter 20, *Haemophilia Therapy – The Period up to the Early 1980s*.<sup>58</sup>

<sup>48</sup> Dr Smith – Day 59, pages 30–31

<sup>49</sup> For further details see: Kasper et al, 'Recent evolution of clotting factor concentrates for hemophilia A and B', *Transfusion*, 1993; 33:422–434 [SGH.002.1947] at 1950; and SNBTS Briefing Paper on the Development of Heat Treatment of Coagulation Factors [PEN.013.1309] at 1323

<sup>50</sup> Dr McClelland's statement on the use of blood products in Scotland [PEN.015.0307] at 0320 and SNBTS Briefing Paper on the Development of Heat Treatment of Coagulation Factors [PEN.013.1309] at 1323

<sup>51</sup> Professor Cash – Day 43, pages 14–15

<sup>52</sup> Dr Perry – Day 45, page 13; Dr Cuthbertson – Day 46, page 19

<sup>53</sup> Dr Foster – Day 41, pages 70–71; SNBTS Briefing Paper on the Development of Heat Treatment of Coagulation Factors [PEN.013.1309] at 1323

<sup>54</sup> Kasper et al, 'Recent evolution of clotting factor concentrates for hemophilia A and B', *Transfusion*, 1993; 33:422–434 [SGH.002.1947]. Colombo et al, 'Transmission of non-A, non-B hepatitis by heat-treated Factor VIII concentrate', *The Lancet*, 6 July 1985; 1–5 [LIT.001.0369]

<sup>55</sup> SNBTS Briefing Paper on the Development of Heat Treatment of Coagulation Factors [PEN.013.1309] at 1340–41

<sup>56</sup> Dr McClelland's statement on viral inactivation to 1985 [PEN.011.0062] at 0062

<sup>57</sup> Dr Foster's statement on viral inactivation to 1985 [PEN.012.1438] at 1446

<sup>58</sup> Dr Foster – Day 41, pages 109–110; Minutes of MRC Working Party on Post-Transfusion Hepatitis, 14 February 1980, paragraphs 3.3 and 3.4 [DHF.002.4845] at 4847; Dr Foster's statement on viral inactivation to 1985 [PEN.012.1438] at 1446

**23.32** Bayer (Cutter Laboratories) filed an original application for protection of a pasteurisation process on 5 March 1980.<sup>59</sup>

**23.33** Towards the end of 1980, however, news had started to filter through to the PFC of the apparent breakthrough by Behringwerke AG ('Behring') in the pasteurisation of Factor VIII already noted. The news was broken to the fractionation community during the First International Haemophilia Conference in Bonn, Germany between 3 and 7 October 1980<sup>60</sup> which was attended by Professor Cash. On his return to the UK, Professor Cash told Dr Foster that the company had claimed that it had succeeded in pasteurising Factor VIII.<sup>61</sup> Subsequently, on 27 October 1980, he wrote a letter to Mr John Watt in which he said:

During the meeting in Bonn I learnt, for the first time, that Behringwerke are getting rather excited – following chimpanzee studies – that their preparations of factor VIII, made from HBsAg positive plasma (starting at 90 ng/ml), appear to be safe. The reason given is that they are heat treating the product for 10 hours at 60°C in the presence of glycine and sucrose. Apparently the glycine and sucrose protect the VIII from denaturation. Sounds unbelievable: thought you might be interested.<sup>62</sup>

**23.34** Dr Foster said in his witness statement that he was 'quite shocked' when he heard of this claim. The notion that Factor VIII might be able to be heat-treated under conditions that would destroy hepatitis viruses was inconceivable to him.<sup>63</sup> In his oral evidence, he said that on hearing the news he was, 'completely gobsmacked'.<sup>64</sup> Dr Robert Perry was not directly involved, but it was clear from his evidence that the claims were widely discussed within the SNBTS and the PFC and that there was a sense of incredulity that the process could take place.<sup>65</sup> Dr Foster was asked whether, intuitively, treating Factor VIII at 60°C would not work. He said:

I can't admit that I ever considered that. It was just so – literally inconceivable. I didn't sit down and say, 'Would this work or would it not work?' it was something I didn't even consider, it was inconceivable.<sup>66</sup>

**23.35** Dr Frank Boulton did not believe that it could possibly be true and expected that it would be found out to have been a mistake.<sup>67</sup> When Dr Foster and others reported some of their own research in this area later,<sup>68</sup> Dr Garrott Allen wrote, expressing surprise, commenting on his own failure, and asking for details.<sup>69</sup> The value of the Behring discoveries was that they demonstrated that in principle Factor VIII could be pasteurised, if suitably protected, in a high purity product. The PFC could not copy the Behring patented process: it would have to produce its own.<sup>70</sup>

<sup>59</sup> Fernandes P and Lundblad JL 1982. *Pasteurized therapeutically active protein compositions*. US Patent 4,440,679, filed 20 December 1982 and issued 3 April 1984 [SNB.004.5922]. Continuation of application number 127,351, filed 5 March 1980.

<sup>60</sup> Dr Foster's statement on viral inactivation to 1985 [PEN.012.1438] at 1447

<sup>61</sup> Ibid [PEN.012.1438] at 1447

<sup>62</sup> Professor Cash's letter [SNB.007.2646]

<sup>63</sup> Dr Foster's statement on viral inactivation to 1985 [PEN.012.1438] at 1448

<sup>64</sup> Dr Foster – Day 41, page 114

<sup>65</sup> Dr Perry – Day 45, page 11

<sup>66</sup> Dr Foster – Day 41, page 116

<sup>67</sup> Dr Foster's statement on viral inactivation to 1985 [PEN.012.1438] at 1449

<sup>68</sup> Welch et al, 'Non-A, non-B hepatitis from intravenous Immunoglobulin', *The Lancet*, 19 November 1983 [LIT.001.3924]

<sup>69</sup> Dr Allen's letter of 7 December 1983 to Dr Welch [SNB.007.4036]; Dr Foster's reply dated 22 February 1984 [SNB.007.4287]; Dr Foster – Day 41, pages 117–118; Dr Foster's statement on viral inactivation to 1985 [PEN.012.1438] at 1449–50

<sup>70</sup> Dr Pepper's statement on viral inactivation to 1985 [PEN.013.1391] at 1394

**23.36** The reasons for Dr Foster's disbelief mirror the general points outlined above by Dr Smith.<sup>71</sup> According to Dr Foster, the established view at the start of the 1980s remained that plasma proteins would be damaged by the level of heat needed to kill viruses. That also accorded with Dr Foster's first-hand experience of working with Factor VIII, as noted at the end of Chapter 20, *Haemophilia Therapy – The Period up to the Early 1980s*, at paragraph 20.75. He had found that Factor VIII from human plasma was considerably more sensitive and more difficult to work with than any of the other proteins that he had encountered.<sup>72</sup>

**23.37** Professor Cash appears to have been the first SNBTS official to become aware of Behring's progress on the heat treatment of Factor VIII.<sup>73</sup> At the end of 1980, however, the specific details of the process were not available to the PFC. After the meeting in Bonn, Behring disclosed certain details in an internal Behring journal called *Die gelben Hefte* (the Golden Notebook).<sup>74</sup> The journal would not have been readily available in the UK. Dr Foster first received a copy of this article when attending a conference in Budapest in 1982.<sup>75</sup> Professor Pier Mannucci saw a copy of the article in 1980. He wrote:

I, like other clinicians, was unimpressed with the claim because clinical evidence was meager and the design of the study retrospective and poor.<sup>76</sup>

Behring's product, Haemate P, was first licensed in Germany in 1981, where it was claimed to be the first effectively virus-inactivated Factor VIII product. The claims advanced for the Behring process are set out in the Preliminary Report at paragraphs 11.45–11.47.

**23.38** In summary, by the end of 1980 Behring had carried out research into the pasteurisation of Factor VIII which appeared to have promise, but an unacceptably low yield. A yield of about 8% of the initial plasma was confirmed in 1981.<sup>77</sup> The details of this research do not appear to have been made public at this time. Behring's approach to publication was described by Dr Smith as a 'teasing process'. The manufacturer would not disclose enough to invalidate his patent, but would hint at developments to come.<sup>78</sup> However, the PFC was aware of the general development.

## 1981

**23.39** Limited information about the procedures used by Behring were published in 1981 in the journal *Haemostasis*.<sup>79</sup> Details of the procedures were ultimately published in April 1981 in an article in the German journal *Arzneimittel Forschung/Drug Research*.<sup>80</sup> Dr Foster obtained a reprint of this document in May 1981 from the Behring trade stand at a symposium in Cambridge on 'Advances in Blood Transfusion' which was organised for Transfusion Directors by Travenol Ltd and which was by invitation only.<sup>81</sup> The article was

<sup>71</sup> See paragraph 23.15

<sup>72</sup> Dr Foster's statement on viral inactivation to 1985 [PEN.012.1438] at 1448–49. For the full explanation of Dr Foster's disbelief on hearing the news regarding Behring's heat treatment process see Dr Foster's statement at 1448–50 and Dr Foster – Day 41, pages 114–117

<sup>73</sup> Dr Foster's statement on viral inactivation to 1985 [PEN.012.1438] at 1447

<sup>74</sup> Heimburger et al, 'Factor VIII concentrate – now free from hepatitis risk; progress in the treatment of haemophilia', *Die gelben Hefte*, 1980; 4:165–174 [SNB.004.5880]

<sup>75</sup> Dr Foster – Day 41, pages 112–113

<sup>76</sup> Mannucci, 'AIDS, hepatitis and haemophilia in the 1980s: memoirs from an insider', *Journal of Thrombosis and Haemostasis*, 2003; 1:2065–69 [LIT.001.1101]

<sup>77</sup> Heimburger et al, 'A Factor VIII concentrate, highly purified and heated in solution', *Haemostasis*, 1981; 10/1:204 [SNB.007.3300]

<sup>78</sup> Dr Smith – Day 59, page 20

<sup>79</sup> Heimburger et al, 'A Factor VIII concentrate, highly purified and heated in solution', *Haemostasis*, 1981; 10/1:204 [SNB.007.3300]

<sup>80</sup> Heimburger et al, 'Faktor VIII-Konzentrat, hochgereinigt und in Lösung erhitzt', *Arzneimittel Forschung/Drug Research*, (31) 619–622 [SNB.008.6794]

<sup>81</sup> Dr Foster's statement on viral inactivation to 1985 [PEN.012.1438] at 1451 and Dr Foster's supplementary statement on viral inactivation to 1985 [PEN.012.1797] at 1798

in German and was translated into English by Dr Werner Zolg, a German post-doctoral researcher at Edinburgh University who was at that time involved in a collaboration on a different project with Dr Alex MacLeod – a research scientist at the PFC.<sup>82</sup>

**23.40** Shortly afterwards, Dr Foster became ill and did not return to work until mid-October 1981. During this period, Dr MacLeod obtained the translation from Dr Zolg and, on his own initiative, on 2 September 1981 started a set of experiments aimed at reproducing Behring's findings.<sup>83</sup> The view in the PFC, differing from Professor Mannucci, was that Behring was a well-respected company, and, if they said a process was feasible, it was worth pursuing even if one remained sceptical about the yield and about proof that the viruses were sufficiently inactivated.<sup>84</sup> According to Dr Foster:

The early research of Dr MacLeod was essentially exploratory and aimed to confirm the findings of Behring and to establish whether or not the approach taken by Behring might be feasible and suitable for the PFC to pursue.<sup>85</sup>

A particular focus for this research was on identifying stabilisers and conditions which might allow pasteurisation to be developed without breaching Behring's patent.<sup>86</sup>

**23.41** Thus, by the end of 1981, as a response to Behring's work, research into the pasteurisation of coagulation factors had begun at the PFC. However, the published yield of eight per cent was a serious draw-back from the point of view of the PFC. In Dr Perry's recollection, the low yield meant that the process had no practical applicability in Scotland (where all coagulation factor production, of necessity, came from the limited Scottish donor population).<sup>87</sup>

**23.42** On 17 December 1981, Professor Cash wrote to Mr Watt, Dr Perry, Dr Foster, Dr Prowse, Dr Boulton, Dr Pepper and Dr G S Gabra intimating the setting up of the SNBTS Factor VIII Concentrate Study Group (Factor VIII Study Group) and inviting them to be members. The group was to have as its remit the exploration of:

[N]ew developments in the widest possible sense with regard to the production of factor VIII concentrates and thereby create the opportunity for cross fertilisation and for co-ordinated research within the SNBTS.<sup>88</sup>

**23.43** This group later formed an important forum for the discussion of matters relating to viral inactivation.

## 1982

### The PFC continues its research into heat treatment options and Behring's pasteurisation process

**23.44** The first meeting of the Factor VIII Study Group took place on 28 January 1982. The minutes of the meeting indicate that Dr Christopher Prowse mentioned pasteurisation in the context of inactivating viruses.<sup>89</sup> He said that the HQ laboratory unit of the SNBTS was

---

<sup>82</sup> Dr Foster – Day 41, pages 121–122; Dr Foster's statement on viral inactivation to 1985 [PEN.012.1438] at 1451–52; for Dr Werner Zolg's translation see [SNF.001.0881]

<sup>83</sup> Dr MacLeod prepared a report on this work dated 10 February 1982 [PEN.012.1489]

<sup>84</sup> Dr Foster – Day 41, page 115; Dr Perry – Day 45, page 12

<sup>85</sup> Dr Foster's statement on viral inactivation to 1985 [PEN.012.1438] at 1452

<sup>86</sup> Dr Perry's statement on viral inactivation to 1985 [PEN.012.1759] at 1761

<sup>87</sup> Dr Perry – Day 45, pages 11–12

<sup>88</sup> Professor Cash's letter of 17 December 1981 [SNB.001.3587]

<sup>89</sup> Minutes of the Factor VIII Study Group, 28 January 1982 [SNF.001.3813] at 3813

carrying out experiments using gamma-irradiation.<sup>90</sup> Viral inactivation was not highlighted in the list of current research priorities, however, and Dr MacLeod's research into Behring's process was not referred to.<sup>91</sup> During the meeting, Professor Cash recommended the setting up of a separate sub-committee with a view to improving 'the safety of the product, eg by irradiation to remove viral infectivity'.<sup>92</sup>

**23.45** This sub-committee became known as the Safety Action Group and held its first meeting on 9–10 February 1982.<sup>93</sup> A discussion document set out what was known and what might be attempted. The meeting summarised the existing knowledge within the SNBTS as regards methods of viral inactivation as well as outlining proposals for action and resources required. Gamma-irradiation was discussed as was the possible use of a combination of b-propiolactone and ultraviolet irradiation.<sup>94</sup> Behring's pasteurisation method was also mentioned, and it was noted that:

An alternative to g-irradiation is heating (pasteurisation). This has been attempted by Behringwerke who now market 'Faktor VIII HS' in which HS implies, "safe from hepatitis". Unfortunately only one paper has been published (in German) and no details are given of solution compositions or yields. However, estimates by P.F.C. indicate 8% yield which is rather low.<sup>95</sup>

**23.46** Although Behring's work was discussed, once again no mention was made during this meeting of the fact that the PFC had already begun investigations, under Dr MacLeod, into whether Behring's findings could be confirmed. Dr MacLeod's work was not included in the proposals for action. The Inquiry has asked whether the lack of a mention of Dr MacLeod's research in this meeting and the earlier meeting of the Factor VIII Study Group could be interpreted as meaning that this research was not a priority for the PFC at this time, or that Professor Cash was not aware of the research.<sup>96</sup> Dr Foster said that, in his view, this was not the case. He explained that:

The first meeting of the Factor VIII Study Group was held on the 28th January 1982, some two weeks before Dr MacLeod had completed his preliminary evaluation. I am sure that Dr Cash was aware of our work on pasteurisation when he arranged the first meeting of the Factor VIII Study Group but, as the exploratory experiments of Dr MacLeod were incomplete, it is understandable that he did not include this topic in the agenda of the first meeting of the Group.

Similarly the meeting of the Safety Action Group of 9–10 February 1982 ... preceded the report of Dr MacLeod.<sup>97</sup>

**23.47** Dr Perry's evidence to the Inquiry also explains that any perceived lack of focus on pasteurisation at this time should be seen in the context of the more general goals of the Factor VIII Study Group:

The Factor VIII study group was an important development in SNBTS and was established to coordinate all available resources in SNBTS to meet the

<sup>90</sup> Minutes of the Factor VIII Study Group, 28 January 1982 [SNF.001.3813] at 3817–18; Dr Pepper's statement on viral inactivation to 1985 [PEN.013.1391] at 1393

<sup>91</sup> As already noted, Dr MacLeod did not report his work until 10 February 1982 [PEN.012.1489]

<sup>92</sup> Minutes of the Factor VIII Study Group meeting, 28 January 1982 [SNF.001.3813] at 3818–19

<sup>93</sup> Factor VIII Study Group: First report of the Safety Action Group, 16 March 1982 [SNB.005.8387]

<sup>94</sup> Preliminary Report, paragraphs 11.57–11.58

<sup>95</sup> Factor VIII Study Group: First report of the Safety Action Group, 16 March 1982 [SNB.005.8387] at 8390

<sup>96</sup> Inquiry's schedule of questions on viral inactivation to 1985 [PEN.012.1531] at 1532

<sup>97</sup> Dr Foster's statement on viral inactivation to 1985 [PEN.012.1438] at 1452

challenges of self-sufficiency and to establish this as a national priority. I attended this meeting together with Dr Foster and Mr Watt from PFC. At this time the PFC work on virus inactivation was only at a preliminary stage without any clear reportable outcomes. My recollection from the meeting is that safety issues were discussed in general leading to agreement to establish a safety sub group. Whilst this is not recorded in the report of the meeting this would not necessarily be unusual for such internal reports. The importance of product safety was certainly recognised in these discussions but so was the recognition that any method likely to improve safety would reduce product yield. Thus consideration of FVIII processing yield and FVIII content of plasma were considered essential prerequisites to progress on product safety if the goal of self sufficiency was to be achieved and maintained.<sup>98</sup>

**23.48** So, even at this early stage, there appears to have been a recognition that improvements in safety had to be balanced against the general goal of self-sufficiency and the need to improve yield to offset any losses caused by viral inactivation.<sup>99</sup>

**23.49** Dr MacLeod's initial findings on his preliminary studies, following the methodology in the Drug Research paper, were summarised shortly thereafter in a PFC R&D report of 10 February entitled 'Preliminary studies on the heat treatment of PFC FVIII concentrate'.<sup>100</sup> The document reported briefly on the initial PFC experiments with heating Factor VIII using glycine and sucrose as stabilisers and concluded that further purification of the PFC's Factor VIII concentrate seemed necessary in order to be able to pasteurise the product.

**23.50** Dr Foster's view was that:

The immediate challenge was therefore two-fold. To discover a means of increasing purity to allow the pasteurisation process to be applied, whilst at the same time substantially increasing the yield ... to enable the SNBTS to provide the quantity of factor VIII concentrate required.<sup>101</sup>

**23.51** This became a major consideration of the Safety Action Group at the PFC.<sup>102</sup> An account of their discussions between February and July 1982 is given in the Preliminary Report at paragraphs 11.57–11.68. In the background was a commitment to self-sufficiency that implied that any strategy that led to failure to meet the escalating demand for product for all of Scotland's patients was not viable.<sup>103</sup> Self-sufficiency was, in Dr Perry's words, 'the only game in town'. He said:

[T]hat culture and that ethos really pervaded everything we did. And for very good reason. It was clearly understood why we had that particular position .... [E]very bottle of product or every vial of product, every dose of product that we could make from Scottish donors avoided the need to import material from what we perceived and believed were less safe parts of the world, and particularly the American commercial material. So it wasn't just a sort of random process of pride or national pride that we would be self-sufficient, there was a very good reason underlying it. And certainly I internalised that at a very early stage. Every morning I woke up, basically the reason for going to work was

---

<sup>98</sup> Dr Perry's statement on viral inactivation to 1985 [PEN.012.1759] at 1762

<sup>99</sup> Dr Perry – Day 45, pages 17–18

<sup>100</sup> Dr MacLeod's report [PEN.012.1489]

<sup>101</sup> Dr Foster's statement on viral inactivation to 1985 [PEN.012.1438] at 1453; see also Dr Perry – Day 45, pages 17–19

<sup>102</sup> Dr Foster's statement on viral inactivation to 1985 [PEN.012.1438] at 1453

<sup>103</sup> Dr Perry – Day 45, pages 18–19

to make sure that we could avoid having to import product from areas that were believed to be less safe than Scottish donors. So where it actually came from, I think certainly pre-dated me. I think certainly Professor Cash – and this is from me reading the sort of historical archives. There were discussions when he took over as national medical director that, I think, one of the clear discussions he had before taking up the post was, you know: is part of the job here to establish self-sufficiency? And I think the answer to that was yes .... [L]eading from that process were discussions between Professor Cash and George MacDonald in the West of Scotland and various other haematologists and haemophilia directors, where they sought to establish what that meant, and the figure that I always had in mind was 2.75. That was the magic figure.<sup>104</sup>

**23.52** There were no policy statements or documents to that effect. But:

It was in the fabric of the building, it was in the fabric of everything that was discussed, that, you know, the PFC was established at great expense to the taxpayer and its job was to meet the needs for Scottish patients. So, you know, I guess I'm just a single point in this process, but for me it became very clear very early on what we were there for and that included – and in a sense, failing to supply was – it sounds a bit romantic but failure to supply was not an option .... [I] think it would have been seen as an admission of failure of delivery against our mission and purpose. Certainly that's how I perceived it anyway.<sup>105</sup>

Dr Perry did not think that the Common Services Agency (CSA) and its committees lived and breathed self-sufficiency to the extent the SNBTS did.<sup>106</sup>

**23.53** Further meetings of the Factor VIII Study Group and the Safety Action Group followed throughout spring/summer 1982. The meeting of the Safety Action Group of 30 March 1982 proposed that work should be carried out into filtration, that Dr MacLeod's research into Behring's pasteurisation process should be pursued and that Dr Duncan Pepper should investigate aspects of irradiation. Practical aspects of these strands of proposed research (laboratory accommodation, access to infected material, which animals could be used to test for infectivity – so-called 'animal models' – and funding) were also discussed.<sup>107</sup> The issue of possible animal models was also discussed during the Factor VIII Study Group meeting on 3 June 1982.<sup>108</sup> It was also dealt with in more detail during the meeting of the Safety Action Group on 23 June 1982, which investigated the possibility of infecting Tamarin monkeys with known NANB Hepatitis infected material and carrying out titrations to measure the effectiveness of various inactivation processes: heat, gamma-irradiation, adsorption, purification and the use of detergent.<sup>109</sup> Therefore, by the middle of 1982, the PFC was continuing its examination of the options for viral inactivation. However, no one option had yet been chosen.

**23.54** Dr Bruce Cuthbertson characterised much of the work of the Safety Action Group as 'blue sky thinking'.<sup>110</sup> However, the discussion focused on what were seen at the time as real possibilities. For example the animal studies were seen as a serious prospect in

<sup>104</sup> Dr Perry – Day 45, page 32–33

<sup>105</sup> Dr Perry – Day 45, page 34

<sup>106</sup> Dr Perry – Day 45, pages 34–35

<sup>107</sup> Minutes of the Factor VIII Study Group meeting, 30 March 1982 [SNF.001.3793] at 3796

<sup>108</sup> Minutes of the Factor VIII Study Group meeting, 3 June 1982 [SNB.001.3902] at 3905

<sup>109</sup> Report of the meeting of the FVIII Safety Action Group on 23 June 1982 [SNB.001.3917]

<sup>110</sup> Dr Cuthbertson – Day 46, page 30

May 1982. SNBTS scientists in this respect reflected the ambition of the organisation, notwithstanding that it was a small operation in a small country.<sup>111</sup> Dr Smith had a more positive view of the work of the group:

I would like to reaffirm just how wide-ranging SNBTS's experiments were. In fact, on theoretical grounds, it would seem to most people far more likely that radiation would distinguish between proteins and an assembled entity like a virus. This simply did not happen. Nature did not cooperate in this case but it does exemplify the lengths that this study group went to in exploring every avenue.<sup>112</sup>

### **Protein Fractionation Centre obtains further information on current viral inactivation research at an International Congress in Budapest**

**23.55** Dr Foster attended the International Society of Haematology/International Society of Blood Transfusion Congress in Budapest between 2–5 August 1982 and produced a detailed report which, among other things, summarised information about recent viral inactivation research publicised during the conference.<sup>113</sup>

**23.56** Behringwerke did not present at the conference. However, it did provide copies of certain documents as part of a trade stand which was held in conjunction with the Congress.<sup>114</sup> These included:

- A Behring paper on Factor VIII published on 16 July 1982 which emphasised the variation in purity and Factor VIII activity of a range of commercial products as compared to Behring's highly purified product.<sup>115</sup>
- A typewritten version of the paper, referred to at paragraph 23.37 above, on the Behring pasteurisation process which had been published in *Die gelben Hefte* in 1980.<sup>116</sup>

**23.57** The introduction to the typewritten paper on the Behring pasteurisation process stated that:

Until recently it has been impossible to eliminate the danger of hepatitis from certain plasma products, in particular clotting factor concentrates. When using factor VIII concentrate for haemophilia it was therefore necessary to weigh the benefits against the hazards. Now, however, thanks to a new manufacturing process, a safe Factor VIII concentrate is available. Experimental and clinical trials have confirmed its freedom from hepatitis risk.

**23.58** It also emphasised the medical need for a safer product, noting that:

Haemophiliacs, because they require lifelong replacement therapy with coagulation factor concentrates, are exposed to considerable risks of hepatitis. Twenty years ago, before the introduction of effective replacement therapy, haemorrhage was the major hazard, but today its place has been taken by chronic liver disease.

---

<sup>111</sup> Dr Cuthbertson – Day 46, pages 34–36

<sup>112</sup> Dr Smith – Day 59, page 35

<sup>113</sup> Dr Foster's report on the conference [SNB.010.4452]

<sup>114</sup> Dr Foster's statement on viral inactivation to 1985 [PEN.012.1438] at 1453

<sup>115</sup> Kröniger et al, 'Factor VIII concentrates: problems and protein-chemical characterization', *Die Medizinische Welt*, 1982; 33:1027–1033 [SNF.001.0921]. Note that the paper made no explicit claims that the Behring product was hepatitis safe.

<sup>116</sup> Heimburger et al, 'Factor VIII concentrate – now free from hepatitis risk; progress in the treatment of haemophilia', undated typescript [SNF.001.0929]



**23.59** The paper included a discussion of the various perceived options for reducing the risk of hepatitis transmission, indicating that: (i) vaccines and immunoglobulins were not available for NANB Hepatitis; (ii) single donor cryoprecipitate derived from medically supervised regular donors would have solved the problem only for a very small number of patients; and (iii) the combination of  $\beta$ -propiolactone and ultraviolet irradiation, which had been used in Factor IX, was not applicable to Factor VIII. Consequently:

In view of these facts we endeavoured to work out a method for producing hepatitis-free Factor VIII concentrate. We chose heat sterilisation, because it had been used for albumin for many years and was of established value. The removal of hepatitis risk by the albumin production process is based essentially on three stages: 1. Screening of all donor plasmas by a third generation test and rejection of HBsAg-positive donations. 2. Elimination of hepatitis virus (BV) during the fractionation process. 3. Inactivation of any residual virus particles by heating the final product to 60° for 10 hours. The Factor VIII molecule is highly susceptible to elevated temperatures and the heating process was made feasible only by addition of stabilizers which protect the molecule from thermal inactivation.<sup>117</sup>

**23.60** The paper outlined experiments which had been carried out to establish whether the viral inactivation protocol had been effective, concluding that:

In the light of the experimental and clinical results it may be said that the possibility of transmission of hepatitis B by Factor VIII HS can be ruled out. Furthermore, non-A/non-B hepatitis has so far not been observed and the characteristic ... signs have not been seen. However, long-term observation is being continued so that a definitive statement can be made.<sup>118</sup>

**23.61** Thus, although there was no final proof at this stage that the Behring product was free from NANB Hepatitis, the company claimed to have had encouraging indications of possible success.<sup>119</sup>

**23.62** In addition to receiving more information on the Behring process in Budapest, Dr Foster learned that Biotest were making progress with  $\beta$ -propiolactone and ultraviolet treatment; and that an independent research company, Rubenstein and Rubenstein, were pursuing dry heat treatment. He also became aware of Hyland/Baxter's announcement that it had developed a heat-treated product. In his report, Dr Foster indicated that Hyland's method 'was said to involve pasteurisation'.<sup>120</sup> However in his evidence to the Inquiry, Dr Foster indicated that 'at the time I didn't know what it was and it was only later that we discovered it was a dry heat process'.<sup>121</sup> More specifically, in his written evidence Dr Foster stated that:

The method of heat treatment was not disclosed at the Congress. Some months later, Dr Chris Prowse of the SNBTS learned from Dr Henry Kingdon, the Medical Director of Hyland/Baxter, that the procedure involved dry-heat treatment at 60°C. What had been done to enable the Hyland/Baxter Factor VIII concentrate (Hemofil) to withstand this degree of heat treatment was not disclosed and, to the best of my knowledge, has never been disclosed.<sup>122</sup>

<sup>117</sup> Ibid [SNF.001.0929] at 0932

<sup>118</sup> Ibid [SNF.001.0929] at 0941

<sup>119</sup> See also Preliminary Report, paragraphs 11.74–11.78

<sup>120</sup> Dr Foster's report on the Budapest conference [SNB.010.4452] at 4456

<sup>121</sup> Dr Foster – Day 41, page 129

<sup>122</sup> Dr Foster's statement on viral inactivation to 1985 [PEN.012.1438] at 1454

**23.63** At the time Dr Foster regarded Hyland's product as having potential, noting in his report that:

The Hyland product is perhaps the most interesting. If the yield indicated (200 iu/l) is confirmed this is probably higher than the present method of manufacture for Hemofil and therefore represents a definite break-through in FVIII stabilisation. Will this ever be published?<sup>123</sup>

**23.64** However, when asked at the Inquiry how he would characterise the information from Hyland, Dr Foster remarked that it should be viewed as 'tantalsing' and that 'it was a heat-treated product that gave no indication as to whether it might deal with viruses or not .... So the questions were still waiting to be answered'.<sup>124</sup> Dr Smith commented in his written statement that the paper would have served to increase interest in pasteurisation, and perhaps increase its priority.<sup>125</sup> As outlined in more detail below, the product was ultimately found to transmit NANB Hepatitis.<sup>126</sup>

**23.65** Dr Foster described the work carried out by Rubenstein,<sup>127</sup> using labile factors in their freeze-dried state, as 'very interesting'.<sup>128</sup> But he thought that freeze-drying was also likely to protect the virus and infectivity data were essential. In his written evidence, Dr Foster indicated that it was at this conference that he first became aware of the possibility of heat-treating freeze-dried factor concentrates, commenting that:

It was also at the 1982 ISBT Congress that I first learned of the concept of applying heat treatment to coagulation factor concentrates in the freeze dried state (ie. dry-heat treatment). These were listed in the programme as poster presentations at which the authors would be present to answer questions on their work. In the event, the posters were not displayed nor were the authors present at the poster session to answer questions.<sup>129</sup>

### *Pasteurisation selected as preferred viral inactivation option*

**23.66** The Factor VIII Study Group met again on 14 October 1982 and discussed the activities of the Safety Action Group. The minutes of the Safety Action Group record that:

Heat Treatment was now the first option of the group in view of developments which had occurred since the last meeting. Dr Alex McLeod [sic] (PFC) would continue studies of heat process using high purity product. Edinburgh BTS to assist if necessary.<sup>130</sup>

**23.67** A number of witnesses were asked the reason for the decision of the Factor VIII Study Group to focus on the heat treatment of a high-purity product.<sup>131</sup> In his written evidence Dr Perry stated that:

By October 1982 SNBTS had eliminated irradiation and virus removal as options for increasing FVIII safety. Irradiation in particular led to complete destruction of the product at doses necessary to achieve a sufficient degree of virus inactivation.

---

<sup>123</sup> Dr Foster's report on the Budapest conference [SNB.010.4452] at 4459

<sup>124</sup> Dr Foster – Day 41, page 128

<sup>125</sup> Dr Smith – Day 59, pages 34–35

<sup>126</sup> Preliminary Report, paragraph 11.160

<sup>127</sup> Dr Foster's supplementary statement on viral inactivation to 1985 [PEN.012.1797] at 1798–99

<sup>128</sup> Dr Foster's report on the Budapest conference [SNB.010.4452] at 4459

<sup>129</sup> Dr Foster's statement on viral inactivation to 1985 [PEN.012.1438] at 1453–54

<sup>130</sup> Minutes of Factor VIII Study Group meeting, 14 October 1982 [SNB.001.3932] at 3932

<sup>131</sup> Inquiry's schedule of questions on viral inactivation to 1985 [PEN.012.1531] at 1532

Therefore heat (pasteurisation) was selected as the preferred option not only because of the reported success of Behring but also because other lines of research had proven unsuccessful.<sup>132</sup>

**23.68** Dr Foster explained in his witness statement that the reasons for prioritising heat treatment were as follows:

- a). Although I was not a member of the Safety Action Group, I believe that there were three principal reasons why pasteurisation was, by 14 October 1982, *'the first option of the group'*.
- b). The first reason concerned the promising results that had been presented by Behring at the ISBT Congress in August 1982.
- c). The second reason was the discovery of a suitable means of reducing the fibrinogen content of Factor VIII. This discovery had been made at PFC in conjunction with Dr Milan Bier of the University of Arizona and involved the addition of zinc,<sup>133</sup> which preferentially caused fibrinogen to precipitate, whilst leaving factor VIII in solution (Bier M & Foster PR. USA Patent 1983, No. 4,406,886). This discovery enabled the purity of factor VIII to be increased prior to pasteurisation with little loss of yield and addressed the need for an increase in purity which Dr MacLeod had identified in his report of 10th February 1982. This was the *'high purity product'* that was noted in the minute of the meeting of the Factor VIII Study Group of 14th October 1982.
- d). The third reason was the promising results that Dr MacLeod had obtained using sorbitol instead of sucrose to stabilise factor VIII during pasteurisation [Preliminary Report para 11.86], which reduced the loss of factor VIII during the heat treatment process.<sup>134</sup>

**23.69** Witnesses were also asked whether the decision to focus on heat treatment could have been due to the PFC's existing knowledge of and experience in the pasteurisation of albumin.<sup>135</sup> In his evidence to the Inquiry Dr Foster explained that, although the heat treatment of albumin *'represented a bench-mark against which new procedures could be compared'*,<sup>136</sup> it could not simply be copied for other coagulation factors since *'the chemical stabilisers were not able to stabilise other plasma proteins, including the coagulation factors'*.<sup>137</sup>

**23.70** Dr Perry, in his written evidence, commented that it was not correct to assume that the choice of pasteurisation by either Behring or the SNBTS was based simply on prior experience with equipment and facilities for albumin production.<sup>138</sup> He, too, emphasised that albumin was a relatively stable protein in the liquid state. Pasteurisation of albumin involved the addition of non-toxic stabilisers which did not require to be removed following pasteurisation. In contrast coagulation factor proteins were known to be unstable in the

<sup>132</sup> Dr Perry's statement on viral inactivation to 1985 [PEN.012.1759] at 1763. See also Dr Cuthbertson's statement [PEN.013.0025] at 0029 for similar reasoning.

<sup>133</sup> For more details on zinc precipitation see 'SNBTS Briefing Paper on the Development of Heat Treatment of Coagulation Factors' [PEN.013.1309] at 1332–33

<sup>134</sup> Dr Foster's statement on viral inactivation to 1985 [PEN.012.1438] at 1454–55

<sup>135</sup> Inquiry's schedule of questions on viral inactivation to 1985 [PEN.012.1531] at 1533

<sup>136</sup> Dr Foster's statement on viral inactivation to 1985 [PEN.012.1438] at 1457

<sup>137</sup> Dr Foster's statement on viral inactivation to 1985 [PEN.012.1438] at 1455

<sup>138</sup> Dr Perry's statement on viral inactivation to 1985 [PEN.012.1759] at 1763–64

liquid state and were rapidly destroyed at elevated temperatures. There were no known stabilisers which could prevent destruction of the coagulation proteins present in the concentrates when exposed to elevated temperatures. In developing virus-safe coagulation factor products with acceptable yield, pharmaceutically suitable stabilisers capable of protecting unstable coagulation factor proteins from the effect of heat, and reducing the concentration of other heat-labile proteins in the product, were required, as were processing methods (including potentially the removal of stabilisers after pasteurisation). These were complex scientific problems. Dr Perry said:

Following the discovery by Behring of suitable stabilisers, SNBTS embarked on a programme to develop a similar process which was capable of delivering an acceptable product yield and which did not infringe the Behring patents.

SNBTS (and probably Behring also) selected pasteurisation at 60 degrees for 10 hours because such established processes were already known to produce safe albumin products and it was thought likely that such processes would similarly deliver safe coagulation factors.

The availability or otherwise of equipment to carry out the specific pasteurisation step in the overall process was a relatively minor consideration.<sup>139</sup>

As noted above at paragraph 23.67, Dr Perry also said that SNBTS research into the use of gamma radiation and methods of physically removing virus from Factor VIII had proven unsuccessful.

**23.71** Dr Cuthbertson's written evidence gave a slightly more positive view of the attractions of the existing albumin process of heating for 10 hours at 60°C noting that 'it was not surprising that Behringwerke chose this time and temperature combination for their process and it had clear attractions for the PFC in that pasteurisation equipment was already available in the PFC facility'.<sup>140</sup> However, Dr Cuthbertson also indicated that 'the outstanding safety record which applied to albumin could not be directly extrapolated'<sup>141</sup> to Factor VIII and that the key issue was finding stabilisers which would preferentially protect Factor VIII (but not viruses) from heat.<sup>142</sup>

### **Cooperation between Protein Fractionation Centre and Blood Products Laboratory**

**23.72** Shortly after the Factor VIII Study Group meeting of 14 October 1982, correspondence followed between the PFC and the BPL regarding heat treatment. Dr Foster wrote to Dr Smith of the BPL on 19 October 1982:

On the FVIII front we are still grinding away at the yield problem and have started to look again at the high purity situation. We are currently pursuing precipitation by metal-ions, which is something we stumbled on with Milan Bier a few months ago. The early results are interesting but its going to be stuck on the lab bench for a long time yet. Everyone is getting very hot about pasteurisation, especially since Budapest. The little work that we have done

<sup>139</sup> Dr Perry's statement on viral inactivation to 1985 [PEN.012.1759] at 1764

<sup>140</sup> Dr Cuthbertson's statement on viral inactivation to 1985 [PEN.013.0025] at 0029

<sup>141</sup> Ibid [PEN.013.0025] at 0029

<sup>142</sup> Dr Cuthbertson – Day 46, page 43; see also Dr Smith's written statement [PEN.012.1551] at 1568 'JKS Note 2' where he emphasises the difficulty of removing the stabilisers from the resultant solution.

suggests that higher purity material is needed and so far FVIII (using Duncan's CAG assay) has always gone into the solids phase!<sup>143</sup>

Dr Smith replied on 3 November 1982 indicating that:

We are doing a little on heating factor VIII, but only for the moment on the gentle conditions for fibrinogen removal. I cannot see us doing the infinitely factorial experiments and infusions required to 'solve' factor VIII and would appreciate any small signal of success from your efforts.<sup>144</sup>

**23.73** In his written statement Dr Smith outlined the background to this comment noting that:

Brief heating at temperatures around 60°C, without stabilisers, was being considered as a means of precipitating fibrinogen as a solid while leaving most F.VIII in solution – by no means an original idea, but we were ready to try almost anything short of voodoo. There was no intention to inactivate NANBH. The letter goes on to say that BPL was in no shape to start serious work on pasteurisation (anticipating a very long haul) and that I would be very pleased if PFC's work might offer some encouragement.<sup>145</sup>

**23.74** When asked during the Oral Hearings what the ultimate aim of the BPL's research was, Dr Smith gave the following explanation of the attempt to remove fibrinogen:

[A]ll the time we had been working with Factor VIII, you are yearning to get rid of fibrinogen, and over ten years we were working continuously on every possible avenue which presented itself to us or in some publication to achieve that ....

So although this looks like pasteurisation in pursuit of killing non-A non-B Hepatitis, the aim of the gentle heating was solely to try and find a shortcut to reduce the amount of fibrinogen at a cost in Factor VIII which might be acceptable. It did not work.<sup>146</sup>

It was an attempt to achieve a more pure product with all the advantages that that would bring.

**23.75** There were close working relationships between the BPL and the PFC. The relationship went beyond Dr Smith and Dr Foster. Dr Cuthbertson and Dr Perry had close relationships with Dr Smith and Dr Snape, and later Dr Harrison.<sup>147</sup> But the relationship between Dr Smith and Dr Foster was particularly close. Mr Watt had heard Dr Foster speak at University College, London in 1970. He suggested to Dr Smith, then at the SNBTS, Edinburgh, that he should visit and discuss Dr Foster's research. Dr Foster gave further details of this stage which are set out later. He was recruited by Edinburgh and in and after January 1973 worked closely with Dr Smith until he left in 1975. They agreed to maintain close contact.<sup>148</sup> Their contacts, at professional level, were known to other managers at the PFC and the SNBTS and news and information gathered was passed on.<sup>149</sup> Dr Perry

---

<sup>143</sup> Dr Foster's letter to Dr Smith [SNB.007.3253]

<sup>144</sup> Dr Smith's letter to Dr Foster [SNB.007.3267]

<sup>145</sup> Dr Smith's statement on viral inactivation to 1985 [PEN.012.1551] at 1555–56

<sup>146</sup> Dr Smith – Day 59, page 51

<sup>147</sup> Dr Cuthbertson – Day 46, page 43

<sup>148</sup> Dr Foster's statement on viral inactivation to 1985 [PEN.012.1438] at 1457

<sup>149</sup> Dr Perry – Day 45, pages 24–25

noted that Dr Smith and Dr Foster were both recognised experts in their field and thought that there was nothing surprising or remarkable about the degree of disclosure.<sup>150</sup> Dr Cuthbertson never had any sense of being constrained in his contacts with colleagues in England. He said:

I think in those days probably at scientific and technical level we had slightly more freedom than we later had to actually indulge personal communications. I mean, it was well enough known that at senior management level there was not a meeting of minds between the directors of the two institutions but I think we all just worked round that rather than through it, if that makes sense.<sup>151</sup>

Dr Richard Lane and Mr Watt did not always see eye to eye. Within the SNBTS tensions between Mr Watt and Professor Cash did not inhibit scientific work either.<sup>152</sup> Externally, within the constraints of commerciality, there was free exchange of data and information with scientists in industry.

**23.76** Meanwhile, initial experiments led by Dr MacLeod into the pasteurisation of factor concentrates had led to what he referred to as 'good results' using sorbitol or sorbitol/glycine as stabilisers.<sup>153</sup> More work was, however, needed and investigations were underway into whether the SNBTS process was sufficiently distinctive and could be protected by patent.<sup>154</sup>

**23.77** Later in the year there was more correspondence between the PFC and the BPL on the subject of heat treatment, with Dr Foster writing to Dr Smith on 1 December 1982 outlining heat treatment experiments which the PFC had carried out on Factor IX. He enclosed a copy of Behring's patent, and an abstract relating to Hyland's work. He also discussed at some length the PFC's freeze-drying experiences.<sup>155</sup>

**23.78** When asked to describe the nature of cooperation between himself and Dr Foster at this time, Dr Smith explained in his written evidence:

I would characterise it as decidedly lopsided at this point, insofar as virus inactivation in F.VIII was concerned. BPL was in a delicate transitional condition and had few resources to tackle the problem seriously.

It was a correspondence between scientists with a clear sense of their responsibilities. We were both well aware of a degree of tension between the upper layers of our respective organisations but agreed (without as I recall having to discuss the question) that this must not be an obstacle to pooling what information we could each gather.

It will also be evident from [Dr Foster's letter of 1 December 1982] that, during my tenure at BPL Elstree, PFC visitors were welcomed and technical information shared openly. My colleagues and I invariably received an equally warm welcome from everyone at PFC and the rest of SNBTS.<sup>156</sup>

---

<sup>150</sup> Dr Perry's statement on viral inactivation to 1985 [PEN.012.1759] at 1771

<sup>151</sup> Dr Cuthbertson – Day 46, page 46

<sup>152</sup> *Ibid*

<sup>153</sup> Memorandum from Drs Foster and MacLeod to Mr Watt, dated 12 November 1982 [SNF.001.3497]

<sup>154</sup> Preliminary Report, paragraphs 11.87–11.89

<sup>155</sup> Dr Foster's letter to Dr Smith [SNB.007.3341]

<sup>156</sup> Dr Smith's statement on viral inactivation to 1985 [PEN.012.1551] at 1556

**23.79** Dr Smith added during his oral evidence:

[T]here were very few telephone conversations. Most of the things we wanted to share with each other involved detailed evidence, as you see, and we would not present each other with rumours or rumours of rumours, which we knew would simply tend to confuse the other. We would wait until we had something which we could stand by and provide in sufficient detail to be useful to the other. We were not in each other's pockets or on the phone every other day. Most of it was done by detailed letters and topping up the background with the occasional visits.<sup>157</sup>

**23.80** Dr Foster characterised the nature of cooperation between himself and Dr Smith as follows:

- a). I had a very good relationship with Dr Smith and always found him to be extremely co-operative.
- b). I first met Dr Smith in 1970 when he visited me at University College London to discuss my PhD research. After joining the PFC in January 1973, I worked closely with Dr Smith until he left in August 1975. Before leaving the PFC, Dr Smith gave a number of seminars in which he very generously shared his knowledge and expertise. I then visited Dr Smith at the PFL (Oxford) in 1976, when we agreed to maintain close communication.
- c). One way of learning of progress elsewhere was to attend international conferences and symposia. As it was difficult for any one person to attend all of the conferences, Dr Smith suggested that we should share reports if one of us had attended a conference that the other had missed. Dr Smith did not attend the 1982 ISBT Congress and it was because of this arrangement that I sent my report ... to him.<sup>158</sup>
- d). I believe that it was on reading my report of the 1982 ISBT Congress that Dr Smith first learned that research was being undertaken on pasteurisation and dry-heat treatment of coagulation factors. It is therefore not surprising that only 'a *little*' research on heat treatment was being undertaken at PFL (Oxford) at November 1982.<sup>159</sup>

**23.81** The Inquiry also asked what degree of importance viral inactivation had in the research and development priorities of the BPL at this point. Dr Smith's response in his written evidence indicated that the Director of the BPL, Dr Lane, viewed NANB Hepatitis as 'a very serious problem in recipients of plasma products', but that 'there were many obstacles to tackling the problem, other than the local ones of resources in a difficult period at Elstree'.<sup>160</sup>

### **Clinical trials and commercial heat-treated products**

**23.82** A meeting took place at the BPL on 15 December 1982 to discuss the 'implications for the Haemophilia and Blood Transfusion Services of Commercial Introduction of "Hepatitis-Safe" Factor VIII and IX'. The minutes of the meeting reported on the expected

---

<sup>157</sup> Dr Smith – Day 59, page 62

<sup>158</sup> Dr Foster's report on the Budapest conference [SNB.010.4452]

<sup>159</sup> Dr Foster's statement on viral inactivation to 1985 [PEN.012.1438] at 1457

<sup>160</sup> Dr Smith's statement on viral inactivation to 1985 [PEN.012.1551] at 1556

introduction of commercial heat-treated concentrates into the UK market and expressed a need for, 'centralised, fully controlled prospective trials of "HS" materials, best operated through a properly executed National Clinical Trial lodged with the Regulatory Authority'. It was proposed that: (a) random exploitation of the haemophilia service by commercial organisations for the study of 'hepatitis-safe' products should be discouraged; (b) the haemophilia services should create a formal basis for controlled clinical trial of alleged 'hepatitis-safe' products in line with the requirements of the Medicines Act; (c) the haemophilia services, the PHLS and the NBTS should combine resources in a manner likely to advance economic treatment of NHS haemophilia patients with safe products.<sup>161</sup>

**23.83** Professor Cash's reaction to the proposals illustrated the difficult relationships between representatives of senior management from time to time. He described it as a 'very difficult' meeting. He felt that English colleagues were party to a proposition that UK clinical trials of the new products should be encouraged, to the advantage of England. He thought that the proposals were a sophisticated marketing exercise set up by US fractionators, and that the meeting had been designed to undermine the Scottish service's commitment to self-sufficiency and, though less obviously, collaboration between BTS and SNBTS scientists.<sup>162</sup>

**23.84** In his view the Scots were considered to be troublesome, not only by the commercial sector, but by the DHSS. Professor Cash believed that Scottish opposition to such a proposal would have been known. He was also somewhat upset that his co-operation was being sought when he had pressed without success for some years for a closer relationship between the two fractionators in research and manufacture.<sup>163</sup> He was anxious that the UK's small cohort of previously untreated patients should not be used to test US products and so be lost to clinical testing of domestic products. He recognised that the products required to be tested, but thought that that might be done in Italy or New York.<sup>164</sup>

**23.85** Professor Cash's evidence reflected his attitude at the time. He believed there was a lack of commitment at the level of senior management of the National Blood Transfusion Services in the two countries to integration of research and production. Professor Cash commented that relationships between Mr Watt and Dr Lane were seriously strained.<sup>165</sup> He thought Dr Smith had left the PFC after falling out with Mr Watt.<sup>166</sup> He himself had serious disagreements with the BPL management.<sup>167</sup> Professor Cash was never sure how far Dr Smith had the support of senior management with regard to his collaboration with Dr Foster.<sup>168</sup> Professor Cash commented that he had lost control at the meeting, and that discussion had become heated.<sup>169</sup>

**23.86** Following this meeting, Professor Cash sent Dr Lane a letter dated 17 December 1982,<sup>170</sup> with a copy to Dr Harold Gunson, in which he outlined his objections to the course of action proposed. In his letter Professor Cash indicated that:

<sup>161</sup> Minutes of meeting [DHF.003.0059]. The meeting was attended by Professor A Bloom, Dr C Rizza, Dr H Gunson, Dr J Craske, Dr R Lane and Dr M Harvey, as well as Professor Cash of the PFC and Dr Smith of BPL/PFL. See also Preliminary Report, paragraph 11.90.

<sup>162</sup> Professor Cash – Day 43, page 37

<sup>163</sup> Professor Cash – Day 43, pages 18–27; Professor Cash's statement on viral inactivation to 1985 [PEN.012.1912] at 1917

<sup>164</sup> Professor Cash – Day 43, pages 28–29

<sup>165</sup> Professor Cash's statement on viral inactivation to 1985 [PEN.012.1912] at 1915

<sup>166</sup> Ibid [PEN.012.1912] at 1916

<sup>167</sup> Ibid [PEN.012.1912] at 1916–19

<sup>168</sup> Ibid [PEN.012.1912] at 1915

<sup>169</sup> Professor Cash – Day 43, page 31

<sup>170</sup> Professor Cash – Day 43, pages 31–32; Professor Cash's letter [SNB.004.3163]



I do not believe it is in the best interests of the NHS Fractionation Centres, at this time, to encourage the commercial manufacturers to undertake clinical trials with a view to obtaining product licences ....

I would therefore conclude that, at the present time, it is in our (British Transfusion Services) best interests to permit the commercial people all the freedom they desire. I fully sympathise with the sentiments expressed at our meeting, but I am totally convinced that the proposed action is tactically wrong at this time, and will have serious consequences for us all if pursued.

The solution to our problem rests, as I said at the meeting on the 15th December, in thinking and acting very much more positively – I refer to the problem of getting BPL and PFC to work together at all levels. I now deeply regret that the joint PFC/BPL meeting on factor VIII concentrates that I proposed in a letter to you dated 19th December, 1980 did not take place. However, we must now surely consider this as ‘water under the bridge’ and get down to the urgent task of bridge building. I’m bound to conclude that up to the present time we, as professionals, have failed and the time has come for a joint meeting of the top managers. I include in this context senior members of our respective employing authorities. It is my intention to see what I can do to build these bridges. I do not regard the existing furtive arrangements, as regards factor VIII, between Jim Smith and Peter Foster, however good they may be, as a sound basis upon which the NHS fractionators can combat the commercial people.

**23.87** Dr Lane replied to Professor Cash on 21 December 1982 suggesting that it had been agreed that: ‘Arthur Bloom and Charles Rizza should inform the Haemophilia Directors of their reasonable right to know the proper basis supporting manufacturers’ claims of safety for products in connection with hepatitis-reduced Factor VIII now about to reach the UK market’ and informing Professor Cash that: ‘since you clearly have altered your view since the meeting, it would seem right that your letter should have been addressed to the Chairman or at least copied to him, since he might feel that further discussion was necessary’.<sup>171</sup> Professor Cash replied on 29 December 1982, in more conciliatory terms, suggesting that ‘perhaps the best way forward would be for you to discuss the matter with Harold and feel entirely free to further discuss the problem with Arthur, if you so wish’.<sup>172</sup>

**23.88** The correspondence between Professor Cash and Dr Lane following the meeting of 15 December 1982 indicated a degree of tension between the BPL and the PFC concerning the approach to be taken with regard to the likely introduction of commercial heat-treated products and, more generally, as regards cooperation/bridge-building between the BPL and the PFC on viral inactivation (and in particular the relationship between Dr Foster and Dr Smith).<sup>173</sup> There is a problem with Professor Cash’s position generally that was highlighted by Professor van Aken: there was a conflict of interest inherent in Professor Cash advising government on the approach to adopt to commercial producers in a competitive market, and in heading the SNBTS which was a producer of products in that market.<sup>174</sup> The Netherlands had a different administrative and licensing structure.<sup>175</sup>

<sup>171</sup> Dr Lane’s letter [SNB.004.3160]. It is clear from [SNB.004.3159] that the Chairman of the meeting held on 15 December 1982 was Arthur Bloom.

<sup>172</sup> Professor Cash’s letter to Dr Lane [SNB.004.3159]

<sup>173</sup> Professor Cash – Day 43, page 36; Professor Cash’s statement on viral inactivation to 1985 [PEN.012.1912] at 1917–18. See also Dr Perry’s statement on viral inactivation to 1985 [PEN.012.1759] at 1765–66

<sup>174</sup> Professor van Aken – Day 47, page 65

<sup>175</sup> Professor van Aken – Day 47, pages 66–68

**23.89** Professor Cash's conclusion that it was in the best interests of the British Transfusion Services to permit commercial producers all the freedom they desired, which might have included sale of commercial products without clinical trials in the UK, might have conserved the British haemophilia population for trial of domestic products, but that would have been a particularly partial case to advance.

**23.90** Professor Bloom and Dr Rizza wrote to the Haemophilia Centre Directors on 11 January 1983 indicating that the Hepatitis Working Party was discussing plans for clinical trials of these products.<sup>176</sup> On 10 January, the Public Health Laboratory Service (PHLS) wrote to the DHSS enclosing a draft letter intended for publication in *The Lancet* supporting prospective trials of commercial products.<sup>177</sup> It appears that by the end of March 1984 clinical trials had been completed of one product, Hemofil HT, at St Thomas' hospital in London.<sup>178</sup> The Scottish response to the invitation to participate in clinical trials of the commercial products is discussed in Chapter 15, *Knowledge of Viral Hepatitis 2 – 1975 to 1985*, at paragraphs 15.143 to 15.144. Professor Christopher Ludlam refused to participate.<sup>179</sup> Professor Cash promoted a Scottish study of patients who had received PFC heat-treated products. The difference in interests between Scotland and the rest of the UK, which had its origins in the dependence of England and Wales on imported products and Scotland's commitment to self-sufficiency, was implicit in these developments.

### Evidence on state of cooperation between Dr Foster and Dr Smith

**23.91** Professor Cash also expanded in his written evidence on what was meant by the mention in his letter of 17 December of 'the existing furtive arrangements' between Dr Foster and Dr Smith, noting that:

There is no doubt that when I look in 2010 at the proposition that Peter Foster and Jim Smith's interactions were 'furtive', an apology is due. I'm afraid the temperature in this meeting got too high and some of us became extremely anxious that all the SNBTS had stood for was to be swept aside by market place considerations. I suspect that Jim Smith and Peter Foster were aware that in 1980 I had sought to persuade Jim's boss (Dr Lane) that we really ought to be making collaboration between BPL and PFC open, intensive and a high priority, and that this proposal had been rejected. Despite this, and at that time unknown to me, Dr Smith elected to work closely with former PFC colleagues.<sup>180</sup>

**23.92** During his oral evidence Professor Cash was asked whether 'furtive' was perhaps simply the wrong word and replied as follows:

Yes, I have no hesitation. I think the fundamental problem I had – and it wasn't about Peter and Jim Smith – it was about: how did the SNBTS as a whole – this working group that we talked about – get engaged in the area of fractionation?

<sup>176</sup> Professor Cash – Day 43, pages 49–51; Professor Bloom and Dr Rizza's letter [DHF.003.0892]. Note that the date recorded on the letter (11 January 1982) would appear to be incorrect and that a date one year later (11 January 1983) appears correct: see Inquiry Counsel's explanation – Day 27, pages 47–51

<sup>177</sup> Letter from PHLS to DHSS [DHF.001.7106]

<sup>178</sup> Professor Cash – Day 43, pages 39–42; Colombo et al, 'Transmission of non-A, non-B Hepatitis by Heat-treated Factor VIII Concentrate', *The Lancet*, 6 July 1985; 1–5 [LIT.001.0369]. And see Memorandum to Haemophilia Centre Directors of 29 March 1984 [DHF.002.8963]

<sup>179</sup> Professor Ludlam's letter to Miss Spooner of 10 April 1984 [SNF.001.3211]

<sup>180</sup> [PEN.012.1912] at 1919

And that was difficult because it was heavily controlled by John Watt and so on, and I felt that Peter and Jim were often in bed. So I didn't regard them as being furtive ....<sup>181</sup>

Professor Cash added that he supported what was going on, and that Dr Smith and Dr Foster were getting on with the work.<sup>182</sup>

**23.93** Professor Cash's concerns appear to have been related not to the state of the cooperation between Dr Foster and Dr Smith itself, but rather to the lack of a formal structure surrounding their cooperation. Professor Cash also appears to have been impressed by Dr Foster's abilities, going so far as to note at one point during his evidence – admittedly with exaggeration – that, 'if we had had 25 Peter Fosters, we would have been fractionating on the moon'.<sup>183</sup>

**23.94** Dr Foster's written evidence to the Inquiry also expressed the view that the issue raised by Professor Cash at the time was the lack of a formal structure for cooperation rather than any breakdown in cooperation with the BPL and Dr Smith.<sup>184</sup>

**23.95** Dr Foster's written evidence indicated, however, that his preference was 'to exchange information with Dr Smith and his staff on a less formal basis than Professor Cash may have preferred', although he 'would have been happy to accept a more formal arrangement, if this had been requested'.<sup>185</sup> When asked to expand on this point during the Oral Hearings, Dr Foster said that with scientists who are dealing with the same problems, talking face-to-face was the best way to proceed in terms of communications, over the phone and having meetings, and obviously in correspondence, and in reciprocal visits to each other's facilities.<sup>186</sup>

**23.96** When asked, both Dr Foster and Dr Smith confirmed that, in their view, the reporting between the PFC and the BPL was reciprocal. Dr Foster noted in his written evidence that:

To the best of my knowledge the exchange of information between the SNBTS and the BPL/PFL was reciprocal, except when precluded by a requirement for confidentiality, such as the arrangements between the PFC and Dr Johnson ... and the period when BPL were planning to patent the process used to prepare 8Y ....<sup>187</sup>

**26.97** Dr Smith's response was:

I would have continued to inform PFC without constraint of anything notable coming out of our still very tentative work on pasteurisation, and later dry-heating, in 1983. But I cannot document that.<sup>188</sup>

---

<sup>181</sup> Professor Cash – Day 43, page 44

<sup>182</sup> Professor Cash – Day 43, pages 44–45

<sup>183</sup> Professor Cash – Day 57, page 138

<sup>184</sup> See also Dr Perry's statement on viral inactivation to 1985 for a similar view – [PEN.012.1759] at 1766

<sup>185</sup> Dr Foster's statement on viral inactivation to 1985 [PEN.012.1438] at 1460

<sup>186</sup> Dr Foster – Day 41, pages 140–141

<sup>187</sup> Dr Foster's statement on viral inactivation to 1985 [PEN.012.1438] at 1461

<sup>188</sup> Dr Smith's statement on viral inactivation to 1985 [PEN.012.1551] at 1558

**23.98** Dr Perry said:

Although there continued to be no formal collaboration or reporting between Scotland and England the established cooperation continued particularly between senior operational managers at PFC (myself and Dr Foster) and their counterparts at BPL (Drs Smith and Snape).<sup>189</sup>

Dr Perry's most important contribution on this issue was that it did not have any impact on the local PFC development programme, which continued to focus on the development and preparation of a pasteurised product for initial clinical trial.<sup>190</sup> He emphasised that it was important to recognise that the pursuit and maintenance of self-sufficiency and product yield were of high priority for the SNBTS, particularly in light of the knowledge that the eventual introduction of NHS heat-treated products would, as a result of yield penalties, potentially reduce the overall amount of Factor VIII available to patients.<sup>191</sup>

**23.99** Notwithstanding the written exchanges, and the background of difficult relationships among senior management of the public sector organisations which they reflect, Dr Smith and Dr Foster continued their dialogue.<sup>192</sup> In addition, there were more formal joint projects involving the two organisations.<sup>193</sup> In the ordinary course of business, the exchange of information was reciprocal except where there was a requirement for confidentiality, arising from external contracts or from patent proceedings.<sup>194</sup>

**23.100** On a wider front, informal contacts with scientists in the pharmaceutical industry provided intelligence on developments that were not widely publicised. Dr Prowse of the PFC had thus heard that Baxter/Hyland's product disclosed at Budapest was dry heat-treated.<sup>195</sup> After testing, the dry heating applied to Hemofil T proved less effective than pasteurisation.<sup>196</sup> That was consistent with information circulating informally within the industry, and within UK Government circles, in 1983 and 1984.<sup>197</sup> It appears that while regulatory reporting on Hemofil awaited completion of the formal studies required by International Society of Blood Transfusion (ISBT) protocols, dissemination of the adverse results was a priority for researchers.

**23.101** Against this background of increased industry interest in heat treatment, the PFC (Dr Cuthbertson and Dr Pepper) did some experiments in dry heat treatment of Factor VIII.<sup>198</sup> Meanwhile, work on pasteurisation continued. There was considerable activity at the beginning of 1983 (summarised in paragraphs 11.96 to 11.115 of the Preliminary Report), leading up to the agreement of Professor Forbes and Professor Ludlam on 22 March 1983 to take part in clinical trials of the PFC Factor VIII product as part of a strategy for developing heat-treated products for general use.<sup>199</sup> However, within a few weeks AIDS among haemophilia patients in the USA was widely publicised and the context

<sup>189</sup> Dr Perry's statement on viral inactivation to 1985 [PEN.012.1759] at 1767. Dr Perry agreed during his oral testimony (Day 45 – page 35) that the order of Drs Smith and Snape should be reversed so as to reflect the correct counterparts at the PFC and the BPL. Dr Perry also noted that Dr Snape was the quality assurance manager at the BPL.

<sup>190</sup> Dr Perry's statement on viral inactivation to 1985 [PEN.012.1759] at 1766

<sup>191</sup> Dr Perry – Day 45, pages 28–29

<sup>192</sup> Dr Foster – Day 41, pages 140–141

<sup>193</sup> Dr Foster's statement on viral inactivation to 1985 [PEN.012.1438] at 1459–60

<sup>194</sup> Dr Foster – Day 41, page 141; Dr Foster's statement on viral inactivation to 1985 [PEN.012.1438] at 1461

<sup>195</sup> Dr Foster – Day 41, pages 142–143

<sup>196</sup> Dr Foster – Day 41, pages 143–145; Mannucci, 'AIDS, hepatitis and haemophilia in the 1980s: memoirs from an insider', *Journal of Thrombosis and Haemostasis*, 2003; 1:2065–69 [LIT.001.1101]; Colombo et al, 'Transmission of non-A, non-B Hepatitis by Heat-treated Factor VIII Concentrate', *The Lancet*, 6 July 1985: 1–5 [LIT.001.0369]

<sup>197</sup> Dr Foster – Day 41, pages 145–148

<sup>198</sup> Dr Foster – Day 41, page 143

<sup>199</sup> Minutes of Haemophilia and Blood Transfusion Working Group, 22 March 1983 [SNB.001.5183]

changed from elimination of NANB Hepatitis. Developments in 1983 are considered in the context of that new threat.

**23.102** The change of emphasis was reflected in the Netherlands also. Professor van Aken said of the early 1980s:

The growing concern was mainly related to AIDS and with regard to non-A, non-B hepatitis that was at that time more or less, I would say, accepted as a side effect of transfusion and of the administration of plasma components. That had not the same urgency as it gradually got later on because in the beginning, when I came in board in CLB on the board, that was not the main concern we had. The first real concern about transmission of the diseases, of viral diseases, was AIDS.<sup>200</sup>

### Research at the Protein Fractionation Centre: Progress in 1983 and 1984

#### 1983

**23.103** In the first few months of 1983 the PFC continued its work on the pasteurisation of Factor VIII. Dr Foster reported on developments to Dr Smith and the PFC appears to have been keenly aware that commercial companies were likely to launch heat-treated Factor VIII in the near future.<sup>201</sup> In a memo to Mr Watt, Heads of Department, Section Managers and Dr MacLeod dated 11 January 1983, Dr Foster explained that 'this could well have major implications for the NHS ... and it is therefore recognised that there is some urgency in demonstrating that the NHS has the capability to manufacture products of this kind'.<sup>202</sup> Clinical trials of small amounts of high purity zinc-precipitated Factor VIII which had been heated at 60°C for 10 hours were planned with the aim of developing a product with a 'reduced risk of transmitting hepatitis'.<sup>203</sup> During the meeting of the Haemophilia and Blood Transfusion Working Group on 22 March 1983, it was decided that Professor Charles Forbes and Professor Ludlam were to carry out these trials in coordination with Professor Cash.<sup>204</sup>

**23.104** As regards Factor IX, research into heat treatment to reduce the risk of hepatitis was reported to be underway.<sup>205</sup> However, it was noted that animal studies would be needed in order to confirm that heat-treated Factor IX was not thrombogenic.<sup>206</sup>

#### Recognition by fractionators of the risks posed by AIDS

**23.105** During the first few months of 1983 the focus of the PFC's research and development programme remained on methods which could inactivate hepatitis in blood products. However, a subtle shift had begun to take place. Fractionators were becoming alive to the possible risks which AIDS might pose to the blood supply (and hence the possible enhanced need for viral inactivation processes which could deal with such risks).

<sup>200</sup> Professor van Aken – Day 47, pages 74–75

<sup>201</sup> See letter from Dr Foster to Dr Smith dated 20 January 1983 including technical details of the PFC's work on pasteurisation [SNB.007.3407]

<sup>202</sup> Dr Foster's memorandum [SNB.005.8435]. See also the minutes of the meeting of Directors of the SNBTS and Haemophilia Directors of 21 January 1983 [SNB.001.5160] at 5163, where a similar view was expressed.

<sup>203</sup> Minutes of the meeting of Directors of the SNBTS and Haemophilia Directors of 21 January 1983 [SNB.001.5160] at 5163

<sup>204</sup> Minutes of Haemophilia and Blood Transfusion Working Group, 22 March 1983 [SNB.001.5183] at 5184

<sup>205</sup> Minutes of the meeting of Directors of the SNBTS and Haemophilia Directors of 21 January 1983 [SNB.001.5160] at 5164

<sup>206</sup> Minutes of the meeting of Directors of the SNBTS and Haemophilia Directors of 21 January 1983 [SNB.001.5160] at 5164. See also the memo from Dr Foster to Mr Watt and Dr Perry dated 17 February [SNB.007.3474] in which Dr Foster proposed setting up a dog colony to test for thrombogenicity. For further details of the period January–April 1982 see Preliminary Report, paragraphs 11.96–11.115.

**23.106** This issue of AIDS was referred to very briefly (admittedly with a question mark) as a ‘problem’ in a presentation entitled ‘Methods for Preparing Non-infective Blood Products’ given by Dr Foster to the Haematology Department of the Royal Infirmary of Edinburgh (RIE) on 8 March 1983.<sup>207</sup> When asked to expand on what this meant, Dr Foster explained that he was beginning to think that AIDS might be caused by an infectious agent that would potentially have to be taken into consideration in research on virus inactivation: research was not going to be focusing exclusively on hepatitis.<sup>208</sup>

**23.107** AIDS was also discussed (in general terms and in the context of high-risk donors) during the meeting of the Haemophilia and Blood Transfusion Working Group on 22 March 1983, the minutes of which note that members were reminded of the recent articles both at home and abroad about AIDS, and that there was concern that AIDS might appear in the UK.<sup>209</sup> However, there is no record that the potential impact of AIDS on the PFC’s viral inactivation programme was discussed. According to Dr Perry, the apparent lack of a cross-reference between AIDS and heat treatment in this discussion was unsurprising as, in his view, ‘at that time it was far from established or accepted that AIDS had a virus aetiology’.<sup>210</sup> Dr Foster was of the same view, although his oral evidence on his presentation of 8 March 1983, referred to at paragraph 23.106 above, indicates a degree of ambivalence. He stated in his written evidence:

At this time (22 March 1983), the cause of AIDS was not known. Even if an infectious agent was assumed to be responsible, neither the nature of the infectious agent, nor its sensitivity to heat were known. Therefore there was no basis, other than speculation, for a ‘cross-reference’ between the topics of heat treatment and AIDS.<sup>211</sup>

**23.108** Dr Perry advanced another possibility for the lack of a cross-reference between AIDS and heat treatment in the minutes of this meeting. According to Dr Perry, the failure to make a connection between these two issues in the minutes did not necessarily imply that the meeting had not discussed the two potentially related topics. He suggested instead that it seemed more likely that any such discussion had been inconclusive and therefore had not been recorded.<sup>212</sup> Professor Cash, in contrast, was of the view that the lack of a reference was to be expected indicating that, ‘heat treatment was a process that was assumed might inactivate all viruses transmitted by plasma products. Thus in March 1983 a specific link between the two would have been taken for granted’.<sup>213</sup>

**23.109** Only a few weeks later, in May 1983, the potential impact of AIDS on the PFC’s strategy had become more apparent. On 3 May 1983 Dr Foster sent a memo entitled ‘Heat Treatment of FVIII. A strategy’ to Mr Watt and the PFC’s Heads of Department.<sup>214</sup> The memo indicated that:

Until very recently the objective of our heat treatment programme was to cope with the hepatitis problem in haemophiliacs.

Because severe haemophiliacs have already been heavily exposed to untreated products then only mild and moderate haemophiliacs could benefit from a

<sup>207</sup> Dr Foster’s presentation [SNB.007.3503] at 3507

<sup>208</sup> Dr Foster – Day 41, pages 150–151

<sup>209</sup> Minutes of Haemophilia and Blood Transfusion Working Group, 22 March 1983 [SNB.001.5183] at 5184

<sup>210</sup> Dr Perry’s statement on viral inactivation to 1985 [PEN.012.1759] at 1768

<sup>211</sup> Dr Foster’s statement on viral inactivation to 1985 [PEN.012.1438] at 1461

<sup>212</sup> Dr Perry’s statement on viral inactivation to 1985 [PEN.012.1759] at 1767–68

<sup>213</sup> Professor Cash’s statement on viral inactivation to 1985 [PEN.012.1912] at 1920–21

<sup>214</sup> Dr Foster’s memorandum [SNB.007.3635]

treated product (in the foreseeable future). It was estimated that the mild/moderate group could use up to 30% of the total FVIII. This estimate, plus the fact that these patients are presently likely to be treated with single donor cryoprecipitate have determined our present strategy i.e. that we will:

- (1) Plan for 4–6 pilot scale lots during 1983.
- (2) Design a full-scale plant to handle 30% production for 1984/85 at the earliest.
- (3) Mild and moderate haemophiliacs can continue to receive single donor cryo meanwhile.

The possibility that another more serious infectious agent (AIDS) is now involved suggests that we may need to review this strategy. In the new scenario:-

- i) The haemophiliacs most at risk are the severes rather than the mild and moderates.
- ii) There is already evidence of a panic recourse to cryoprecipitate.

In the absence of any hard data, heat treatment (of everything) looks at the moment to be the most likely possibility that we have to face up to. If this is so then we will have to plan to pasteurise all of the FVIII (rather than 30%) and we may also want to review the timescales noted above.

**23.110** The memo indicated further that decisions will probably be taken according to a 'worst case' hypothesis and suggested that:

There may therefore be a case for accelerating our heat treatment programme. While I do not disagree with point (2) above it may be possible to introduce an intermediate stage, still using the pasteurisation cabinets. We probably have most of the equipment to do this already.<sup>215</sup>

**23.111** A worked example followed outlining how this 'intermediate stage' would operate in practice based on an input of 1000kg of fresh frozen plasma.

**23.112** Two days later, on 5 May, Mr Watt wrote to Professor Cash.<sup>216</sup> His letter outlined the existing pilot-scale approach to heat treatment and preliminary results of heat treatment studies which showed that heating for a shorter period at a higher temperature (70°C for less than an hour) was more effective in killing virus than heating for 60°C at 10 hours. The letter also advocated an acceleration of the pasteurisation programme, noting that:

In view of recent news exposure of (?) [*sic*] infectivity of Factor VIII concentrates we have made a re-assessment of heat treated concentrate based on a careful step-by-step appraisal of a series of pilot-scale lots.

In most areas of the development I believe we now possess sufficient data to allow, by adopting a few calculated risks, this programme to be speeded up substantially .... My colleagues are engaged in a costing for the expedited programme in case public opinion rather than science may dictate the best course of action.<sup>217</sup>

<sup>215</sup> The memo included Dr Foster's tentative suggestions as how such a process would operate [SNB.007.3635] at 3636

<sup>216</sup> Mr Watt's letter [SNB.007.3638]

<sup>217</sup> Mr Watt's letter [SNB.007.3638] at 3640

**23.113** Professor Cash responded to this letter on 1 June 1983 noting that he considered the last part of Mr Watt's letter (ie the proposal to accelerate the heat treatment programme) to be the most important and that 'as you say, public opinion may eventually press us heavily'.<sup>218</sup> However, the letter also indicated that there were insufficient funds:

Right now we must conclude that with the existing set of instructions the Agency [the CSA] has received from SHHD with regard to the way it is to spend its development monies, and noting the reaction of the Deputy Chief Medical Officer to the concept that heat treated factor VIII is related to the interests of the Medicines Inspectorate, then there are no funds available in 1983–1984 for your proposals. However, in the light of the current pressures (AIDS etc.) the Department may wish to reconsider its instructions to the CSA and/or find additional monies (less likely!). In any event, I think we can be certain that a full and separate case will be required by the SHHD as soon as possible and your Report on PFC's needs will be of considerable importance.

**23.114** The letter drew Mr Watt's attention to two 'inextricably linked items' ('implications for PFC of optimal additive blood bags' and 'pilot stage of heat-treatment of factor VIII') and went on to ask Mr Watt to 'take these two items' and 'put them together in a single package (story) directed towards the heat treatment of factor VIII' – ie a proposal which could be put before the SHHD.

**23.115** The Inquiry asked various witnesses questions focused on gaining an understanding of: the circumstances which led Dr Foster to write his memo of 3 May 1983; the plans outlined in this memo; the subsequent correspondence between Mr Watt and Professor Cash; and the plan to seek more funds from the SHHD for the acceleration of the pasteurisation programme.<sup>219</sup>

**23.116** In his written evidence,<sup>220</sup> Dr Foster explained that the trigger for his memo was the report in *The Lancet* of 30 April 1983 of AIDS infections in 11 haemophiliacs in the USA and three in Spain who had been treated with commercial factor concentrates.<sup>221</sup> According to Dr Foster, 'these reports caused me to consider the potential implications for our strategy on the development of heat treatment, should it be found that this syndrome was caused by an infectious agent'.<sup>222</sup> Severe haemophiliacs were more at risk of AIDS as they 'received much more treatment'.<sup>223</sup>

**23.117** Dr Smith's view was that, at this time, most fractionators thought it likely that AIDS was caused by a blood-borne virus, indicating that Montagnier and Barré-Sinoussi's seminal article of 20 May on the isolation of the HIV virus<sup>224</sup> offered 'strong support' for this 'working hypothesis'.<sup>225</sup> The Montagnier/Barré-Sinoussi article post-dated Dr Foster's memo and could not have been something he would have been aware of in preparing his

<sup>218</sup> Professor Cash's response [SNB.007.3708]

<sup>219</sup> Inquiry's schedule of questions on viral inactivation to 1985 [PEN.012.1531] at 1534, paragraphs 17–18

<sup>220</sup> Dr Foster's statement on viral inactivation to 1985 [PEN.012.1438] at 1461

<sup>221</sup> Gordon, 'Factor VIII products and disordered immune regulation', *The Lancet*, 30 April 1983; 991 [LIT.001.0911]; Lissen et al, 'AIDS in haemophilia patients in Spain', *The Lancet*, 30 April 1983; 991 [LIT.001.0403]

<sup>222</sup> Dr Foster's statement on viral inactivation to 1985 [PEN.012.1438] at 1461–62

<sup>223</sup> Dr Foster – Day 41, pages 153–154

<sup>224</sup> Barré-Sinoussi et al, 'Isolation of a T-lymphotropic retrovirus from a patient at risk for acquired immune deficiency syndrome (AIDS)', *Science*, 1983; 220:868–871 [LIT.001.0058]

<sup>225</sup> Dr Smith's statement on viral inactivation to 1985 [PEN.012.1551] at 1559



memorandum of 3 May.<sup>226</sup> Dr Smith further explained in his oral evidence that the insight that he had at this time (based on information probably provided by Dr Cumming) was that:

[There was] a huge overlap between the sexually transmitted diseases and the blood borne diseases. So anyone with that mindset would tend to be making a conclusion perhaps before the evidence really justified it.<sup>227</sup>

**23.118** Professor Cash also confirmed in his written evidence that the threat of AIDS was becoming clearer by May 1983, noting that:

As far as I recall, by May 1983 we were a little more certain that AIDS was transmitted by plasma products and that the clinical consequences were very much more serious than viral hepatitis. It follows that Dr Foster's reported efforts to accelerate our heat treatment programmes were entirely appropriate.<sup>228</sup>

**23.119** In his oral evidence, Dr Foster explained how the plan outlined in his memo of 3 May 1983 was intended to operate. He noted that he had difficulty recollecting exactly what he meant by the introduction of an 'intermediate stage' for the acceleration of the heat treatment programme.<sup>229</sup> However, when asked, he indicated that the phrase should be read as meaning a plan which could advance heat treatment as quickly as possible<sup>230</sup> and that, in practice, this meant a 'temporary arrangement pending the fully engineered process design' (ie pending the design of a full-scale plant).<sup>231</sup> The plan would, therefore, have amounted to a wholesale move to pasteurisation using the existing pasteurisation cabinets, albeit on a temporary basis.<sup>232</sup>

**23.120** Dr Foster gave further background information in his written statement. He indicated that the original plan for the pasteurisation process involved 'heating large volumes of protein in a concentrated sugar solution' in a single large vessel, but that:

[E]arly large-scale experiments demonstrated that the heating-up and cooling-down of the mixture took a very long time, during which more factor VIII was destroyed than had been experienced in small-volume laboratory experiments.<sup>233</sup>

**23.121** To prevent this loss of Factor VIII, Dr Foster considered the design of a recirculating system in which the solution would be passed through a heat exchanger to accelerate heating-up and cooling-down. However, according to Dr Foster, this was not straightforward. An alternative process was adopted which involved 'dispensing the mixture into 1 litre bottles which could then be heat-treated in the PFC spray cabinet that was used to pasteurise albumin'. Dr Foster explained that this procedure enabled pilot-scale production of Factor VIII to be accelerated.<sup>234</sup> This pilot-scale process did not extend to the wholesale switch to pasteurisation using pasteurisation cabinets which was proposed in his memorandum of 3 May 1983.<sup>235</sup> As outlined further below in the discussion of the events of 1984, wholesale switch to pasteurisation ultimately never occurred.

---

<sup>226</sup> Dr Foster – Day 41, page 159

<sup>227</sup> Dr Smith – Day 59, page 72

<sup>228</sup> Professor Cash's statement on viral inactivation to 1985 [PEN.012.1912] at 1921

<sup>229</sup> Dr Foster – Day 42, pages 2–3

<sup>230</sup> Dr Foster – Day 42, page 3: 'I was looking to see how we can advance this as quickly as possible'.

<sup>231</sup> Dr Foster – Day 42, page 5

<sup>232</sup> Dr Foster – Day 42, page 4

<sup>233</sup> Dr Foster's statement on viral inactivation to 1985 [PEN.012.1438] at 1462

<sup>234</sup> Ibid [PEN.012.1438] at 1462

<sup>235</sup> Dr Foster – Day 41, pages 11–12

## Funding issues

**23.122** The Inquiry posed various questions to witnesses aimed at clarifying the outcome of Professor Cash's request in his letter of 1 June 1983 for the PFC to put together a funding proposal for the heat treatment programme.

**23.123** In summary, the position appears to have been as follows:

- At the end of May 1983, the Blood Transfusion Service Sub-Committee of the Common Services Agency (CSA) agreed that a funding proposal for the 'pilot stage of heat treatment of factor VIII' should be submitted to the SHHD as a bid against certain of the money available to meet the costs of the recommendations arising from the Medicines Inspectorate inspection of the PFC.<sup>236</sup> The reason for attempting to link heat treatment to the recommendations of the Medicines Inspectorate appears to have been largely a pragmatic one, based on the fact that a large sum of money (circa £650,000) had already been allocated for compliance with the Medicines Inspectorate's recommendations relating to the quality of the PFC's facility.<sup>237</sup>
- A proposal was duly submitted by the CSA to the SHHD in June 1983.<sup>238</sup> The funding sought for the heat treatment of Factor VIII was for capital of £74,000 for equipment and £13,400 revenue.<sup>239</sup>
- In September 1983, the SHHD responded that the expenditure on heat treatment was not a requirement arising from the recommendations of the Medicines Inspectorate, but asked the CSA to consider making a separate submission for funding.<sup>240</sup>
- On 22 February 1984, the Blood Transfusion Service Sub-Committee approved a separate submission to the SHHD for funding for the heat treatment of Factor VIII.<sup>241</sup>
- On 23 May 1984, Dr Albert Bell of the SHHD wrote to Mr Alexander Murray (also SHHD) outlining the policy case for the heat treatment of Factor VIII, concluding, '[I]t is not for me to say how this development should be financed but I can say that it is a genuine technological advance and a failure to bring it about would be very difficult to defend'.<sup>242</sup>
- Formal authorisation of a sum of £90,000 for the heat treatment of Factor VIII was ultimately made by the SHHD in mid-August 1984.<sup>243</sup>

**23.124** There was, therefore, a delay of more than one year between the submission of the initial request for funding for heat treatment of Factor VIII and the authorisation of the amount requested, arising largely from these administrative exchanges.<sup>244</sup> Funding was one of the few aspects of the SNBTS operations in which the CSA and its committees had an active role.

<sup>236</sup> Minutes of Blood Transfusion Service Sub-Committee, 25 May 1983 [SGH.001.9769] at 9770 and 9775

<sup>237</sup> Professor Cash – Day 43, pages 66–69; Dr Perry – Day 45, pages 54–56; and Dr Cuthbertson's oral evidence – Day 46, pages 47–48 and his written statement [PEN.013.0025] at 0033

<sup>238</sup> Letter from Mr Wooller, CSA, to Mr Murray, SHHD, dated 6 June 1983 [SNB.003.7641]

<sup>239</sup> Dr Perry – Day 45, pages 47–49; Annex to Mr Wooller's letter of 6 June 1983 [SNB.003.7643] 7645

<sup>240</sup> Letter from Mr Wastle, SHHD, to Mr Wooller, CSA, dated 20 September 1983 [SNB.011.1251]; Professor Cash – Day 43, pages 74–76; See also papers for the Blood Transfusion Service sub-committee of 23 November 1983 [SGH.001.9496] at 9497

<sup>241</sup> Minutes of Blood Transfusion Service Sub-Committee, 22 February 1984 [SGH.001.9972] at 9974

<sup>242</sup> Dr Bell's letter [SGF.001.1986]

<sup>243</sup> Letter from Dr Perry to Mr Wooller, dated 13 August 1984 [SNB.007.4523] and Mr Wooller's response, dated 17 August 1984 [SNB.007.4527]

<sup>244</sup> Dr Perry – Day 45, pages 39–56 and Professor Cash – Day 43, pages 56–79 for more details on the issue of funding.

**23.125** An important question is whether this delay in the authorisation of funding resulted in a delay to the heat treatment programme. According to the witnesses asked this question by the Inquiry, the heat treatment development programme was not delayed. Dr Perry stated in his written evidence that: ‘my recollection is that notwithstanding the above funding issues concerning scale up of production and its routine introduction the development programme continued to progress at pilot scale within existing resources’.<sup>245</sup> Dr Foster echoed this view in his oral evidence:

Q. But just before we drop for today the question of funding, do you have any memory of its also being an obstacle ... that money had to be found?

A. No, it didn’t seem to me to be an issue. I thought this is so important that I thought, ‘If this is what it costs, this is what it costs and the money will come through,’ and I left that to Mr Watt and Professor Cash to sort out. It wasn’t something that seemed to me to be an obstacle.<sup>246</sup>

**23.126** During his oral evidence, Professor Cash ‘instinctively’ concurred with Dr Foster’s view.<sup>247</sup>

**23.127** Both Dr Perry and Dr Foster also explained that, in their view, the key factor which determined the progress of the pasteurisation project in the latter half of 1983 was the organisation and conduct of clinical trials and not funding.<sup>248</sup>

### Progress at PFC

**23.128** Meanwhile, on 13 June 1983 Professor Cash wrote a letter to Professor Ludlam asking him to carry out clinical trials of the first batch of pasteurised Factor VIII (batch NY 761).<sup>249</sup>

**23.129** On 15 June 1983 a meeting of the Factor VIII Safety Action Group was held, which was attended by Dr Bruce Cuthbertson, Dr Bobby Sommerville and Dr Duncan Pepper. The minutes of the meeting provide a detailed overview of the research which the PFC was undertaking at this time, which involved heating at 60°C for 10 hours followed by a 30 minute period at 70°C and testing for virus kill (using vaccinia, polio 2 and herpes simplex as model viruses) and Factor VIII loss.<sup>250</sup> The research was summarised as follows:

Considerable progress has been made at P.F.C. in producing heat treated FVIII and clinical trials should start towards the end of the summer in Glasgow and Edinburgh. No infectious model for non-A, non-B has been produced yet. The putative ‘AIDS’ virus must be considered as a potential hazard in FVIII concentrates.<sup>251</sup>

**23.130** On 27 June 1983 Dr Foster met Dr Johnson at a World Federation of Hemophilia meeting in Stockholm and learned of a potentially promising method which could be used to increase the purity of Factor VIII.<sup>252</sup> Dr Foster explained in his written evidence that the process:

<sup>245</sup> Dr Perry – Day 45, pages 54–55; Dr Perry’s statement on viral inactivation to 1985 [PEN.012.1759] at 1769

<sup>246</sup> Dr Foster – Day 42, page 14

<sup>247</sup> Professor Cash – Day 43, page 79

<sup>248</sup> Dr Perry – Day 45, pages 57–58; Dr Perry’s statement on viral inactivation to 1985 [PEN.012.1759] at 1769; Dr Foster – Day 42, page 13

<sup>249</sup> Professor Cash’s letter to Professor Ludlam [SNB.006.5498]

<sup>250</sup> Minutes of FVIII Safety Sub-Committee, 15 June 1983 [SNF.001.3730] at 3731

<sup>251</sup> Minutes of FVIII Safety Sub-Committee, 15 June 1983 [SNF.001.3730]; Preliminary Report, paragraphs 11.130–11.134

<sup>252</sup> SNBTS Briefing Paper on the Development of Heat Treatment of Coagulation Factors [PEN.013.1309] at 1364

[I]nvolved the chromatographic purification of factor VIII, in which chemicals were added to subtly modify the conformation of the factor VIII molecule to promote its attachment to a conventional ion exchange matrix.<sup>253</sup>

**23.131** In practical terms this meant that:

[I]t was conceivable that the increased purity promised by the method of Dr Johnson would enable the volume of solution to be pasteurised to be reduced about 50-fold, making the pasteurisation in 1 litre bottles potentially feasible for full-scale manufacture as well as for pilot-scale processing.<sup>254</sup>

**23.132** Dr Foster passed on this information to Mr Watt who wrote to Dr Johnson on 1 August 1983, proposing collaboration (initially on a confidential basis) and outlining various procedural issues which would have to be dealt with.<sup>255</sup> The letter to Dr Johnson also intimated Mr Watt's decision to leave the PFC on grounds referred to as 'multifactorial'.<sup>256</sup>

### Infectivity of Hyland product

**23.133** Meanwhile, on 1 July 1983, Dr Diana Walford of the DHSS wrote to Dr Harold Gunson of the Regional Transfusion Centre (RTC) in Manchester indicating that three chimpanzees given Hyland's dry-heated Factor VIII product had developed hepatitis.<sup>257</sup> It would appear that the reference to hepatitis in this letter meant Hepatitis B.<sup>258</sup> The suggestion was that Hyland's product might not be hepatitis-safe. It is not clear at exactly what point this information filtered through to the PFC for the first time. However, it is clear that Hyland had already proposed a study during the World Federation of Hemophilia meeting in Stockholm in June to evaluate whether its dry-heated Factor VIII product transmitted hepatitis.<sup>259</sup> Professor Mannucci of the University of Milan took part in this study which was carried out in Milan, Heidelberg, Paris and London, and noted in his 2003 memoirs that:

[I]t was evident from the follow up of the first few patients enrolled in our study that a large number of them had developed hepatitis. Such information was verbally communicated by me to a large number of hemophilia treaters who met in Barcelona on the occasion of the Congress of the European Society of Haematology in September 1983.<sup>260</sup>

**23.134** The ultimate outcome of the research carried out by Professor Mannucci and others into the safety of the Hyland product, which was published in July 1985, was that patients given Hyland's dry-heated product had a high prevalence of NANB Hepatitis and an absence of Hepatitis B, whereas for chimpanzees the results were the reverse (ie an absence of NANB Hepatitis and a prevalence of Hepatitis B). So, in simple terms, the fact that a chimpanzee which had been given Hyland dry-heated Factor VIII was free from NANB Hepatitis provided no guarantee that the product would not transmit NANB

---

<sup>253</sup> Dr Foster's statement on viral inactivation to 1985 [PEN.012.1438] at 1465

<sup>254</sup> Dr Foster's statement on viral inactivation to 1985 [PEN.012.1438] at 1462

<sup>255</sup> Mr Watt's letter to Dr Johnson [SNB.007.3794]

<sup>256</sup> For further details on Mr Watt's departure from the PFC and the possible impact this may have had on the PFC's heat treatment programme, paragraphs 23.244 to 23.252 below.

<sup>257</sup> Letter from Dr Diana Walford, DHSS, to Dr Harold Gunson dated 1 July 1983 [DHF.002.5668]

<sup>258</sup> Dr Foster – Day 41, page 145. The fact that the chimpanzees had developed Hepatitis B can be derived from the conclusion to Professor Mannucci's research – see paragraph 23.134 below.

<sup>259</sup> Dr Foster – Day 41, pages 143–144

<sup>260</sup> Mannucci, 'AIDS, hepatitis and haemophilia in the 1980s: memoirs from an insider', *Journal of Thrombosis and Haemostasis*, 2003; 1:2065–69 [LIT.001.1101] at 1103

Hepatitis to humans. The conclusion of Professor Mannucci's research was therefore that, 'the animal model is not reliable for NANB hepatitis transmission studies'.<sup>261</sup>

**23.135** The results of the research were already widely known before publication in 1985. By late summer 1983, knowledge of the failure of the Hyland dry-heated product to inactivate hepatitis appeared to be fairly widespread. By January 1984, the SNBTS was certainly aware that the Hyland product was infective as evidenced by the minute of the meeting of the Factor VIII Study Group of 12 January 1984 which indicated that 'the current Hyland product ... is still infective'.<sup>262</sup>

### Progress in England

**23.136** By late July 1983, consideration by the authorities in England of their own approach to heat treatment was ongoing. A report by Dr Craske, which was subsequently incorporated into the annual report of the UK Haemophilia Centre Directors Hepatitis Working Party for 1982–83, included a general overview of the viral inactivation landscape outlining the various forms of viral inactivation which were being developed (ie using chemicals, pasteurisation and dry heat treatment), and the commercial heat-treated products which were likely to become available. The report commented that it was possible that Factor VIII concentrate prepared from plasma donations obtained in the USA might be contaminated with a putative infectious agent associated with the cause of AIDS.<sup>263</sup> It did not, however, suggest a specific direction which should be taken.

**23.137** An unpublished Central Blood Laboratories Authority (CBLA) paper on heat treatment dated 26 July 1983 did comment on the direction which was likely to be taken in England, though for marketing rather than purely scientific reasons.<sup>264</sup> It noted that pasteurisation was 'more homogeneous and efficient' than dry heat treatment, but that it was 'associated with more molecular damage of heat unstable proteins than occurs by the dry heat route' and appeared to favour dry heat treatment on the basis that this 'will allow BPL to present to clinical managers of haemophilia a product carrying equivalent weight of claims for safety as those of rival commercial organisations'. The report also indicated that 'it [had] been shown possible to maintain greater than 95% of factor VIII activity in the finished product after heating at 75°C for ten hours or heating at 60°C for 24 hours' and that this dry-heated product was 'being advanced with high priority to enable manufacture to become routine by the late summer 1983'. At this point, therefore, shortly before Mannucci was giving preliminary indications of the lack of efficacy of the dry-heated Hyland product in Barcelona, dry heat treatment was the preferred viral inactivation process in England.

**23.138** Various witnesses commented critically on aspects of the CBLA report of 26 July 1983. Dr Smith did not know who had written it and indicated that the date for routine manufacture of 'summer 1983' was 'extraordinarily optimistic' as by 'late summer 1983 we only had our very first results on dry heating'.<sup>265</sup> Dr Smith also pointed out that, while correct in principle, the reference to pasteurisation being 'associated with more molecular damage' had to be read loosely as one would not pasteurise or dry heat in the same

<sup>261</sup> Colombo et al, 'Transmission of NANBH by heat-treated factor VIII concentrate', *The Lancet*, 1985; 2:1–4, [LIT.001.0369] at 0371. See Dr Cuthbertson – Day 46, pages 59–61 for discussion of the failure of the chimpanzee animal model.

<sup>262</sup> Minutes of Factor VIII Study Group, 12 January 1984 [SNB.007.4059] at 4063; See also Dr Foster – Day 41, page 146 and Dr Foster's statement on viral inactivation to 1985 [PEN.012.1438] at 1467–68

<sup>263</sup> UK Haemophilia Hepatitis Working Party Annual Report for 1982–83 [SNF.001.0948]; Preliminary Report, paragraphs 11.148–11.150

<sup>264</sup> CBLA report [DHF.002.4489]

<sup>265</sup> Dr Smith – Day 59, page 117

medium and account would have to be taken of other elements used to protect Factor VIII in the pasteurisation process.<sup>266</sup> Dr Foster shared this view indicating that the statement on the molecular damage caused by pasteurisation was a 'bit of a generalisation' and that it failed to take account of the amount of heat applied or the use of stabilisers in the pasteurisation process.<sup>267</sup> Similarly, Dr Cuthbertson indicated that the reference to 'heating at 75°C for ten hours or heating at 60°C for 24 hours' was too simplistic noting that 'it's not simply a question of heat and time, it's a question of the stabilisers, the format that the product is in and a whole range of other complex things that lead to the level of inactivation that you finally get'.<sup>268</sup>

### Scottish developments

**23.139** Returning to Scotland, on 23 August 1983, Dr Foster updated Dr Smith on the progress of the pilot-scale pasteurisation programme for Factor VIII and explained that, since Factor VIII survived 'fairly well' for up to one hour at 70°C, an amended regime of 9.25 hours heating at 60°C followed by 0.75 hours at 70°C would be followed in the next trials.<sup>269</sup> According to Dr Foster, Dr Smith visited the PFC on 8 September and 2 November 1983 to discuss coagulation factor research and development and the heat treatment of coagulation factor concentrates.<sup>270</sup>

**23.140** Research into heat treatment continued at the PFC during the second half of 1983. Progress at the end of the year was summarised as part of a more general report by Dr Foster entitled *Progress Report on Studies to Improve Yield and Quality of FVIII Concentrate* dated 20 December 1983. As regards pasteurisation, the report explained that:

Extensive studies have been carried out on the stability of FVIII:C and a range of model viruses to heating in solution in the presence of sorbitol and glycine.

Compared to an albumin control ... the sugar solutions ... showed substantial stabilisation of virus (vaccinia and mumps). Improved heating conditions have been identified to achieve further viral inactivation ....

Even more severe heating results in substantial loss of FVIII activity and the improved conditions are probably the best that can be achieved without an unacceptable loss of yield.<sup>271</sup>

**23.141** The report also indicated that the PFC was carrying out experiments in dry heating, using the same model viruses. Dr Cuthbertson indicated in his witness statement that he carried out the dry heating experiments together with Dr Pepper on 21 November 1983. He described the work:

Vials were either left unheated as controls or were heat treated at 60 or 70°C. The vials heated at 70°C were completely insoluble, so it was not possible to assess the extent of viral inactivation. The vials heated at 60°C were tested and showed a modest degree of inactivation of vaccinia virus, which was significantly less than that found in our pasteurisation studies.<sup>272</sup>

---

<sup>266</sup> Dr Smith – Day 59, page 118

<sup>267</sup> Dr Foster – Day 42, page 33

<sup>268</sup> Dr Cuthbertson – Day 46, pages 58–59

<sup>269</sup> Dr Foster's letter to Dr Smith [SNB.007.3841]

<sup>270</sup> SNBTS Briefing Paper on the Development of Heat Treatment of Coagulation Factors [PEN.013.1309] at 1364

<sup>271</sup> Progress Report on Studies to Improve Yield and Quality of FVIII Concentrate, 20 December 1983 [PEN.012.1500] at 1503

<sup>272</sup> Dr Cuthbertson's statement on viral inactivation to 1985 [PEN.013.0025] at 0036; see also Dr Foster – Day 42, page 38

The report commented that 'initial results suggest that the viral kill is less than that achieved by heating in sugar solutions at 60°C for 10hrs'.<sup>273</sup>

**23.142** Dr Cuthbertson was asked by the Inquiry to provide further information and documentation describing these experiments.<sup>274</sup> He duly provided his handwritten summary of the experiments<sup>275</sup> together with a typewritten copy for ease of reading.<sup>276</sup> In his oral evidence, Dr Cuthbertson explained that the purpose of the experiments was to see whether dry heating would give equivalent inactivation to what the PFC was seeing in the liquid process. It was a kind of control. The temperatures applied, 60°C and 70°C, were chosen because they were the temperatures used for the pasteurised product.<sup>277</sup> Dr Cuthbertson also explained in more detail the difference in viral inactivation between the dry-heated and wet-heated products, noting that in the dry-heated product heating led to 'a 3 log reduction, whereas in the ... liquid product, we were looking at an 8 log reduction' and adding, in reference to the dry-heated product, that:

Just to put that into perspective, an 8 log reduction means 100 million viruses per inoculum being inactivated, whereas this shows about 10,000 viruses per 0.1 ml being inactivated. So the difference in them, because it is a logarithmic scale, is enormous. So it was a much less effective virus inactivation process than the liquid process that we were studying and for that reason we kept going with the liquid process at that time.<sup>278</sup>

**1984**

**23.143** On 5 January 1984, Dr Smith sent Dr Foster a memorandum outlining details of the results of the PFL's experiments on the dry heat treatment of Factor VIII.<sup>279</sup> The memorandum commented on the impact of different heating conditions on solubility and Factor VIII activity and indicated that the experiments showed 'the promising preservation of factor VIII:C<sup>280</sup> and solubility of one batch'.<sup>281</sup> The Inquiry asked whether what was disclosed in this memorandum was new and what effect, if any, this news had on those working at the PFC.<sup>282</sup> Dr Foster's response in his written statement was that:

The memorandum from Dr Smith to myself, of 5<sup>th</sup> January 1984 ... concerned the ability of the current BPL Factor VIII concentrate to withstand dry heat treatment under different conditions. Although these data were more extensive than those that had been obtained by the SNBTS, the results were consistent with those of Dr Cuthbertson and Dr Pepper and were not regarded as representing new findings.

The absence of any data from BPL concerning the inactivation of any viral markers, meant that the data from Dr Smith were of limited value. Virus inactivation data were available for pasteurisation, from laboratory studies with marker viruses by the SNBTS, as well as studies in animals and in patients by Behring, all pointing to pasteurisation being more likely to succeed in making

<sup>273</sup> Progress Report on Studies to Improve Yield and Quality of FVIII Concentrate, 20 December 1983 [PEN.012.1500] at 1504

<sup>274</sup> Dr Cuthbertson's statement on viral inactivation to 1985 [PEN.012.1692] at 1693

<sup>275</sup> Dr Cuthbertson's handwritten notes [PEN.012.1669]

<sup>276</sup> Transcript of Dr Cuthbertson's notes [PEN.012.1673]

<sup>277</sup> Dr Cuthbertson – Day 46, pages 65–66

<sup>278</sup> Dr Cuthbertson – Day 46, page 67

<sup>279</sup> Dr Smith's memorandum [SNB.007.4052]; Preliminary Report, paragraph 11.156

<sup>280</sup> ie Factor VIII activity.

<sup>281</sup> Dr Smith's memorandum [SNB.007.4052] at 4053

<sup>282</sup> Inquiry's schedule of questions on viral inactivation to 1985 [PEN.012.1531] at 1536

coagulation factor concentrates safe with respect to non-A, non-B hepatitis than dry-heat treatment. Consequently the information from Dr Smith did not alter the opinion in Scotland that pasteurisation should continue to be the main focus of research on virus inactivation.<sup>283</sup>

**23.144** Dr Smith indicated that:

There does appear to be some gap in technical correspondence, but Dr Foster and I both understood perfectly well that we were pursuing different approaches in the short term, for our respective pressing reasons. For example, during this period PFC was greatly preoccupied with preparing a pasteurised product for clinical trial. My letter would not be intended in any sense to divert PFC from pasteurisation ... simply to show that the Oxford and larger-scale Elstree products were capable of withstanding heat treatment, as Rubinstein predicted. I had no information (and at the time little hope) that this treatment would inactivate NANBH, which remained the goal of pasteurisation.<sup>284</sup>

**23.145** Thus, on Dr Smith's approach, the information in his memorandum did not indicate that the BPL results suggested that the procedure reported would inactivate NANB Hepatitis, and only alerted the PFC to the fact that the BPL's Factor VIII could survive certain forms of dry heat treatment.

**23.146** On 11 January 1984, Professor Ludlam wrote to Professor Cash reporting that the clinical trial of the PFC's pasteurised Factor VIII (batch NY 761) had led to an adverse reaction in one patient:

I write to let you know the outcome of infusing the heat treated factor VIII. The above batch of material was given to a single severe haemophiliac on three separate occasions ....

Infusions were accompanied by reactions on all three occasions. On the first the recipient had a short episode of diarrhoea beginning an hour after the infusion. On the second and third occasion he felt ill towards the end of each infusion. He developed transient central chest pain, pallor and [retching]. There was no change in his pulse, BP or temperature. To ascertain whether this was likely to be an organic reaction to the concentrate we gave him a 'placebo' infusion of ordinary SNBTS factor VIII. He was told that it was the heated material and the infusion protocol was identical. He had no adverse reaction to this standard product.<sup>285</sup>

**23.147** Professor Ludlam therefore concluded that that batch of material 'genuinely gave rise to significant and unacceptably adverse reactions in the recipient'.

**23.148** Professor Cash replied on 16 January 1984 agreeing with Professor Ludlam's conclusions, and expressing the hope that a further batch, with improvements in heat treatment and lower sorbitol content, would be available in April.<sup>286</sup> On 25 January 1984, Dr Gillon wrote to Dr Boulton expressing the view that sorbitol was unlikely to be the cause of the adverse reaction.<sup>287</sup>

---

<sup>283</sup> Dr Foster's statement on viral inactivation to 1985 [PEN.012.1438] at 1468–69

<sup>284</sup> Dr Smith's statement on viral inactivation to 1985 [PEN.012.1551] at 1562

<sup>285</sup> Professor Ludlam's letter to Professor Cash [SNB.001.5311]

<sup>286</sup> Professor Cash's reply to Professor Ludlam [SNB.006.4695]

<sup>287</sup> Dr Gillon's letter to Dr Boulton [SNB.007.4127]



**23.149** The information regarding the possibly adverse outcome of the clinical trial had already been intimated at the meeting of the Haemophilia and Blood Transfusion Working Group on 14 November 1983. During this meeting Professor Ludlam appears to have mentioned that the patient experienced, 'minor adverse reactions', possibly implying that the severity of the reactions was less than the 'significant and unacceptable reactions' outlined in the letter of 11 January 1984.<sup>288</sup>

**23.150** The Inquiry asked witnesses for an explanation of the difference in the description of the adverse reaction in the letter of 11 January and the memo of 14 November 1983.<sup>289</sup> Professor Ludlam's response in his written statement was as follows:<sup>290</sup>

At the meeting of the Haemophilia Directors with SNBTS at SHHD on 14<sup>th</sup> November the Minutes record that I reported that there had been 'minor adverse reactions on each occasion' when the heated product was infused. This was how the Minute-taker recorded what he thought had been said and may not have accurately recorded what had actually been stated. I have no recollection of exactly what I said. I might have indicated that the reactions were 'minor' but this does not make them acceptable. A 'major' reaction would have been an anaphylactic one in which there is severe hypotension and is immediately life-threatening – this occasionally is seen with infusion of blood products especially cryoprecipitate.

Further details of the infusions and the reactions are given in my letter of 11<sup>th</sup> January 1984 in which I recorded that 'Infusions were accompanied by reactions on all three occasions ....' The reaction to each infusion was sufficiently marked that an injection of piriton (antihistamine commonly given to reduce 'allergic' reactions) was given on each occasion ....

**23.151** Dr Cuthbertson's view in his written statement was that the reaction was probably not severe, but was not one which would be considered acceptable. He noted that Professor Forbes agreed to trial the product with additional patients, which was not consistent with a severe reaction.<sup>291</sup> However, a later letter from Dr Foster to Professor Ludlam dated 10 February 1984 indicated that Professor Ludlam was the only clinician who had been given an 'inferior batch' to test, the implication being that this could have been the reason for the adverse reaction.<sup>292</sup> Therefore, according to Professor Ludlam the description of the adverse reaction as 'minor' during the meeting of the Haemophilia and Blood Transfusion Working Group on 14 November 1983, may have been due to an inaccurate recording by the minute taker, or may have been accurate and consistent with the letter of 11 January 1984. According to him, the fact that he was prepared to arrange a control experiment with unheated product was evidence that the reactions were 'clinically significant'.<sup>293</sup>

**23.152** On 12 January 1984 the Factor VIII Study Group met.<sup>294</sup> Dr Cuthbertson presented the results of the PFC's research into the viral inactivation of Factor VIII (including the results of viral inactivation experiments using model viruses) and referred to the BPL's work on dry heat treatment and the fact that this work suggested that, 'there is no yield penalty

---

<sup>288</sup> Minutes of the Haemophilia and Blood Transfusion Working Group, 14 November 1983 [SNB.001.5188]

<sup>289</sup> Inquiry's schedule of questions on viral inactivation to 1985 [PEN.012.1531] at 1537

<sup>290</sup> Professor Ludlam's statement on viral inactivation to 1985 [PEN.012.1688] at 1689

<sup>291</sup> Dr Cuthbertson's statement on viral inactivation to 1985 [PEN.013.0025]

<sup>292</sup> Dr Foster's letter to Professor Ludlam [SNB.007.4147]

<sup>293</sup> For similar arguments to Professor Ludlam's see Dr Perry's statement on viral inactivation to 1985 [PEN.012.1759] at 1771

<sup>294</sup> Minutes of Factor VIII Study Group, 12 January 1984 [SNB.007.4059]

for dried FVIII if it is heated to 60°C for 3 days'. As indicated above, mention was also made of the fact that Hyland's heat-treated product was infective.

**23.153** The Inquiry asked witnesses whether the information on the failure of Hyland product had an impact on the perceived significance of the BPL's progress in dry heating Factor VIII and whether there was any suggestion within the PFC of changing to dry heat treatment at this time.<sup>295</sup> Dr Foster's response in his written statement<sup>296</sup> was that the failure of the Hyland product was indeed considered to be evidence against dry heat treatment, as were the disappointing levels of viral inactivation which Dr Cuthbertson and Dr Pepper had found when carrying out their own dry heat experiments in November of 1983.<sup>297</sup> Dr Foster also pointed out that the fact that the BPL's dry heat treatment experiments lacked any measurement of viral kill was a factor in the PFC's decision to continue with its prioritisation of pasteurisation.<sup>298</sup> Dr Perry's answer was to the same effect. He emphasised that there was no information available worldwide to suggest that heat treatment of freeze-dried product at 60°C would be capable of inactivating an AIDS virus.<sup>299</sup>

**23.154** Dr Cuthbertson agreed with this view, noting that the failure of the dry heat-treated Hyland product to inactivate NANB Hepatitis 'made this process look less promising, whereas the virus inactivation data on the SNBTS pasteurised product were very promising indeed' and that for this reason, it was concluded that the PFC should continue with pasteurisation as the primary heat treatment process.<sup>300</sup>

**23.155** At this time the firm focus of the PFC was, therefore, on continuing its research into the pasteurisation of Factor VIII. Work in this regard continued in the early part of 1984. Events of note included:

- Further clinical trials of heat-treated Factor VIII and the conclusion of a successful trial (with no adverse reactions) by Professor Forbes of Glasgow Royal Infirmary by March 1984.<sup>301</sup>
- The availability for formal clinical trial of a pilot batch of pasteurised Factor VIII at the end of April 1984.<sup>302</sup>
- Further collaboration between Dr Foster and Dr Smith in May of 1984.<sup>303</sup>

**23.156** At this point the target date for the introduction of pasteurised Factor VIII for clinical use was April 1985.<sup>304</sup> That target date was described by Dr Foster in his written evidence as 'extremely ambitious for the installation and commissioning of such a large and complex manufacturing process' adding that this is why 'the focus shifted in August 1984 to the incorporation of Dr Johnson's purification procedure in order to substantially reduce the volume of solution to be pasteurised ...'.<sup>305</sup>

<sup>295</sup> Inquiry's schedule of questions on viral inactivation to 1985 [PEN.012.1531] at [PEN.012.1537]

<sup>296</sup> Dr Foster's statement on viral inactivation to 1985 [PEN.012.1438] at 1468

<sup>297</sup> See paragraphs 23.141 to 23.142

<sup>298</sup> Dr Foster's statement on viral inactivation to 1985 [PEN.012.1438] at 1468–69

<sup>299</sup> Dr Perry's statement on viral inactivation to 1985 [PEN.012.1759] at 1772–73

<sup>300</sup> Dr Cuthbertson's statement on viral inactivation to 1985 [PEN.013.0025] at 0037

<sup>301</sup> Letter from Professor Forbes to Professor Cash dated 15 March 1984 [SNB.007.4335]

<sup>302</sup> Letter from Dr Perry to Professor Cash dated 27 April 1984 [SNB.007.4383]; Preliminary Report, paragraph 11.174

<sup>303</sup> Letter from Dr Smith to Dr Foster dated 22 May 1984 [SNB.007.4402] and letter from Dr Foster to Dr Smith dated 24 May 1984 [SNB.007.4403]

<sup>304</sup> Cost estimate for the production of heat-treated Factor VIII concentrate, SNBTS, February 1984 [SGH.002.0068] at 0069

<sup>305</sup> Dr Foster's statement on viral inactivation to 1985 [PEN.012.1438] at 1469–70. For an additional statement indicating that the PFC April 1985 goal was ambitious, see Dr Smith's statement on viral inactivation to 1985 [PEN.012.1551] at 1563. See also Dr Cuthbertson's statement on the same topic [PEN.013.0025] at 0037 for the argument that the proposed timescale was sensible given the number of safety and quality control steps which were needed before issuing a product to patients.

**23.157** The PFC's research into, and focus on, the pasteurisation of Factor VIII continued during the summer of 1984. The collaboration with Dr Johnson of New York University on the development of a high purity Factor VIII product, which it was hoped would allow for pasteurisation in one litre bottles, had stalled due to the delay in applying for a patent and the University's concerns that details of the procedure should not be disclosed before an application was filed.<sup>306</sup> However, on 14 June 1984, Dr Foster met with Dr Johnson in New York and an agreement was made that details of the procedure should be disclosed to the PFC prior to the patent being filed.<sup>307</sup> This agreement paved the way for further work to be carried out at the PFC into the development of a high purity Factor VIII product. Such work included an evaluation by Dr Foster of Dr Johnson's proposed ion-exchange<sup>308</sup> reagent and the setting up of a meeting between Dr Johnson and Dr John Curling of the pharmaceutical company Pharmacia at the ISBT Congress in Munich to look at alternative reagents. The alternative reagent chosen, Q-Sepharose, was delivered to the PFC on 22 August 1984.<sup>309</sup> According to Dr Foster, it was found to be 'very promising', although 'it became clear that further work would be required to fine-tune the chromatography process before it could be integrated into the pasteurisation process'.<sup>310</sup> Due to the additional scientific input needed, Dr Ronald McIntosh was moved from his work on immunoglobulins to take the lead on the high purity project.<sup>311</sup> As indicated above, one of the main aims behind this project was to reduce the volume of solution to be pasteurised, and so facilitate the change from experimental to commercial production.

**23.158** Arrangements for clinical trials of pasteurised Factor VIII were progressing and in June 1984 Professor Cash prepared a report on the activities of the Factor VIII Study Group which contained a separate report outlining 'Preliminary Clinical Evaluation Studies' for heat-treated Factor VIII.<sup>312</sup> The annex explained that:

Preliminary *in vivo* and *in vitro* studies (carried out in Edinburgh and Glasgow), using a 60°C for 10 hours heating procedure demonstrated that the sugar appeared to prevent denaturation of factor VIII. The proposed new studies will be performed using product exposed to the optimal heat treatment (includes a period at 70°C) and are designed to assess biological acceptability, clinical efficacy and residual infectivity.

It is proposed that all heat-treated product made available for patient use until further notice will be issued exclusively for these clinical evaluation studies.<sup>313</sup>

**23.159** The separate report also contained a detailed plan/protocol as to how such studies should be structured as regards assessment of biological acceptability, clinical efficacy and residual infectivity.

<sup>306</sup> Using the chromatographic purification process first discussed between Dr Johnson and Dr Foster on June 27 1983 at a World Federation of Haemophilia meeting in Stockholm. See paragraphs 23.130 to 23.131 above.

<sup>307</sup> Dr Foster – Day 42, page 18; Dr Foster's statement on viral inactivation to 1985 [PEN.012.1438] at 1463

<sup>308</sup> Ion-exchange is a process used to separate or purify proteins where selected proteins are bound to a solid matrix and then removed.

<sup>309</sup> Dr Foster's statement on viral inactivation to 1985 [PEN.012.1438] at 1463

<sup>310</sup> Ibid

<sup>311</sup> Ibid

<sup>312</sup> Report on the activities of the Factor VIII Study Group [SNB.007.4169]

<sup>313</sup> Preliminary Clinical Evaluation Studies report [SNB.007.4407] at 4408

**23.160** On 26 June 1984, Professor Cash wrote to Dr Perry outlining the process for the future issue of the product for clinical evaluation. The letter indicated that this was to be on a named patient basis.<sup>314</sup>

**23.161** On 25–26 June 1984, Dr Smith and other members of staff from the PFL and the BPL visited the PFC to observe the preparation of a pilot-scale batch of SNBTS pasteurised Factor VIII concentrate and took photographs of the process.<sup>315</sup> Dr Foster indicated in his written statement that this was evidence of continuing interest by the BPL and the PFL in pasteurisation in the summer of 1984.<sup>316</sup> Dr Smith confirmed this during his oral evidence. It was suggested to him that progress with dry heat treatment in England was still taking place against the backdrop of a preference, at least in theory, for pasteurisation, as offering a more efficient form of heat treatment. He said:

Very definitely. We were quite near achieving what looked like success in recovering Factor IX from pasteurisation and on Factor VIII we were still working well into the early summer of 1984 on pasteurisation. I think that's the point at which Lowell Winkelman and I went up to [PFC] to see their scaled-up pasteurisation process, and I think even to take photographs.<sup>317</sup>

**23.162** An abstract outlining the PFC's proposed pasteurisation process for Factor VIII (heated at 60°C for 9.5 hours followed by 70°C for 0.5 hours with glycine/sorbitol stabilisers) was drawn up for the 18th Congress of the International Society of Blood Transfusion held in Munich between 22 and 27 July 1984.<sup>318</sup> The abstract also noted that:

A FIX concentrate has been pasteurised in a similar manner giving about 60% recovery of clotting activity over the heating step with no increase in thrombogenicity ....<sup>319</sup>

**23.163** After the summer of 1984, the focus of the PFC's heat treatment programme remained on the pasteurisation of Factor VIII and its clinical evaluation. Dr Foster commented on progress:

During 1983/84, a total of seven pilot batches of pasteurised Factor VIII concentrate (ZHT) were prepared at the PFC for clinical evaluation with the final batch (batch number ZHT-007) being processed on 24/25 September 1984.<sup>320</sup>

**23.164** Thus, by the autumn of 1984 the PFC remained committed to the introduction of a pasteurised Factor VIII product and was actively working towards the introduction of such a product. However, significant developments occurred towards the end of 1984 which, together, would have a crucial impact on the PFC's existing viral inactivation strategy.

<sup>314</sup> Professor Cash's letter to Dr Perry [SNB.007.4447]. 'Named patient basis' meant that, if a clinician considered that a patient would benefit from a medication prior to it being licensed, the clinician could request access to the medication for this patient from the manufacturers – see Professor Leen, Day 33, pages 20–21

<sup>315</sup> Dr Foster – Day 42, page 39 and Dr Smith – Day 59, page 115

<sup>316</sup> Dr Foster's statement on viral inactivation to 1985 [PEN.012.1438] at 1469

<sup>317</sup> Dr Smith – Day 59, page 115

<sup>318</sup> MacLeod et al, 'Pasteurisation of Factor VIII and Factor IX concentrates', *Abstracts of 18th Congress of the International Society of Blood Transfusion*, Munich, 22–27 July, 1984 [SNB.008.6696]

<sup>319</sup> MacLeod et al, 'Pasteurisation of Factor VIII and Factor IX concentrates', *Abstracts of 18th Congress of the International Society of Blood Transfusion*, Munich, 22–27 July, 1984 [SNB.008.6696] at 6677

<sup>320</sup> Dr Foster's statement on viral inactivation to 1985 [PEN.012.1438] at 1464

**23.165** On 1 September 1984, Dr Rachanee Cheingsong-Popov, Professor Robin Weiss, Professor Richard Tedder and others published the results of a major study of the prevalence of antibodies to HTLV-III in UK subjects.<sup>321</sup> Haemophilia clinicians responded to the information that an assay for HTLV-III/HIV antibodies was available by submitting samples from their own patients for testing. By the end of October, there was growing awareness among haemophilia clinicians in the UK generally that HIV infection could be contracted from Factor VIII and that transmission could be associated with domestic as well as imported products.<sup>322</sup> Professor Ludlam submitted samples to Professor Tedder. Independently, Professor Forbes submitted samples from west of Scotland patients to Dr Gallo's laboratory in the USA.

### The Edinburgh Cohort

**23.166** It is not known when SNBTS scientists received information about the west of Scotland results. Information about the results in Professor Ludlam's patients was received first, probably at the end of October 1984. A group of patients treated with standard production PFC Factor VIII at the RIE over the period March to May 1984 (ie the so-called 'Edinburgh cohort') had become infected with HIV.<sup>323</sup> Various witnesses were asked when exactly this information was passed on to the PFC, as this was not clear from the documentation available to the Inquiry.

**23.167** The SNBTS had the information over the weekend 26 to 29 October 1984. Professor Ludlam told Dr McClelland on the evening of 26 October.<sup>324</sup> There had been a meeting of the PFC Heads of Department on the morning of 26 October.<sup>325</sup> Dr Perry thought that he could not have known that the patients had seroconverted, or potentially seroconverted before 26 October.<sup>326</sup> Dr Cuthbertson remembered Dr McClelland telephoning him with the news. He remembered a review of all of the available information a week later.<sup>327</sup> Dr Foster first learned of the infections in late October 1984, when Dr Cuthbertson received a telephone call about it. He had thought he had overheard a conversation between Dr McClelland and Dr Cuthbertson.<sup>328</sup> But he thought later that it may have been Dr Boulton who passed on the news to the PFC, explaining that he now knew that Dr McClelland had been ill.<sup>329</sup> The precise date on which the PFC got to know of the events cannot be specified. But it must have been around the weekend beginning 26 October.

**23.168** The response was fast. In the course of a few weeks, the PFC shelved its pasteurisation programme, experimented with dry heating of Factor VIII, and adopted dry heating for all of its intermediate Factor VIII product. Coinciding with the outbreak of HIV infection in Edinburgh emerging intelligence on the effectiveness of dry heating to kill HIV caused a rapid reassessment of priorities. It was apparent that there was a current problem that had to be dealt with. But, before narrating the events which followed, it is appropriate to take note of the wider research environment at the time.

<sup>321</sup> Cheingsong-Popov et al, 'Prevalence of antibody to human t-lymphotropic virus type iii in aids and aids-risk patients in Britain', *The Lancet*, 1 September 1984 [LIT.001.0417] at 0419. See Chapter 10, *Knowledge of the Geographical Spread and Prevalence of HIV/AIDS 2*, at paragraphs 10.3 to 10.5

<sup>322</sup> See Chapter 10, *Knowledge of the Geographical Spread and Prevalence of HIV/AIDS 2*, at paragraph 10.15

<sup>323</sup> The topic is discussed more fully in Chapter 10, *Knowledge of the Geographical Spread and Prevalence of HIV/AIDS 2*, from paragraph 10.16

<sup>324</sup> Dr McClelland's statement on viral inactivation to 1985 [PEN.011.0062] at 0063

<sup>325</sup> Minutes of PFC Heads of Department meeting, 26 October 1984 [SNB.010.3479]

<sup>326</sup> Dr Perry – Day 45, page 106

<sup>327</sup> Dr Cuthbertson – Day 46, page 76

<sup>328</sup> Dr Foster's statement on viral inactivation to 1985 [PEN.012.1438] at 1472

<sup>329</sup> Dr Foster – Day 42, page 54

### Information about heat inactivation of retroviruses

**23.169** In October 1984 a 'haemophilia meeting' took place in Cardiff.<sup>330</sup> Notes of the meeting were received at the PFC on 6 November 1984. During this meeting, Professor Mannucci discussed the European trials of the dry-heated product Hemofil T. As outlined above, the trials demonstrated that the product was infective for NANB Hepatitis and that the attack rate was 70%.<sup>331</sup> However, as far as AIDS was concerned, Professor Mannucci reported that after one year no patients treated with the product had apparently seroconverted.<sup>332</sup> AIDS was still not reported as a major threat to haemophilia patients.

**23.170** On the other hand, it was being suggested that HTLV-III was heat-labile. Prior to the Cardiff meeting, an article published in *The Lancet* on 29 September 1984 reported substantial inactivation, after several hours of dry heat treatment at 68°C, of a murine (ie mouse) retrovirus which had been added to Factor VIII concentrate.<sup>333</sup> Dr Foster indicated in his written statement that he was aware of this publication in *The Lancet* and noted that, 'as the AIDS virus was also known to be a retrovirus ... these data suggested that HIV might be destroyed by dry-heat treatment at 68°C'.<sup>334</sup>

**23.171** This research on the murine retrovirus was later referred to in the USA Centers for Disease Control (CDC) *Morbidity and Mortality Weekly Report (MMWR)* published on 26 October 1984, which indicated that:

A recently published study evaluated the thermostability of murine retroviruses inoculated into factor concentrates, using a cell transformation assay. After 48 hours at 68 C (154.4 F), viral titers dropped from 10<sup>8</sup> to two infectious particles/ml.<sup>335</sup>

**23.172** The *MMWR* report also referred to studies carried out by the CDC, in cooperation with Cutter laboratories (a subsidiary of Bayer) in which 'AIDS virus was added to factor VIII concentrate (virus titer 10<sup>5</sup>) and the factor was lyophilized and heated to 68 C (154.4 F)'. The report concluded with a statement which was later to prove crucial that 'virus was undetectable after 24 hours of heat treatment'.<sup>336</sup> Although the PFC subscribed to the *MMWR*, Dr Foster explained during his oral evidence that the journal 'took a couple of weeks to arrive' and that, therefore, the PFC were not yet aware of this research when information about the outbreak in the Edinburgh Cohort was received.<sup>337</sup>

### Protein Fractionation Centre response to the discovery of infection in the Edinburgh Cohort

**23.173** Dr Foster indicated in his written statement that, upon overhearing the telephone conversation in which Dr Cuthbertson was given news of the HIV infections, he immediately called Dr MacLeod to his office to ask him to identify R&D samples of

<sup>330</sup> The Inquiry has been unable to discover the exact date of this meeting.

<sup>331</sup> Note of Dr Mannucci's talk on safe treatment of haemophilia at Cardiff meeting [SNB.004.9164]

<sup>332</sup> Note of Dr Mannucci's talk on safe treatment of haemophilia at Cardiff meeting [SNB.004.9164] at 9166

<sup>333</sup> Levy J et al, 'Recovery and inactivation of infectious retroviruses added to Factor VIII concentrates', *The Lancet*, 29 September 1984:722-723 [LIT.001.0434]

<sup>334</sup> Dr Foster's statement on viral inactivation to 1985 [PEN.012.1438] at 1473; See Dr Foster – Day 42, pages 48-52 for further discussion.

<sup>335</sup> 'Update: Acquired Immunodeficiency Syndrome (AIDS) in Persons with Hemophilia', *MMWR*, 1984; 33/42:589-591 [LIT.001.0460]. Results from the studies were published in a peer-reviewed journal in August 1985 – McDougal et al, 'Thermal inactivation of the acquired immunodeficiency syndrome virus, human T lymphotropic virus-III/lymphadenopathy-associated virus, with special reference to antihemophilic factor', *Journal of Clinical Investigation*, 1985; 76/2:875-877, [SNB.010.6169]

<sup>336</sup> 'Update: Acquired Immunodeficiency Syndrome (AIDS) in Persons with Hemophilia', *MMWR*, 1984; 33/42:589-591 [LIT.001.0460] at 0461

<sup>337</sup> Dr Foster – Day 42, page 63

Factor VIII concentrate that were already available which could be used for heat treatment experiments.<sup>338</sup> According to Dr Foster, Dr MacLeod responded immediately coming to Dr Foster's office, 'before Dr Cuthbertson had put the phone down'.<sup>339</sup> Dr Foster also indicated that Dr Macleod returned with a list of available samples and that they 'drew up a plan of investigation to obtain as much information as possible on the impact that the various additives might have on the ability of the PFC Factor VIII concentrate (NY) to withstand dry heat treatment at 68°C'.<sup>340</sup> When asked when this plan was drawn up and whether this was on Friday 26 October, Dr Foster responded that:

[I]t seems to me more likely that that was the Monday morning and that it was Dr Boulton who was phoning Dr Cuthbertson on the following Monday and that that then led us to carry out these further heat treatment experiments. And I do have a set of results of some of these experiments, which are dated Tuesday, 30<sup>th</sup>, which would be consistent with that.<sup>341</sup>

**23.174** Dr Foster explained in oral evidence that there were two relevant sets of experiments – the experiments carried out by Dr MacLeod which involved samples prepared with different additives, and also experiments with existing product carried out by Mr McQuillan of the quality control department.<sup>342</sup> According to Dr Foster, it was the results of Mr McQuillan's tests which were available on Tuesday 30 October.<sup>343</sup> Dr Foster indicated that these involved dry heating Factor VIII to 68°C (and also to 60°C)<sup>344</sup> and explained that it is possible that these experiments were discussed on the Friday afternoon (ie following the Heads of Department meeting on the morning of Friday 26 October), in light of the publication by Levy and others in *The Lancet* (see paragraph 23.170 above) that the murine retrovirus could be inactivated at a temperature of 68°C.<sup>345</sup> Dr Foster also noted in his written statement that he had:

[S]pecified that heating at 68°C be included, not only because of the publication by Levy et al. of 29 September, but also because this was the highest temperature to which a Factor VIII concentrate (Koate HT of Cutter/Bayer) had been dry-heat treated, in addition to having obtained regulatory approval in the USA ....<sup>346</sup>

**23.175** Dr Foster commented further in his written statement that the results of the experiments by Mr McQuillan indicated that 'PFC's Factor VIII concentrate (NY) could withstand dry-heat treatment at either 60°C for 24 hours or at 68°C for about 3 hours'.<sup>347</sup> In his oral evidence he explained that these were the first dry heat treatment experiments to have been carried out by the PFC since the experiments of Dr Cuthbertson and Dr Pepper in November 1983.<sup>348</sup>

<sup>338</sup> Dr Foster's statement on viral inactivation to 1985 [PEN.012.1438] at 1472

<sup>339</sup> Dr Foster – Day 42, page 55

<sup>340</sup> Dr Foster's statement on viral inactivation to 1985 [PEN.012.1438] at 1473

<sup>341</sup> Dr Foster – Day 42, page 56

<sup>342</sup> Dr Foster – Day 42, page 59

<sup>343</sup> Ibid

<sup>344</sup> Dr Foster – Day 42, page 61

<sup>345</sup> Dr Foster – Day 42, page 51

<sup>346</sup> Dr Foster's statement on viral inactivation to 1985 [PEN.012.1438] at 1474

<sup>347</sup> Dr Foster's statement on viral inactivation to 1985 [PEN.012.1438] at 1472

<sup>348</sup> Dr Foster – Day 42, page 60

**23.176** On Wednesday 31 October, the day after the PFC's dry heating results were available, Dr Foster, Dr Perry and Dr Ronald McIntosh travelled to the Netherlands to attend a Plasma Fractionation Conference held by the transfusion centre in Groningen on 1–2 November 1984.<sup>349</sup> The Groningen meeting proved to be a crucial event as, according to Dr Foster, it was there that the PFC became aware, for the first time,<sup>350</sup> of the findings of the CDC/Cutter, which had been published in the *MMWR* on 26 October 1984, that, 'HIV could be substantially inactivated by dry-heat treatment at 68°C for 1 hour'.<sup>351</sup> These findings were contained in an oral presentation by Dr Jason of the CDC made on 2 November 1984.<sup>352</sup> During the public hearings, Dr Perry characterised the Groningen meeting and the knowledge that HIV had entered the Scottish blood supply as a 'strategy-changing moment', explaining that:

For the first time we had evidence from the Groningen meeting that the product that we were making could be inactivated fairly simply but also, and importantly, there was HIV in the UK and certainly the Scottish, blood supply.<sup>353</sup>

**23.177** The Lindsay Tribunal report comments that the results of the research, showing HIV to be sensitive to heat inactivation, were considered highly significant by the CDC and were widely publicised, both formally and informally. There was not yet any clinical proof of the effectiveness of heat treatment against the HIV virus but there was an immediate recommendation in the USA by MASAC<sup>354</sup> that 'Treaters using coagulation factor concentrate should strongly consider changing to heat treating products with the understanding that protection against AIDS is yet to be proved'.<sup>355</sup> This increased the pressure on the manufacturers, including the BPL, to develop methods of viral inactivation. The Lindsay Tribunal found that there was no general move to the use of heat-treated commercial concentrates until after October 1984.<sup>356</sup>

**23.178** So far as Scotland is concerned, Dr Perry said:

This ten-day period brought together, almost coincidentally, the report to Dr Ludlam and the information that we got for the first time from the Groningen meeting, from the CDC and the Cutter people, who demonstrated for the first time that HIV is fairly heat-sensitive and ... the risk/benefit balance changed overnight. It was dramatic and it was quite clear, moving from a position where everyone was very nervous about introducing heat treatment to a position where the advantages clearly outweighed any of the risks.<sup>357</sup>

**23.179** Dr Foster commented in his written statement that the data from the Groningen meeting were discussed by himself and Drs Perry and McIntosh during their return journey from Groningen to Edinburgh and that they 'agreed to propose to Dr Cash that the SNBTS

<sup>349</sup> Dr Foster – Day 42, page 62

<sup>350</sup> Dr Foster – Day 42, page 63

<sup>351</sup> Dr Foster's statement on viral inactivation to 1985 [PEN.012.1438] at 1474

<sup>352</sup> Dr Foster – Day 42, page 61; SNBTS Briefing Paper on the Development of Heat Treatment of Coagulation Factors [PEN.013.1309] at 1366

<sup>353</sup> Dr Perry – Day 45, page 110

<sup>354</sup> The Medical and Scientific Advisory Council of the US National Hemophilia Foundation

<sup>355</sup> Lindsay Tribunal (1999). *Report of the Tribunal of Inquiry into the Infection with HIV and Hepatitis C of Persons with Haemophilia and Related Matters*, page 62. <http://health.gov.ie/blog/publications/report-of-the-tribunal-of-inquiry-into-the-infection-with-hiv-and-hepatitis-c-of-persons-with-haemophilia-and-related-matters/> [Last accessed 21 January 2013]

<sup>356</sup> Lindsay Tribunal (1999). *Report of the Tribunal of Inquiry into the Infection with HIV and Hepatitis C of Persons with Haemophilia and Related Matters* page 154. <http://health.gov.ie/blog/publications/report-of-the-tribunal-of-inquiry-into-the-infection-with-hiv-and-hepatitis-c-of-persons-with-haemophilia-and-related-matters/> [Last accessed 21 January 2013]

<sup>357</sup> Dr Perry – Day 45, pages 110–111



should immediately adopt dry heat treatment at 68°C'.<sup>358</sup> A decision was taken to follow this approach, which Professor Cash characterised in his oral testimony as a very difficult one (both emotionally and on a more practical level):

Q. Do you remember that time, November/December 1984, quite clearly?

A. Yes, I do actually.

Q. Yes.

A At least the panic and alarm and the sweat and the terror and the loneliness of it, when the boys came in and said, 'John, we think we should do this and this and this', and they are all looking at me. It is up to you, you are the medical director, to press the button. And there were two problems: were we going to accept the Groningen view that it was okay, our product was going to be okay? Point 1. The second was, which I think would be refused now: what's the legal position of pulling that product that has already been issued and heating it?<sup>359</sup>

**23.180** As regards the issue of the legal position of rapidly introducing heat-treated product, Professor Cash alluded in his written statement to experiencing a sense of isolation at the time.<sup>360</sup> In an additional written statement on this point, Professor Cash commented that:

Despite a request for SHHD support (through Dr AE Bell, (SHHD)), the responsibility to permit the release of the first PFC heat-treated Factor VIII was not shared by SHHD or CSA officials .... But it was shared by clinical colleagues and, through Dr Perry, informal support was obtained from a senior NIBSC staff member.<sup>361</sup>

**23.181** When asked to comment on this suggestion by Professor Cash, the Scottish Government explained that it had been 'unable to find any documents in which the SNBTS complained of a lack of support, or sought additional support, other than funding', noting however, that 'it would appear from the remaining records that the main contact within SHHD in relation to this issue was Dr Bell, who is no longer alive and therefore cannot be consulted'.<sup>362</sup> The Scottish Government also asserted that in its view, the fact that dry heat treatment was ultimately introduced is evidence that active support and funding was provided to the PFC.<sup>363</sup> When asked about this issue during the public hearings, Dr Perry explained that he did contact Dr Duncan Thomas, who was the Head of Haematology at the National Institute for Biological Standards and Control (NIBSC), but that this was not a formal process and was merely a question of talking him through the PFC's strategy and rationale and establishing the extent to which he thought that the rapid introduction of dry heat treatment was an appropriate thing to do.<sup>364</sup> Dr Perry also appeared to have few concerns over regulatory issues commenting that:

I have to say, as an operational manager in a period of enormous concern but also a belief that we could do something very quickly and very effectively, I

---

<sup>358</sup> Dr Foster's statement on viral inactivation to 1985 [PEN.012.1438] at 1472

<sup>359</sup> Professor Cash – Day 43, page 108

<sup>360</sup> Professor Cash's statement on viral inactivation to 1985 [PEN.012.1912] at 1927

<sup>361</sup> Professor Cash's additional statement on viral inactivation to 1985 [PEN.012.1909] at 1910. There is no evidence that a specific request for support on this matter at that time was made to the CSA.

<sup>362</sup> Letter from Scottish Government to Inquiry Team, 4 May 2011 [PEN.012.1731] at 1732

<sup>363</sup> In the light of the evidence already recited, this assertion cannot be accepted as accurate or justified on any objective view.

<sup>364</sup> Dr Perry – Day 45, page 116

think, even with hindsight, the concerns over the regulatory process weren't at the front of my mind.<sup>365</sup>

**23.182** It appears that Professor Cash had a telephone conversation with Dr M E Duncan of the DHSS Medicines Division (then charged with the control of licensing of medical products) in November 1984. Dr Duncan wrote to Professor Cash on 26 November 1984 referring to the telephone conversation and confirming that 'the licensing authority wishes to encourage all companies involved in the production of Factor VIII to use a dry heat process in the course of manufacture' and that 'we are inviting each company to consider this proposal and, hopefully, to make early (abridged) application for a new product licence'.<sup>366</sup> The PFC did not require a licence under the Medicines Act 1968. But it appears that Professor Cash, via Dr Perry, received from Dr Duncan Thomas in the NIBSC, the 'moral support' he wanted.<sup>367</sup>

**23.183** On returning to Scotland, Dr Foster wrote a letter to Professor Cash on 6 November 1984 in which he described the information provided during the Groningen meeting as 'encouraging'.<sup>368</sup> The letter included Dr Foster's notes of the meeting which, as regards inactivation of HTLV-III, contained the following information:<sup>369</sup>

Heat inactivation studies (probably by Cutter)

Starting level of virus  $10^5$  particles/ml (LAV)

Conditions

68° wet heating (German method)

68° dry heating

Comment

Complete inactivation in 4 minutes

< $10^1$  particle/ml after 1 hour, complete inactivation at 24 – 78 hr

**23.184** Dr Foster later confirmed, during his oral evidence, that the figure of 68°C mentioned in his notes for 'wet heating' was incorrect and should read '60°C' as this – not 68°C – was the temperature used in the pasteurisation experiments in question.<sup>370</sup>

**23.185** In his written statement, Dr Foster explained that one of the key attractions of dry heat treatment was that it could be applied to existing stocks of Factor VIII concentrate.<sup>371</sup> In the SNBTS Briefing Paper on the Development of Heat Treatment of Coagulation Factors he said that reasons for choosing this heating protocol (68°C for two hours) were as follows:

68°C was selected by the SNBTS as it was the highest temperature that had been applied to Factor VIII concentrate by any manufacturer and was known to be well tolerated by recipients. Two hours was specified because this was the longest period of heating that samples of the existing SNBTS Factor VIII concentrate (NY) from a range of different production batches could withstand, as well as being double the period that had been reported to substantially inactivate HIV.<sup>372</sup>

<sup>365</sup> Dr Perry – Day 45, page 117

<sup>366</sup> Dr Duncan's letter to Professor Cash [PEN.013.0125]. For a discussion of the background to the licensing process see Professor Cash's additional statement on viral inactivation to 1985. [PEN.012.1909] and Professor Cash – Day 43, pages 111–114

<sup>367</sup> Professor Cash – Day 43, pages 109–110

<sup>368</sup> Dr Foster's letter to Professor Cash [SNB.007.4557]

<sup>369</sup> Dr Foster's notes on the Groningen meeting of 1–2 November 1984 [SNB.008.6528] at 6529–30

<sup>370</sup> Dr Foster – Day 42, pages 62–63

<sup>371</sup> Dr Foster's statement on viral inactivation to 1985 [PEN.012.1438] at 1464

<sup>372</sup> SNBTS Briefing Paper [PEN.013.1309] at 1345

**23.186** The SNBTS Briefing Paper explained in more detail that the rationale for choosing to heat for two hours at 68°C was as follows:<sup>373</sup>

- There was evidence from the USA that this degree of heat treatment could inactivate HIV.
- As about 12 months stock of unheated Factor VIII (NY) was available, heat treatment of this stock meant that heat treated Factor VIII could be supplied from donations that had been collected at an earlier stage of the HIV epidemic, thereby enabling a product to be supplied with a lower theoretical risk than one prepared from donations collected later in the epidemic.
- The product was immediately available for heat treatment, enabling sufficient heat-treated Factor VIII concentrate for all patients to be provided very quickly.
- A stock of heat-treated product was available to re-fill the supply chain and to have available product in reserve for unplanned use, emergencies and other contingencies.
- Waiting for Factor VIII concentrate to be prepared with a revised formulation, to enable the product to tolerate heating for 24 hours, would have delayed the introduction of heat-treated Factor VIII concentrate by about five months, ie the time taken to re-start production, manufacture a fresh batch of Factor VIII concentrate and to then obtain the necessary clinical data concerning efficacy and tolerability.

**23.187** Following the meeting in Groningen, the PFC focused on attempting to dry heat Factor VIII to 68°C. During a meeting of the Heads of Department/Section Managers held on Tuesday 13 November 1984, Dr Perry indicated that:

[A]s a result of the amount of information being publicised through the press on the subject of AIDS, there was an immediate requirement for PFC to render all FVIII free from HTLV III virus .... R&D and QC were setting up experiments for heating FVIII at a higher temperature to kill the HTLV III virus without compromising the quality of this product and it was noted that Dr Foster had already subjected some material to this heating process ....<sup>374</sup>

**23.188** The minutes of the meeting also noted that Dr Foster had advised that he might need access to the pasteurisation cabinet and a freeze drier for the purpose of this exercise.<sup>375</sup> In his written statement he explained that access to the pasteurisation cabinet (normally used for albumin processing) was needed as there was insufficient time to obtain a dry heat treatment oven, noting that:

Specialist ovens for dry-heat treatment ... had to be manufactured to order and could not be obtained for about 6 months. In order to avoid delay, the spray cabinet that was used to pasteurise albumin was utilised to heat vials of freeze dried Factor VIII, pending the purchase and delivery of a specialised oven.<sup>376</sup>

---

<sup>373</sup> SNBTS Briefing Paper [PEN.013.1309] at 1345–46

<sup>374</sup> Minutes of PFC Heads of Department meeting, 13 November 1984 [SNB.010.3475] at 3476

<sup>375</sup> Ibid

<sup>376</sup> Dr Foster's statement on viral inactivation to 1985 [PEN.012.1438] at 1464. See also Dr Perry's statement on viral inactivation to 1985 [PEN.012.1759] at 1777–78

**23.189** Dr Foster added that 'although the spray cabinet was normally operated at 60°C, it had fortuitously been designed to function up to 70°C'.<sup>377</sup> Dr Foster said that the successful operation of the spray cabinet was confirmed in a validation run on 14 November 1984, enabling routine dry heat treatment of Factor VIII to begin on 18 November 1984.<sup>378</sup> It was this spray cabinet which was ultimately used to heat sealed vials of freeze-dried Factor VIII concentrate for two hours at 68°C (see step A18 in Figure 20.2 appended to Chapter 20, *Haemophilia Therapy – The Period up to the Early 1980s*).

**23.190** On 22 November 1984, the PFC sent Dr Boulton (Edinburgh and South East Scotland BTS) four vials of Factor VIII which had been dry-heated for two hours at 68°C.<sup>379</sup> These were supplied so that solubility tests could be carried out before the planned limited release of the batch the following week once it had cleared quality control.

**23.191** A meeting of Haemophilia Directors and representatives of the SNBTS took place on 29 November 1984 to discuss the implications of recent findings of HTLV-III antibodies in Scottish haemophilia patients, measures being taken by the SNBTS to prevent transmission of AIDS by blood products, and media-related matters.<sup>380</sup> During this meeting Dr Perry explained that it would be some time before the PFC's pasteurised product would be available and that 'having regard to the established sensitivity of retroviruses to heat, and corresponding reports of the efficacy of heat treatment at 68°C in countering HTLV III activity' dry heat treatment of Factor VIII at 68°C for two hours had commenced as a short-term measure.<sup>381</sup> The minutes of this meeting also noted that clinical trials of this dry-heated product were already underway. Thus, at this point a formal decision had also been taken in Scotland to dry heat Factor VIII as a short-term solution aimed at preventing transmission of AIDS.

**23.192** The clinical trials referred to were intended to ensure that the product still had Factor VIII activity and that there were no unacceptable side-effects to its use. These tests could be carried out quickly. Trials to assess whether the dry-heated product did prevent HIV/AIDS transmission would have taken much longer.

**23.193** On 6 December 1984, Dr Perry wrote a letter to all the Regional Transfusion Directors (ie in Belfast, Glasgow, Edinburgh, Inverness, Aberdeen and Dundee) which confirmed that the first infusions of dry-heated Factor VIII had been successful, although recovery and half-life data had yet to be received.<sup>382</sup> The letter also noted that arrangements had been made for dispatch of the first batches of dry heat-treated Factor VIII, with expected delivery on 10 or 11 December 1984 and that the initial quantities dispatched would provide approximately one month's supply. It was also indicated that following this initial supply, plans were in hand to supply further quantities of dry-heated product to each RTC equivalent to twice the minimum/maximum stock level so as to enable continuous supply to patients after 10 December (this second phase would start in the latter half of the week beginning 10 December and was expected to be completed before Christmas). It was also pointed out that 'in the New Year, PFC will arrange for non-heated product to be collected from RTCs' – ie a recall of non-heated products would take place in the New Year of 1985 – and that the RTCs should 'make arrangements for this material to be recalled as widely as possible in preparation for this replacement programme'.

<sup>377</sup> Dr Foster's statement on viral inactivation to 1985 [PEN.012.1438] at 1465

<sup>378</sup> Ibid [PEN.012.1438] at 1465

<sup>379</sup> Letter from Mr McQuillan to Dr Boulton, dated 22 November 1984 [SNB.007.4592]

<sup>380</sup> Minute of meeting of Haemophilia Directors and SNBTS representatives, 29 November 1984 [SNB.001.5256]

<sup>381</sup> Minute of meeting of Haemophilia Directors and SNBTS representatives, 29 November 1984 [SNB.001.5256] at 5257

<sup>382</sup> Dr Perry's letter to Regional Transfusion Directors [SGH.002.6506]. Shortly thereafter, the recovery and half-life data were found to be acceptable – see message from Dr Boulton to Dr Perry [SNB.007.4656]

**23.194** When asked about this general recall programme during the public hearings, Dr Perry explained that 'it was the intention that all product, right down to the patient's domestic refrigerator at home would be recalled and replaced with heat-treated material'.<sup>383</sup> Dr Perry also explained that the PFC arranged this through the RTCs, with the RTCs making the practical arrangements with the patients:

[T]he instruction would have gone from myself to the regional transfusion centres, who were our regional representatives, and they would have liaised with the haemophilia centres and various other holding points because they were the distribution points ... they held the records of where these products were issued to. Therefore in order to effect an effective recall, you had to recall it via the regional transfusion centre.<sup>384</sup>

However, he added that recall from the patients did not occur in order to carry out the initial heat treatment since the SNBTS had sufficient of its own material for this purpose and also because the patients still needed product to treat unexpected bleeds.<sup>385</sup>

**23.195** Dr Cuthbertson also emphasised that the PFC was not directly responsible for the recall, explaining that Dr Perry wrote to the Regional Transfusion Directors who then transacted the recall from individual haemophilia treatment centres, who in turn requested the return of product from their patients.<sup>386</sup>

**23.196** Professor Ludlam described his practice:

Patients were invited to return the bottles of unheated concentrate they had at home and heat treated concentrate was given in exchange. This change over was complete by the end of December.<sup>387</sup>

**23.197** Following on from Dr Perry's letter of 6 December 1984, a meeting of the Heads of Department/Section Managers took place on 7 December 1984 which also confirmed that the clinical trials in question had been successful and that the product would be distributed to the RTCs in the forthcoming week.<sup>388</sup>

**23.198** On 10 December a meeting took place in Elstree between UKHCDO Reference Centre Directors, blood transfusion colleagues and senior staff from Edinburgh and Elstree.<sup>389</sup> The meeting discussed heat treatment and ultimately recommended the heat treatment of NHS products. Although it is not clear what influence, if any, a negative decision by this meeting might have had on the PFC's existing strategy to dry heat its own product, it is worth noting that the meeting appears to have been a difficult one. According to Professor Ludlam's written statement:

It was not an easy decision to make because of the possible adverse effects of heat treatment on the clotting factors and other proteins in the vials which could have had a range of adverse effects on patients. This was particularly difficult because it was very uncertain how effective the heat treatment would be at inactivating the HTLVIII virus ....<sup>390</sup>

---

<sup>383</sup> Dr Perry – Day 45, pages 101–102

<sup>384</sup> Dr Perry – Day 45, pages 103–104

<sup>385</sup> Dr Perry – Day 45, page 102

<sup>386</sup> Dr Cuthbertson – Day 46, pages 84–85

<sup>387</sup> Professor Ludlam's note on long-term safety monitoring for transfusion transmitted infections [PEN.012.0351] at 0355

<sup>388</sup> Minutes of PFC Heads of Department meeting, 7 December 1984 [SNB.010.3462] at 3463

<sup>389</sup> DHSS note from 10 December 1984 meeting [DHF.003.0898] and Note of Haemophilia Reference Centre Directors' meeting, 10 December 1984 [SNF.001.3850]

<sup>390</sup> Professor Ludlam's note on long term safety monitoring for transfusion transmitted infections [PEN.012.0351] at 0355

**23.199** In oral evidence, Professor Ludlam explained further that, in practical terms the problem was that 'if we had altered the molecule slightly and 100 per cent [of patients] developed inhibitors, then we would have virtually no effective treatment for haemophilia, apart from FEIBA'<sup>391</sup> adding that 'a decision was nearly made not to heat-treat and it was only because two or three people were quite forceful in their views that the decision was made'.<sup>392</sup>

**23.200** Professor Cash made a similar general point in his written statement, indicating that 'there was great concern among many of the clinicians that any form of heating might be associated with protein denaturation which could have serious consequences for the patients'.<sup>393</sup>

**23.201** Later, on 17 December 1984, Professor Cash wrote to the Scottish Haemophilia Directors informing them that they would be receiving supplies of the first-generation heat-treated Factor VIII within the next day or so and requesting them to monitor clinical efficacy and the development of neo-antigens and to take serum samples to test for HTLV-III antibody.<sup>394</sup> Professor Cash's letter elicited a critical response from Professor Ian Hann of the Royal Hospital for Sick Children at Yorkhill in Glasgow who queried, in a handwritten letter to Professor Cash dated 19 December 1984, whether adequate studies of 'neo-antigen formation, efficacy and other safety issues' had been made and whether the PFC would know in the near future whether heat treatment had been effective.<sup>395</sup> When asked to expand on this letter during the public hearings Professor Hann explained that:

Certainly I was very nervous about this approach. Without going into great detail, one normally does not launch a product or a drug in children with very, very limited information. Especially when there is a risk of neoantigen formation, therefore severe reactions which could be even life-threatening. There could be a significant risk of the development of inhibitors, which is a disaster, making patients not responsive to treatment, et cetera.<sup>396</sup>

**23.202** He added:

As it turned out, everything was okay, but I just wanted to express the fact that (a), it was very impracticable to do what was being asked, (b), it wasn't necessarily covering all the types of checks that I would like to see with regard to the liver function tests, et cetera and (c), that it really ought to have been instituted, and I would have preferred to see a bit more evidence that there were no neoantigens, et cetera, and that there was some evidence of safety rather than, 'Here it is, get on with it'.<sup>397</sup>

**23.203** Therefore, in summary, by the end of 1984 the PFC had taken a strategic about-turn due to the threat of AIDS and (notwithstanding the lack of clear-cut evidence that such a process would be successful) had chosen to dry heat existing Factor VIII for two hours at 68°C and to recall existing unheated product.

---

<sup>391</sup> ie Factor VIII Inhibitor Bypass Activity.

<sup>392</sup> Professor Ludlam – Day 44, pages 9–10

<sup>393</sup> Professor Cash's statement on viral inactivation to 1985 [PEN.012.1912] at 1927

<sup>394</sup> Professor Cash's letter to Haemophilia Directors [SNB.007.4685]

<sup>395</sup> Dr Hann's letter to Professor Cash [SNB.007.4689]

<sup>396</sup> Professor Hann – Day 21, page 59

<sup>397</sup> Professor Hann – Day 21, page 59

**23.204** At the time, this strategy was seen as a temporary arrangement and, as outlined elsewhere in this Report, further developments (for example dry heat treatment for 24 hours at 68°C) followed. At the time it was not clear whether the heating protocol had been successful in inactivating HIV. However, a later look-back study discussed by Dr Robert Cuthbert and others reported that two of the first batches of PFC Factor VIII heated in November 1984 at 68°C for two hours had been prepared using a donation which was later found to be infected with HIV. It had not subsequently transmitted HIV.<sup>398</sup> The Inquiry is also not aware of any HIV infections associated with Factor VIII heat-treated using this protocol. Therefore, looking back at this period, the evidence suggests that the heat treatment protocol chosen by the PFC (ie 68°C for two hours) was effective in inactivating HIV. As outlined elsewhere in the Report, it was not, however, effective at inactivating NANB Hepatitis.

### General issues

#### *Why did the Protein Fractionation Centre not switch to dry heat treatment earlier?*

**23.205** As outlined above, up until the autumn of 1984 the PFC planned to pasteurise Factor VIII – initially to deal with the threat of NANB Hepatitis and later to deal with the emerging threat of HIV. In late October/early November 1984 this strategy changed and the PFC switched its efforts to dry heat treatment of Factor VIII, which ultimately proved successful at inactivating HIV. Given that the Edinburgh Cohort became infected with HIV in the spring of 1984, one of the key questions for the Inquiry is whether the PFC should have made this switch at an earlier point in time – for example in January 1984.

**23.206** The Inquiry put this question in the following terms to all of the major witnesses who gave evidence:

In retrospect, the infection of the group of people known as the Edinburgh Cohort would have been prevented if PFC had moved to dry heat treated product at the beginning of 1984. It appears that the equipment necessary to do so was either already installed or already obtained. What are the reasons why this did not take place?<sup>399</sup>

At one level, the question was clearly hypothetical. Confirmation that the cause of AIDS was indeed viral, and was to become known as the Human Immunodeficiency Virus, was not available until April 1984, and the first (experimental) test of possible exposure to the virus was not available until August or September 1984. It was important, however, to avoid limiting the issue by prescribing an over-narrow reference period.

**23.207** The Inquiry also posed a similar question to the expert witness, Professor van Aken.

**23.208** As outlined below, the overwhelming response of the witnesses heard by the Inquiry was that the PFC was correct not to introduce dry heat treatment at the beginning of 1984, and that there were rational reasons for not doing so.

---

<sup>398</sup> Cuthbert et al, 'Efficacy of heat treatment of Factor VIII concentrate', *Vox Sanguinis*, 1988; 54:199–200 [LIT.001.0664]

<sup>399</sup> Inquiry's schedule of questions on viral inactivation to 1985 [PEN.012.1531] at 1538–39

## Dr Foster

**23.209** Dr Foster's response to this question in his written statement, with references to paragraphs of the Preliminary Report, was as follows:

a) In my opinion, dry-heat treatment was not introduced by the SNBTS in January 1984 for the following reasons:

- the cause of AIDS was not known (paragraph 8.84),
- the virus responsible for AIDS had not been discovered (paragraph 8.84),
- that the virus responsible for AIDS could be inactivated by heat treatment was not known,
- that the virus responsible for AIDS could be inactivated by dry-heat treatment, under conditions that SNBTS Factor VIII concentrate could withstand, was not known,
- the SNBTS was already preparing pilot batches of a heat treated product (ZHT) for clinical evaluation, similar to a number of other manufacturers,
- no manufacturer in the world had switched from unheated to heat treated Factor VIII concentrate, although some manufacturers were heat treating a small proportion of their Factor VIII,
- it was known that dry-heat treatment had not inactivated agent(s) responsible for non-A, non-B hepatitis (paragraph 11.160),
- there was concern<sup>400</sup> that patients might react adversely to heat treated products ....<sup>401</sup>

**23.210** Dr Foster also made the following additional points in his statement: (i) to the best of his knowledge Scotland was the first country to switch completely to heat-treated Factor VIII and the only country to recall unheated Factor VIII at the end of 1984/start of 1985; (ii) it was not until 26 January 1985 that a peer-reviewed paper was published which reported that HIV was relatively heat-sensitive;<sup>402</sup> (iii) although the BPL issued some batches of dry-heated Factor VIII in early 1985, unheated Factor VIII continued to be issued in England and Wales by the BPL until 1 May 1985.<sup>403</sup>

**23.211** During the public hearings Dr Foster was also asked whether an additional reason for not dry heating at the start of 1984 was the fact that it was not then known that HIV had infected the Scottish blood supply.<sup>404</sup> Dr Foster said:

[I]n January 1984, even if we had known that HIV was in the blood supply, we didn't know how to prevent it and what you are suggesting is based on hindsight.<sup>405</sup>

---

<sup>400</sup> Dr Foster's statement includes a reference to a letter from Professor Cash to Mr Watt, dated 22 April 1983 [SNB.007.3625]

<sup>401</sup> Dr Foster's statement on viral inactivation to 1985 [PEN.012.1438] at 1475–76

<sup>402</sup> Spire et al, 'Inactivation of lymphadenopathy-associated virus by heat, gamma rays and ultraviolet light', *The Lancet*, 1985; 1:188–189 [SNB.007.4724]

<sup>403</sup> For these and other additional background arguments see Dr Foster's statement on viral inactivation to 1985 [PEN.012.1438] at 1476–77

<sup>404</sup> Dr Foster – Day 42, page 77

<sup>405</sup> Dr Foster – Day 42, page 78



**23.212** When asked what the PFC would actually have done in these hypothetical circumstances, Dr Foster explained that:

I am sure we would have sat down and done everything we could have thought of. I doubt we would have done something speculative in terms of some treatment that we had no knowledge would or wouldn't work, which might harm patients.<sup>406</sup>

**23.213** Thus, according to Dr Foster, even if it had been clear at the start of 1984 that HIV had entered the donor pool, given that it was not known then how to inactivate the virus it is unlikely that this knowledge would have led to speculative dry heat treatment.

### Dr Smith

**23.214** Dr Smith's response to this question was as follows:

May I be allowed to speculate, since I was not party to PFC's decision-making but was swimming in the same soup at the time? ....

- Prior to November 1984, there was no reason to believe that dry-heating would succeed in preventing transmission of AIDS, and in fact almost all the early dry-heated (commercial) concentrates caused confirmed transmissions of HIV at later dates. In the wake of Hyland's experience, there was no likelihood that NANBH would be inactivated if dry-heating were applied to PFC's F.VIII at that time.
- I am not sure that, in early 1984, it was generally perceived that AIDS had entered the UK donor population. No test was generally available, validated for application to large populations of donors.
- In about May 1984, three patients in England were given mildly-heated (60°C, 72h) Factor VIII, and by the end of 1984 had contracted neither AIDS nor NANBH. [T]his anecdotal experience had no impact on BPL's policy. If in fact the information was considered significant enough for me to share with SNBTS, I would not have expected it to affect PFC policy.
- At the beginning of 1984, clinical trial of PFC's pilot-scale batches of pasteurised F.VIII was still being considered successful ... and there were detailed plans for scale-up and national issue in a credible time-scale .... There was reason to expect that this pasteurised F.VIII would transmit neither AIDS nor NANBH. For several reasons, it is extremely difficult to envisage running two candidate products full-pelt in a unit with limited resources, so a choice had to be made (England did not have the luxury of choice ... and was perhaps lucky in that – but only with hindsight). It should not be inferred that PFC made the 'wrong' choice at that period, or that PFC was slow to modify its position when the evidence moved on, later in the year.<sup>407</sup>

**23.215** Dr Smith was asked during the public hearing to expand on the second bullet point in his written statement and whether the assessment of risk would have been different if it had been known that HIV had entered the donor population at the start of 1984. Dr Smith responded as follows:

---

<sup>406</sup> Dr Foster – Day 42, page 81

<sup>407</sup> Dr Smith's statement on viral inactivation to 1985 [PEN.012.1551] at 1565–66

Q. [I]f it had been known at the start of 1984 that AIDS was in the donor population, the assessment of the risk and the timescale within which some sort of viral inactivation process would be required would have necessarily have been different. Would you agree with that?

A. Yes, and I could be wrong. This is my recollection from the time but it is a long time ago and, generally perceived, is rather loose. But I have said it here, this would be a factor, how you perceived the balance of risk/benefit in going to heat treatment, which was still being perceived by some people as very dangerous.<sup>408</sup>

**23.216** Dr Smith was also asked whether the assumption that HIV had not entered the donor pool at the start of 1984 was realistic:

THE CHAIRMAN: In retrospect, was there not a degree of naivety in treating the donor population as in some way hermetically sealed within the boundaries of the United Kingdom? Didn't people travel in those days?

A. Yes, they did, and already by 1983 the Fletcher and Rizza paper had shown that there was no safety from non-A non-B but there were inhibitions against – AIDS was being seen as, like TB and leprosy and syphilis in previous times, as a kind of dirty disease, and you do not want readily to think that your patients or your donors are in that category. This is just psychopathology. It's not good reasons for it. But when I say 'perceptions', I don't know how many percentage of which groups – treaters, patients, transfusionists – would have subscribed to that view.<sup>409</sup>

### Dr Perry

**23.217** Dr Perry's written statement indicated that it was only with the benefit of hindsight that one could suggest that dry heat treatment could have been implemented earlier and referred to similar arguments to those mentioned above in support.<sup>410</sup> Dr Perry's statement also referred to the following additional arguments which, in his view, supported his position:

- That the PFC studies carried out in late 1983 indicated that dry heat treatment of the PFC's existing Factor VIII product (i.e. the experiments carried out by Dr Pepper and Dr Cuthbertson on 21 November 1983),<sup>411</sup> rendered the product insoluble;
- That the formal regulatory position in the UK and elsewhere was that there was inadequate evidence of any benefit (in terms of virus safety) from dry heat treatment (for either AIDS or Hepatitis) to justify the licensing of commercial dry heat treated products; and
- That, at that time, the modern 'precautionary principle' was less developed compared with today with the result that interventions on blood or plasma product safety required a greater body of scientific evidence to justify their implementation.<sup>412</sup>

---

<sup>408</sup> Dr Smith – Day 59, pages 137–138

<sup>409</sup> Dr Smith – Day 59, page 139

<sup>410</sup> Dr Perry's statement on viral inactivation to 1985 [PEN.012.1759] at 1778

<sup>411</sup> Dr Perry – Day 45, page 115. See paragraphs 23.141 to 23.142 above. NB – the protocol used by Drs Pepper and Cuthbertson was 70°C for 72 hours and not 68°C for 24 hours as reported in Dr Perry's written statement.

<sup>412</sup> Dr Perry's statement on viral inactivation to 1985 [PEN.012.1759] at 1778. It should be noted that Dr Perry's point regarding the precautionary principle does not accord with his description of the lack of regulatory procedures – see above at paragraph 23.181 and Dr Perry – Day 45, pages 116–117. See also Dr Perry – Day 45, pages 83–84 where Dr Perry makes the argument that today's regulatory procedures are much more stringent than those of the early 1980s.

**23.218** Dr Perry was also asked, during the public hearings, to explain why there appeared to be a belief at the start of 1984 that HIV had not arrived in Scotland (and by implication entered the Scottish blood supply). Dr Perry answered as follows:

[W]e must remember that although HIV is a well-known entity for everybody in this room now, at that time it was a new disease, it wasn't understood, there were still alternative ways to describe the AIDS condition and its causation and so on, and little, if anything, was known about the epidemiology and the extent to which it was travelling around the world .... With hindsight, it could have been clearly proposed or suggested that HIV could indeed be in the UK population. We just hadn't seen any evidence of it.<sup>413</sup>

**23.219** As regards the issue as to whether the PFC's strategy would have been different if it had been aware of HIV infection at the start of 1984 Dr Perry offered the following thoughts:

[M]y best guess is that even if we had had evidence of HIV in the donor population, at that point in time that in itself wouldn't have been sufficient to take what would have been seen at that time as a very dramatic step in terms of potential damage to a Factor VIII product. We might have known that HIV was in the donor population but we would have had no knowledge whatsoever of our ability to inactivate it using heat treatment.<sup>414</sup>

#### Dr Cuthbertson

**23.220** Dr Cuthbertson's written statement also commented that, in his view, 'it is only with the benefit of hindsight that it can be concluded that earlier introduction of heat treatment was a sound option', and that 'more rapid introduction of dry heat treatment was not justified on the basis of knowledge at the time and we could have easily introduced a less safe product with reduced yield which still had the capacity to transmit HIV'.<sup>415</sup> Dr Cuthbertson's arguments mirror those outlined above and also make mention of what Dr Cuthbertson refers to as 'Regulatory constraints' – the understanding that the DHSS did not wish to grant licences to commercial dry heat-treated products at this time due to safety concerns.<sup>416</sup>

#### Professor van Aken

**23.221** Professor van Aken provided the Inquiry with a report in which he reviewed the introduction of dry heat treatment of Factor VIII by the PFC and considered the question whether the PFC could or should have introduced this process at the start of 1984.<sup>417</sup>

**23.222** In his report, Professor van Aken referred to the World Health Organization's 2004 'Guidelines on viral inactivation and removal procedures intended to assure the viral safety of human blood and plasma products'<sup>418</sup> which stipulate that the ability of a process to inactivate/remove viruses should take into account:

---

<sup>413</sup> Dr Perry – Day 45, page 112

<sup>414</sup> Dr Perry – Day 45, page 114

<sup>415</sup> Dr Cuthbertson's statement on viral inactivation to 1985 [PEN.013.0025] at 0043

<sup>416</sup> Ibid

<sup>417</sup> Professor van Aken's statement on the introduction of dry heat treatment of Factor VIII concentrate [PEN.012.1932]

<sup>418</sup> *Guidelines on viral inactivation and removal procedures intended to assure the viral safety of human blood and plasma products*, WHO Technical Report, Series No. 924, Annex 4 2004, [http://www.who.int/bloodproducts/publications/WHO\\_TRS\\_924\\_A4.pdf](http://www.who.int/bloodproducts/publications/WHO_TRS_924_A4.pdf). [Last accessed 23 January 2013]

- the reduction of virus titre achieved;
- for inactivation processes, the rate of inactivation;
- the robustness of the inactivation step in response to changes in process conditions;
- the selectivity of the process for viruses of different classes; and
- validation studies, which need to be well documented.<sup>419</sup>

**23.223** According to Professor van Aken, these requirements meant that the safe introduction of a change in the manufacturing process of plasma products such as Factor VIII required: (i) knowledge about the nature and characteristics of virus(es) to be inactivated; (ii) validation studies and studies in experimental animals, and (iii) yield, manufacturing consistency and integrity of the final product with regard to protein function/structure.<sup>420</sup>

**23.224** As regards the first requirement (knowledge about nature and characteristics of virus(es)) and HIV, Professor van Aken's view was that the first indication of the cause of AIDS did not arise until the publication of Professor Gallo's article in May 1984.<sup>421</sup> Therefore, according to his view, at the start of 1984 there was insufficient knowledge regarding the cause of AIDS and consequently:

[I]f heat treatment for inactivation of HIV [had] been introduced in early or mid 1984 (or earlier) it would not have been based on evidence but rather on speculations about the origin of the virus.<sup>422</sup>

**23.225** When asked during the public hearings why commercial companies appeared to have pushed ahead with dry heat treatment in 1983 before all the necessary information was available, Professor van Aken indicated that the commercial companies had taken a 'pragmatic approach'. He said that commercial companies were able to do so since, unlike public fractionators who were confined to their home country, they operated on a worldwide basis and could, therefore, tailor their approach to different attitudes in different markets. If one country had a particularly stringent approach to the regulation of new products the commercial companies could move to another (less stringent) country.<sup>423</sup> Professor van Aken also pointed out that it was not possible simply to copy the protocols used by commercial companies as the heating conditions were either confidential or patented.<sup>424</sup> In his view, another key difference was the fact that public fractionators were often aiming at a policy of self-sufficiency and were therefore more concerned about the impact of heating on yield than commercial companies.<sup>425</sup> Upon further questioning, Professor van Aken also indicated that the fact that the commercial companies' source plasma may have been of a lower quality than that of public fractionators was likely to have been a factor which made them more likely to use heating protocols even when the evidence was not yet definitive.<sup>426</sup>

<sup>419</sup> Professor van Aken's statement on the introduction of dry heat treatment of Factor VIII concentrate [PEN.012.1932] at 1934–35

<sup>420</sup> Ibid [PEN.012.1932] at 1935–36

<sup>421</sup> Gallo, 'Frequent detection and isolation of cytopathic retroviruses (HTLV-III) from patients with AIDS and at risk of AIDS', *Science*, May 1984; vol. 224 [LIT.001.3769]

<sup>422</sup> Professor van Aken's statement on the introduction of dry heat treatment of Factor VIII concentrate [PEN.012.1932] at 1935

<sup>423</sup> Professor van Aken – Day 47, page 46

<sup>424</sup> Professor van Aken – Day 47, page 47

<sup>425</sup> Ibid, page 47

<sup>426</sup> Ibid, page 51

**23.226** As regards validation studies, Professor van Aken made the point that sufficient HIV virus to allow these studies to take place was only available in mid-1984.<sup>427</sup> Therefore, before this period work had to be done using model viruses, and that would not necessarily have been as accurate as validation using the actual virus.<sup>428</sup>

**23.227** As regards requirement three (yield, manufacturing consistency and integrity of the final product), Professor van Aken explained during the public hearings that the issue was ensuring that the product was still effective after heat treatment and also that it had not been changed in such a way that it might cause harm to patients.<sup>429</sup>

**23.228** On the basis of these arguments, Professor van Aken's conclusion on the question of whether the PFC should have introduced dry heat treatment more quickly was as follows:

The answer to the question 'Should/could PFC have moved more quickly to introduce the dry heating of factor VIII concentrate?' is NO for the following reasons:

- the procedure (the proper conditions) to inactivate blood borne viruses, in particular those present in plasma, by dry heating were not known until the later part of 1984;
- the characteristics of the viruses to be inactivated (HIV and HCV) were not known until the beginning of 1984 (HIV) respectively 1989 (HCV);
- cell lines producing sufficient quantities of HIV and HCV<sup>430</sup> to perform validation studies (virus spiking experiments) in the laboratory were not available until mid 1984;
- methods to improve the yield of factor VIII and to determine that the structure of factor VIII (or other clotting factors) after heating is still intact were not yet available.<sup>431</sup>

***Why did the Protein Fractionation Centre not follow through with the proposed acceleration of pasteurisation in 1983?***

**23.229** As mentioned above, on 3 May 1983 Dr Foster wrote a memorandum suggesting that the PFC's existing pasteurisation programme should be accelerated in order to meet the 'worst case' scenario of having to deal with HIV/AIDS.<sup>432</sup> The Inquiry asked Professor van Aken to comment on the suggestion of taking a decision on the basis of a 'worst case scenario' and asked whether he was aware whether other fractionators were also considering such an approach at the time. Professor van Aken provided a written response to this question in a separate report which was discussed during the public hearing.<sup>433</sup>

**23.230** In his report, Professor van Aken explained that in mid-1983 it was not known if a virus was responsible for AIDS and that Dr Foster's suggestion was, therefore, likely based on a presumption to this effect. Professor van Aken also indicated that in mid-1983 evidence that heat would be an effective means of inactivating the agent which caused

<sup>427</sup> Professor van Aken's statement on the introduction of dry heat treatment of Factor VIII concentrate [PEN.012.1932] at 1936

<sup>428</sup> Professor van Aken – Day 47, pages 52–55

<sup>429</sup> Ibid, page 55

<sup>430</sup> It was only cell lines for HIV which were available in 1984 (ie not for HCV). Professor van Aken corrected this mistake in his oral evidence, Day 47, page 56.

<sup>431</sup> Professor van Aken's statement on the introduction of dry heat treatment of Factor VIII concentrate [PEN.012.1932] at 1937

<sup>432</sup> Dr Foster's memo [SNB.007.3635]

<sup>433</sup> Professor van Aken's statement on the acceleration of the existing pasteurisation programme [PEN.012.1928]

AIDS was also lacking. According to Professor van Aken, it was therefore, 'by no means certain that pasteurisation would be a method to improve the safety of plasma products like factor VIII concentrate'.<sup>434</sup>

**23.231** He also indicated that initial pasteurisation attempts in several laboratories had resulted in low yields and that any pasteurisation programme would have to take this, and the possible impact on self-sufficiency, into account. He also pointed to the possible risk of neo-antigen formation as a second negative effect of any pasteurisation of Factor VIII. This could result in the creation of inhibitors in patients, thus complicating their future treatment. Professor van Aken explained further that these considerations were part of the discussion that took place among fractionators in various different countries and that some chose to carry out heat treatment even though important evidence was not available whereas others, such as the Central Laboratory of the Blood Transfusion Service (CLB) in Amsterdam, did not. In the case of the CLB, his report notes that a decision was made in accordance with recommendations of haemophilia physicians in the Netherlands to restrict the manufacture of Factor VIII so as to have sufficient material for the production of freeze-dried cryoprecipitate (reflecting the view that the risk of virus transmission from small pools of cryoprecipitate would be less than from large plasma pools used to make Factor VIII).<sup>435</sup>

**23.232** Professor van Aken's report concluded as follows:

Acceleration of the pasteurisation program by PFC would most likely have led to a low factor VIII yield and consequently fewer products for haemophilia treatment. To compensate such losses a very large increase in the collection of donor plasma in Scotland would have been necessary. In addition the risk of side effects, such as neoantigen formation by pasteurisation, would have made the treatment of a certain number of haemophilia patients more complicated. This leads me to conclude that although acceleration of the pasteurization program by PFC might have seemed an option in 1983, it is unlikely that (as part of a 'worst case scenario') this would have provided a solution for PFC.<sup>436</sup>

**23.233** When asked during the public hearings to comment on his statement that it was 'by no means certain that pasteurisation would be a method to improve the safety of plasma products like factor VIII concentrate', Professor van Aken explained that he thought that Dr Foster's plan to pasteurise all product was logical, given the amount of time which had already been committed to the project.<sup>437</sup> However, he also indicated that he personally was not convinced that 'this was the way to go,' whilst explaining that this was 'his bias' and that he found it difficult to give a clear or explicit answer given the underlying element of speculation at the time.<sup>438</sup> He also stressed that in the Netherlands the patient organisations were particularly concerned about the potential loss of yield which could be caused by heat treatment and that their preference was for yield/supply over safety.<sup>439</sup>

<sup>434</sup> Ibid [PEN.012.1928] at 1928

<sup>435</sup> Ibid [PEN.012.1928] at 1929. Compare Dr Smith's evidence at paragraph 23.21 above of planning for the BPL at April 1981.

<sup>436</sup> Professor van Aken's statement on the acceleration of the existing pasteurisation programme [PEN.012.1928] at 1929

<sup>437</sup> Professor van Aken – Day 47, page 58

<sup>438</sup> Professor van Aken – Day 47, page 59. See also Page 60 where Professor van Aken admitted that he did not know enough about the pasteurisation developments to be comfortable giving a definitive answer, and pages 60–61 where Professor van Aken indicated that the PFC did more pasteurisation research than the Dutch CLB.

<sup>439</sup> Professor van Aken – Day 47, page 62

**23.234** Thus, in conclusion, Professor van Aken's view was that there were certain difficulties with the proposed plan to accelerate pasteurisation of Factor VIII. However, given the inevitably speculative nature of taking such a decision, and the differing considerations inherent in the decision-making process between the Netherlands and Scotland, he found it difficult to give a clear-cut answer as to whether the PFC's plan to pasteurise was a reasonable one or not.

***Should the Scottish National Blood Transfusion Service have been encouraging clinicians not to let their patients try the commercial heat-treated products?***

**23.235** The Inquiry asked Professor van Aken to give a view on whether the SNBTS should have encouraged clinicians not to let their patients try commercial heat-treated products. In other words, was Professor Cash correct to oppose the introduction of formal clinical trials for commercial heat-treated products as outlined in his letter of 17 December 1982 to Dr Lane?<sup>440</sup>

**23.236** In his written statement Professor van Aken explained that such a set of circumstances would be unlikely to have occurred in the Netherlands as the CLB did not offer opinions about commercial products or encourage clinicians to stop or decrease the use of such products. Instead it provided information on its own products, with the Dutch haemophilia physicians having more of an advisory role. Professor van Aken further explained, in this context, that the Dutch association of physicians treating haemophilia patients agreed in January 1983 on the following advice for haemophilia treatment:

- 1) if possible use cryoprecipitate (notably for newly diagnosed patients and children of less than 4 years);
- 2) if factor VIII concentrate needs to be used, prescribe factor VIII concentrate prepared from plasma of Dutch donors (use commercial concentrates only in case of a severe side effects following the use of Dutch concentrate);
- 3) for the treatment of haemophilia B patients use only factor IX concentrate prepared from plasma of Dutch donors.<sup>441</sup>

**23.237** When asked during the public hearings to comment further on Professor Cash's position as expressed in his letter to Dr Lane, Professor van Aken said that, coming from a small country, he understood Professor Cash's fear that clinical trials of commercial products could reduce the number of patients available for any SNBTS trials.<sup>442</sup> However, he also pointed out that he did not think that it was the role of a fractionator to take this stance, noting that:

[I] always have felt that we have to be very cautious when you were going to direct or try to give directions for what other products, what other commercial products should or should not be used, because you are in a competitive market and in my experience it doesn't work when you are trying, as a manufacturer, to influence. That you have to leave to the government or to physicians treating haemophiliacs, but as a producer that is not your personal

---

<sup>440</sup> Professor Cash's letter to Dr Lane [SNB.004.3163]

<sup>441</sup> Professor van Aken's statement on the acceleration of the existing pasteurisation programme [PEN.012.1928] at 1929–30. Professor van Aken's statement also notes that there was one blood bank in the Netherlands which had a different policy and which recommended the use of commercial heat-treated products. For further discussion of the situation in the Netherlands at this time see Professor van Aken – Day 47, pages 66–70.

<sup>442</sup> Professor van Aken – Day 47, page 65

responsibility. I interpreted that Dr Cash was director here of the SNBTS. So he was in fact the director of a producing institution. And therefore I would be more restrictive. I would try other ways to do this instead of so openly giving a recommendation how it should be done.<sup>443</sup>

***Should commercial heat-treated products (Hemofil T) have been adopted in advance of locally produced products?***

**23.238** As outlined above, the commercial heat-treated product Hemofil T (dry heat for 72 hours at 60°C), which was licensed in the USA by the US Food and Drug Administration (FDA) in March 1983,<sup>444</sup> was later found not to have led to HIV seroconversions. The product was not granted a licence in the UK until February 1985.<sup>445</sup>

**23.239** The Inquiry asked Professor van Aken whether, in his view, Hemofil T should have been adopted in the UK in advance of locally produced heat-treated products. There are two aspects to the question: whether the product should have been granted a licence earlier, and whether it should have been prescribed on a named patient basis. Professor van Aken discussed the first of these.

**23.240** He explained in his report that Hemofil T was later found to transmit NANB Hepatitis (the outcome of Professor Mannucci's 1985 study mentioned above). According to Professor van Aken, looking back, this was one reason to justify the lack of a licence since:

If the marketing efforts of commercial companies such as Hyland would have led to introduce such a product for haemophilia treatment in the UK it would subsequently have created uncertainty and critique when it was shown that the claim of non-transmission of NANB hepatitis proved to be unjustified.<sup>446</sup>

**23.241** Professor van Aken explained that his view was that the adoption of heat-treated products was justified when it could be established that the agent responsible for AIDS was inactivated by the heating procedure. In his view, since the safety of commercial plasma as source material for the manufacturing of Factor VIII was questionable, 'it was prudent not to introduce commercial factor VIII concentrate until it was shown that such products were safe'.<sup>447</sup> Professor van Aken also argued that alternative products such as cryoprecipitate were available which, because they were prepared from small pools of plasma from non-remunerated donors, were less risky than Factor VIII concentrates prepared from very large pools of remunerated donors.

**23.242** Given the above arguments, Professor van Aken concluded that:

[T]he adoption of commercial heat treated products in the UK in advance of locally produced products would have been justified once there was sufficient and reliable data from clinical studies demonstrating the safety and efficacy of such commercial products. *Hemofil-T* did not meet such criteria.<sup>448</sup>

<sup>443</sup> Professor van Aken – Ibid

<sup>444</sup> Kasper et al, 'Recent evolution of clotting factor concentrates for hemophilia A and B', *Transfusion*, 1993; 33/5: 422–434 [SGH.002.1947] at 1954

<sup>445</sup> SNBTS Briefing paper on the development of heat treatment of coagulation factors [PEN.013.1309] at 1323; HC Hansard, Vol 75, Col. 117, 12 March 1985 [SGF.001.0854]

<sup>446</sup> Professor van Aken's statement on the acceleration of the existing pasteurisation programme [PEN.012.1928] at 1930

<sup>447</sup> Ibid [PEN.012.1928] at 1930

<sup>448</sup> [PEN.012.1928] at 1930–31



**23.243** The issue of the safety, or otherwise, of Hemofil T as regards HIV was also discussed with Dr Foster during the Inquiry's public hearings.<sup>449</sup> Dr Foster referred to a report which he had drawn up for the Archer Inquiry<sup>450</sup> entitled, 'Response to Questions raised at the Inquiry in Contaminated Blood and Blood Plasma Products'.<sup>451</sup> The report explained, amongst other things, that:

- (i) it was known in September 1983 that Hemofil T had transmitted NANB Hepatitis;
- (ii) the UK Committee on the Safety of Medicines had rejected a licence application for Hemofil T in September 1983;
- (iii) it was not until February 1985 that reports became available that 18 patients treated exclusively with Hemofil T were HIV-negative (according to Dr Foster, although these results were encouraging they did not prove that HIV had been inactivated as there was no evidence that the batches in question were infected);
- (iv) a January 1986 study on the inactivation of viruses in Factor VIII did not contain any data on Hemofil T.<sup>452</sup> According to Dr Foster, to suggest, as had been suggested at the Archer Inquiry, that it was known in May 1983 that the HIV virus could be inactivated by a particular heat treatment protocol, such as that used for Hemofil T, reflected a misunderstanding.<sup>453</sup>

***Did Mr Watt's resignation have an impact on the heat treatment programme?***

**23.244** As outlined above, Mr Watt, the Director of the PFC, decided to leave the PFC in the summer of 1983. This decision was officially communicated to Professor Cash by letter dated 4 July 1983 in which Mr Watt outlined the reasons for his resignation. The reasons included personal matters (including increased domestic commitments and medical issues), as well as a desire on the part of Mr Watt to finish his career as a consultant working in the field of fractionation in a role outwith the PFC.<sup>454</sup> Professor Cash subsequently drew up a confidential document entitled 'Replacement of the Director of PFC (Preliminary Notes)', dated August 1983.<sup>455</sup> In this document, Professor Cash discussed certain problem areas which, in his view, had arisen during Mr Watt's management of the PFC (in particular the lack of management control which the National Medical Director had over the Director of the PFC) and suggested possible solutions. From the tone and content of this confidential report, it is clear that Professor Cash viewed the relationship between himself and Mr Watt as not being in good repair. Although the original plan was that Mr Watt would leave at the end of March 1984, it is evident from a memo from Dr Perry to the Heads of Department and Section Managers dated 30 December 1983 that Mr Watt actually left at the end of December 1983<sup>456</sup> with Dr Perry taking over as Acting Director.<sup>457</sup>

<sup>449</sup> Dr Foster – Day 42, page 46

<sup>450</sup> Independent Public Inquiry into Contaminated Blood and Blood Products – <http://www.archercbbp.com/report.php> [Last accessed 14/12/2014]

<sup>451</sup> Dr Foster's report to the Archer Inquiry [PEN.012.1506]

<sup>452</sup> Ibid [PEN.012.1506] at 1507

<sup>453</sup> Dr Foster – Day 42, page 48

<sup>454</sup> Mr Watt's letter to Professor Cash [SNB.011.1214]

<sup>455</sup> Professor Cash's note on replacement of the Director of PFC [SNB.011.1217]

<sup>456</sup> Dr Perry's memorandum of 30 December 1983 [SNB.009.4290]

<sup>457</sup> See letter from Professor Cash to Mr Mutch (Secretary CSA) dated 23 May 1984 confirming that Dr Perry was Acting Director of the PFC [SNB.011.1688]

**23.245** The Inquiry asked various witnesses for more details on the impact of Mr Watt's departure and, more importantly, whether his departure adversely affected the PFC's viral inactivation programme.<sup>458</sup>

**23.246** In his oral evidence Professor Cash confirmed that he was of the view that Mr Watt's departure did not affect the heat treatment programme. The main reason for this was that 'Peter Foster, the solid rock, was still there, as far as that programme was concerned'.<sup>459</sup> As regards the departure of staff, Professor Cash explained that two staff at a senior technical level ultimately left the PFC to work with Mr Watt's consultancy.<sup>460</sup>

**23.247** Dr Foster stated in his written evidence that he learned on Monday 11 July 1983 on his return from Stockholm that Mr Watt had resigned. He was informed by a colleague that Mr Watt was planning to establish a company to fractionate animal plasma and that he was seeking to recruit staff from the PFC.<sup>461</sup> When asked, Dr Foster informed Professor Cash that he had not been approached by Mr Watt and that, if approached, he had no intention of leaving the PFC. According to Dr Foster:

It was evident to me that Dr Cash was worried that the PFC might be damaged by the loss of key staff. Later, he told me that he had discussed the matter with Mr Watt, who had indicated that he intended to recruit only a small number of staff from the PFC to avoid any damage to the PFC. Nevertheless, I believe that it was concern over the potential loss of key PFC staff that led to Mr Watt leaving at the end of December 1983, rather than at the end of March 1984.<sup>462</sup>

**23.248** In his written statement Dr Foster also expressed the view that Mr Watt's resignation did not adversely affect the virus inactivation programme, stating that:

I do not believe the resignation of Mr Watt adversely affected the virus inactivation programme or influenced the SNBTS strategy. According to his CV,<sup>463</sup> Mr Watt continued to be a member of the Biologicals sub-committee of the Committee on Safety of Medicines until 1986. In March 1984 this committee approved an application from Behring for a licence for its pasteurised Factor VIII and, in July 1984, rejected an application for a licence from Armour for its dry-heat treated Factor VIII. I do not know the advice, if any, that Mr Watt offered at these meetings, but the fact that the SNBTS strategy was consistent with both of these decisions does not suggest that Mr Watt would have encouraged the SNBTS to take a different position if he had remained in post.<sup>464</sup>

**23.249** In oral evidence Dr Foster said that the departure of staff to Mr Watt's consultancy did not impact on the heat treatment programme. A few people at section manager, senior technical level left the PFC to join him when he had established his own business. In particular, a person who managed one of the quality control laboratories and also a person who managed one of the areas in production at a senior technical level joined Mr Watt. But these losses were coped with within normal turnover of staff arrangements.<sup>465</sup>

---

<sup>458</sup> See the Inquiry's Schedule of Questions [PEN.012.1531] at 1535 – paragraphs 21–22

<sup>459</sup> Professor Cash – Day 43, page 83

<sup>460</sup> Professor Cash – Day 43, pages 83–84

<sup>461</sup> Dr Foster's statement on viral inactivation to 1985 [PEN.012.1438] at 1467

<sup>462</sup> Dr Foster's statement on viral inactivation to 1985 [PEN.012.1438] at 1467

<sup>463</sup> Mr Watt's curriculum vitae [PEN.012.1491]

<sup>464</sup> Dr Foster's statement on viral inactivation to 1985 [PEN.012.1438] at 1466

<sup>465</sup> Dr Foster – Day 42, pages 30–31

**23.250** Dr Perry was also of the view that Mr Watt's resignation did not adversely affect the viral inactivation programme, stating that:

Mr Watt resigned in July 1983 and following his earlier than planned departure in December 1983 I was appointed as acting Director of PFC.

It is not possible to meaningfully judge the general impact of his departure but by this time the PFC programme on heat treatment was well advanced and there are no specific instances of delays or failures of the development programme attributable to his departure.<sup>466</sup>

**23.251** In line with Dr Foster, Dr Perry also explained in his oral evidence that, in his view, the departure of two staff to Mr Watt's consultancy did not adversely affect the heat treatment programme, stating that:

[I] don't think there were any, what you might describe as absolutely key individuals, that left taking with them intellectual capability or intellectual property. I think that the programme that had been established prior to Mr Watt's departure carried on, ably led by Dr Foster.<sup>467</sup>

**23.252** Dr Perry also provided background to his appointment as Acting Director of the PFC in January 1984, explaining that Professor Cash asked him informally to take on the role and that this was followed up on a formal basis by the secretary of the CSA, Mr Mutch, with confirmation of the permanent role being made a year later in 1985.<sup>468</sup>

## Discussion and conclusions

**23.253** The transmission, in the spring of 1984 (discovered in the autumn of 1984), of HIV infection to haemophilia patients treated in Scotland at the RIE with PFC Factor VIII concentrate was an event of critical importance for this Inquiry. It had a devastating impact on the lives of the patients involved, and on the lives of their families. Most of the patients infected with HIV had died before the Inquiry was instructed. The circumstances in which the patients came to be infected are discussed in Chapter 10, *Knowledge of the Geographical Spread and Prevalence of HIV/AIDS 2*. As is clear from the evidence that has been analysed in this chapter, discovery of the transmission of HIV was a factor that immediately and significantly impacted on the PFC's research and development and production priorities. And what proved to be an effective response, dry heat treatment of Factor VIII concentrate, was quickly put into effect.

**23.254** The evidence sought from documents, written statements and oral testimonies from witnesses, could not be narrowly specified: in fairness to patient interests and to the manufacturers, it was necessary to explore the background in depth. But there were some obvious questions that provided focus for the investigation and presentation of the evidence:

- Was there a risk of HIV infection in blood donated in Scotland that affected the safety of PFC products?
- When was such a risk was understood to exist?
- Was or should that risk have been taken into account by the SNBTS and the PFC in the processing of blood products?

---

<sup>466</sup> Dr Perry's statement on viral inactivation to 1985 [PEN.012.1759] at 1770

<sup>467</sup> Dr Perry – Day 45, page 61

<sup>468</sup> Dr Perry – Day 45, pages 64 and 67

- More specifically, should the threat of AIDS have caused the PFC to accelerate its heat treatment programme in or around May 1983?
- Was adherence to the pasteurisation programme until October/November 1984 justified? In particular was that course justified after January 1984?
- Was there sufficient liaison/cooperation between the fractionation services in Scotland and England over the period 1980 to 1984 in relation to viral inactivation?
- Did any management problems impact on the PFC's viral inactivation programme?
- Would closer collaboration, and UK-wide policy guidance, have avoided the pursuit of different courses by the Transfusion Services in Scotland and England, and would it have been more effective?
- Did the PFC have sufficient resources/staff and access to information/academic research for its viral inactivation programme?
- Should commercial heat-treated products have been adopted in advance of locally produced products or could/should the PFC have bought in a commercial heat-treated process<sup>469</sup> instead of developing its own?
- In general, was the approach taken to viral inactivation at the PFC in the period 1980 to 1984 reasonable?
- In general, was the degree of priority accorded to viral inactivation by the PFC during this period reasonable?

***The risk of HIV infection in blood donated in Scotland that affected the safety of Protein Fractionation Centre products***

**23.255** As discussed in Chapter 33, *An Investigation into the Systems in Place for Informing the Patients about the Risks – HIV/AIDS*, it was understood within the SNBTS by May 1983 (though not reflected in uniform action throughout Scotland) that certain groups of individuals presented a risk of transmission of the presumed infective agent causing AIDS if they donated blood, and were therefore asked not to present themselves as donors. The advice was based on reports of the US experience rather than on reported cases of transmission in the UK involving any of the groups identified. The aetiology of AIDS, and therefore the precise nature of the risk, was not at that stage well understood. The preparation and issue of leaflets reflected apprehension that there might be a risk rather than knowledge of an existing risk.

**23.256** By late July 1983, the Central Blood Laboratories Authority had concluded that AIDS was likely to include in its aetiology transmission of an infective virus, and noted that this had prompted more activity in the area of blood products pasteurisation.<sup>470</sup> At this stage it was thought that domestic products presented a low risk.<sup>471</sup> The view of the Biological Sub-Committee of the Committee on the Safety of Medicines, who at that stage were opposed to the withdrawal of imported products, was that:

Efforts are ... being made to secure UK independence of foreign suppliers of clotting factor concentrates. This should reduce markedly, although not

---

<sup>469</sup> See Dr Smith's statement on viral inactivation to 1985 [PEN.012.1551] at 1573 for a very brief mention of this point.

<sup>470</sup> CBLA paper on AIDS, dated 26 July 1983 [DHF.002.4489] at 4490

<sup>471</sup> Summary of main points from a consideration of AIDS and licensed blood products by CSM(B), 13 July 1983 [DHF.002.8865]

eliminate, the risks to recipients of these products, and the Sub-Committee strongly supports this aim.<sup>472</sup>

**23.257** At that time virus inactivation of Factor VIII and Factor IX products was a 'promising future development', and the assessment of risk was related to the presumed low level of infection in domestic blood donations. As stated in paragraph 8.45 of the Preliminary Report, self-sufficiency was seen as part of the answer to the problem of AIDS. The possibility that the agent of transmission was already present in the UK blood supply had not been specifically acknowledged.

**23.258** The death of a haemophilia patient in England in August 1983 was associated with imported products.<sup>473</sup> A further patient had received English therapy. The products he had received were under investigation, but no link had been established. An article by Dr Peter Jones in the *British Medical Journal*, published on 10 December 1983, noted that two AIDS cases had been reported in haemophilia patients in the UK.<sup>474</sup> At the end of the year there was media comment on the number of AIDS cases.<sup>475</sup> Apprehension that there was a present risk arising from UK products was beginning to appear in some quarters.

**23.259** A meeting arranged by the NIBSC to examine the infectious hazards of blood and blood products, with particular reference to hepatitis and AIDS, was held on 9 February 1984.<sup>476</sup> It was reported that the most recent information indicated that two UK patients and nine other European patients with haemophilia had contracted AIDS. A report by the Centres for Disease Control and Prevention (CDC) had identified 31 recipients of blood transfusion in the USA who had contracted AIDS. Association with UK products was not reported.

**23.260** It was not until the development of tests for anti-HIV and the report of research by Dr Cheingsong-Popov, Professor Weiss, Professor Tedder and others was published on 1 September 1984 that any data on the prevalence of anti-HIV seropositivity among 'at risk' groups in England were available.<sup>477</sup>

**23.261** The period when the SNBTS and the PFC might have acknowledged that the domestic product might be infected with HIV runs from the turn of the year 1983–84 until early September 1984. During that period the risk to haemophilia patients in Scotland was real: the Edinburgh Cohort patients were infected by PFC product.

**23.262** However, on the evidence as a whole, there was no basis on which it could be inferred that an actual present risk was known, or should have been known, to the SNBTS, the PFC, or, indeed, the haemophilia clinicians. They shared, with colleagues in England and Wales, the understanding that there was a potential risk. The second and third questions have to be considered in that context.

<sup>472</sup> Ibid [DHF.002.8865] at 8866

<sup>473</sup> Haemophilia Centre Directors AIDS Investigation – Surveillance of AIDS patients in patients with blood coagulation disorders; Update 10.9.83 [SNB.001.7556]

<sup>474</sup> Jones, 'Acquired immunodeficiency syndrome, hepatitis and haemophilia', *British Medical Journal*, 10 December 1983; 6407:1737–38 [LIT.001.0243]

<sup>475</sup> *The Guardian*, 9 December 1983 [SGF.001.0944]

<sup>476</sup> Draft minutes of NIBSC meeting on the infectious hazards of blood products, 9 February 1984 [SNB.004.8628]

<sup>477</sup> Cheingsong-Popov et al, 'Prevalence of antibody to human T-lymphotropic virus type III in AIDS and AIDS-risk patients in Britain', *The Lancet*, 1 September 1984; 477–480 [LIT.001.0417]

***Steps taken by The Scottish National Blood Transfusion Service/Protein Fractionation Centre to take account of the potential risk of transmission of HIV in the processing of blood products***

**23.263** As the narrative of the evidence shows, the PFC's research relating to virus infection concentrated on hepatitis until early 1983. Then there was the beginning of a subtle change of focus as the possible risks which AIDS might pose to the blood supply began to be understood. From then the scientists realised that research would focus, not exclusively on hepatitis, but also on AIDS. By March 1983 recognition of the importance of AIDS was tentative: explanations of the absence of a formal record of discussion of the subject at the Haemophilia and Blood Transfusion Working Group meeting on 22 March 1983 demonstrate that opinion had not become firm on the relevance of the topic.<sup>478</sup>

**23.264** Dr Foster's memorandum of 3 May 1983 marked the beginning of a substantial shift towards recognising the relevance of the AIDS risk. By the end of the year there had been a substantial programme of research, set out in paragraphs 23.128–23.132 and 23.139–23.142 above. The potential risk was clearly taken into account and influenced the programme of research into the formulation and processing of the PFC's products.<sup>479</sup>

***Should the threat of AIDS have caused the Protein Fractionation Centre to accelerate its heat treatment programme in or around May 1983?***

**23.265** This question was prompted by Dr Foster's memorandum of 3 May 1983. It implies that, in acknowledging the potential risk from AIDS, not only should the direction of research have been altered, but that the progress of that research should have been accelerated. Dr Foster identified the issues clearly. NANB Hepatitis was thought to have infected all severely affected haemophilia patients because of the inherent infectivity of large-pool concentrates. So long as the focus was on hepatitis, strategy could focus on those who had received little treatment, and a proportion only of total production had to be treated for virus inactivation. With AIDS, those who needed most treatment were exposed to the greatest risk of infection. It would not be possible to differentiate, and all production would require to be heat-treated. It was possible that the timetable would require to be reviewed.

**23.266** Mr Watt's letter to Professor Cash dated 5 May 1983 supported the speeding-up of the programme.<sup>480</sup> The initial request sought funding from the budget set aside to cover costs arising from compliance with the Medicines Inspectorate recommendations. Unfortunately, this request was turned down. The subsequent submission for funds was successful. However, it was not until August 1984 that the funding issue was resolved. If the scientists at the PFC had waited until the resolution of that issue, there would have been a very considerable delay in progress.

**23.267** That did not happen. There was progress, and the question whether there should have been acceleration must be considered in the light of the evidence of what happened in fact rather than on the implementation of the specific scheme put to Professor Cash.

**23.268** A batch of pasteurised Factor VIII was sent out for clinical trial on 13 June 1983. There was a review of the research programme on 15 June. By that time, the heating protocol had been developed to specify pasteurisation at 60°C for 10 hours and at 70°C

---

<sup>478</sup> See paragraphs 23.107 and 23.108 above

<sup>479</sup> Dr Foster's memorandum to Mr Watt of 3 May 1983 [SNB.007.3635] referred to in paragraphs 23.109 to 23.111

<sup>480</sup> Mr Watt's letter [SNB.007.3638] at 3640

for half an hour. Tests of virus kill were in place using model viruses, and loss of Factor VIII activity was being monitored. In the light of experience, an amended regime of heating at 60°C for 9.25 hours followed by 0.75 hours at 70°C had been developed for testing in the next round of trials. Dr Foster's report dated 20 December 1983 on progress in the studies to improve yield and quality of Factor VIII concentrates included comment on extensive work on the stability of FVIII:C (activity) and a range of model viruses used in heating in solution in the presence of sorbitol and glycine in conditions which were, in his opinion, probably the best that could be achieved without an unacceptable loss of yield.<sup>481</sup>

**23.269** There is no basis in the evidence on which it could be found that that programme could have been accelerated to any significant extent. On the contrary, the evidence indicates that progress was acceptable.

**23.270** The scientific witnesses were generally in agreement that the funding issue did not affect progress which went ahead according to the development programme. Dr Perry's evidence was that despite the funding issues, the programme was carried out. Dr Foster's evidence illustrates an aspect of the conduct of business at the PFC which was to arise in other contexts. The scientists got on with the work they considered relevant and important, and left questions of administration and funding to others. In their separate views, what did hold up progress of the pasteurisation programme in the latter part of 1983 was the organisation and conduct of clinical trials (in part another administrative issue) and not funding.

**23.271** As narrated in paragraphs 23.155 to 23.156, research and development work was well advanced in the early part of 1984, and an ambitious target for the installation and commissioning of the necessary production facilities had been set. The impression reasonably gained from the evidence as a whole is that the scientists made good progress, conscious of the threat of AIDS as it was understood at the time, and that there is no basis on which they could have accelerated the work.

***Was adherence to the pasteurisation programme until October/November 1984 justified, and in particular was that course justified after January 1984?***

**23.272** By December 1983, Dr Foster was reporting good progress in the pasteurisation of Factor VIII in the presence of sorbitol and glycine. The CBLA report of 26 July 1983 had indicated that pasteurisation was more homogeneous and efficient than dry heating.<sup>482</sup> The adverse comments on pasteurisation in the report were subject to significant criticism by the witnesses who gave evidence to the Inquiry. It is not possible to treat the comments on pasteurisation in the CBLA report as substantial or as likely to be material to a decision whether to persist with pasteurisation in 1983. Until the end of the year there is no reasonable criticism that can be made of the PFC's pursuit of a solution to the problem of virus inactivation that employed 'wet' heating (pasteurisation).

**23.273** In January 1984, Dr Smith sent Dr Foster a memorandum on the PFL's experiments on the dry heat treatment of Factor VIII. Findings reflected in the memorandum were set out in paragraph 11.156 of the Preliminary Report. Written and oral evidence now available to the Inquiry provides a fuller insight into the report and its significance. Dr Smith's evidence (paragraph 23.144) indicates the limited scope of the memorandum, and is in line with

---

<sup>481</sup> Progress Report on Studies to Improve Yield and Quality of FVIII Concentrate, 20 December 1983 [PEN.012.1500]

<sup>482</sup> CBLA report on AIDS [DHF.002.4489]

Dr Foster's understanding. The two English facilities had demonstrated, at laboratory scale at Oxford and large-scale at Elstree, that the English Factor VIII products could withstand heat treatment, as Rubenstein had predicted at the International Society of Haematology/International Society of Blood Transfusion Congress in Budapest in August 1982. It had not been demonstrated that the treatment applied would inactivate NANB Hepatitis, and Dr Smith at that time had little hope that it would. Dr Foster considered that the results, though more extensive, were consistent with the PFC's own findings on dry heating. His view was that, without evidence of inactivation of any viral markers, the data were of limited value. The SNBTS had data from laboratory studies using model viruses, and published data from Behring, which pointed to the relative effectiveness of pasteurisation in making concentrates safe from transmission of NANB Hepatitis viruses.

**23.274** In the light of this evidence, the PFC was fully justified in pursuing the pasteurisation project undeterred by the information provided by Dr Smith in January 1984.

*Was there sufficient liaison/cooperation between the fractionation services in Scotland and England over the period 1980 to 1984 in relation to viral inactivation? Did any management problems impact on the PFC's viral inactivation programme?*

**23.275** It is not inevitably the case that closer collaboration would have been of advantage to either service. If that had involved restricting the scope of research, the benefit of having two independent, and skilled, teams of investigators could have been lost. The issue is, rather, whether there was sufficient contact and exchange of information to ensure cross-fertilisation of research, giving each team the benefit of the other's work.

**23.276** The Inquiry considered two factors that might have influenced the exchange of information between Scotland and England: firstly, any formal structures providing links between the two transfusion services and their fractionation facilities; and secondly, the nature of personal contacts and communications between staff at the PFC and the BPL.

**23.277** As far as formal links were concerned, the transfusion services in England and Scotland and their associated fractionation facilities reported to different government departments and Ministers. While collaboration in specific research and development projects was arranged from time to time, there were no formal structures in place to ensure communication between the PFC and the BPL/PFL or to coordinate their work generally.<sup>483</sup>

**23.278** Professor Cash maintained that he had been anxious to foster collaboration. In oral evidence, he said:

It has always been my belief that had the two organisations (BPL and PFC) been able to pool their limited R&D resources, and perhaps some manufacturing resources, it may have ... made a significant difference, throughout the 1980s, to the availability of desirable plasma products in the UK.<sup>484</sup>

---

<sup>483</sup> In the 1980s there was collaboration in virus inactivation studies of 8Y, and on the thrombogenicity of heat-treated FIX concentrates, for example, [PEN.013.1309] at 1338–39

<sup>484</sup> Professor Cash – Day 57, page 135; See also Professor Cash's statement on viral inactivation from 1985 to 1987 [PEN.017.1085] at 1089



**23.279** In his view it was in the public interest that there should be formal links.<sup>485</sup> Consistent attempts to try and forge closer relationships between the Scottish and English transfusion services, in different areas, were a constant theme of his tenure as national medical director.<sup>486</sup> He believed that there was a critical shortage of research staff – the background to the comment in paragraph 23.93 about the value of Dr Foster.

**23.280** In a paper for the chairman of the CSA dated January 1984, Professor Cash provided some background information describing the comparative roles of the Central Blood Laboratories Authority (CBLA) and CSA. Having described the position generally, he wrote:

[T]he formal relationships between BPL (originally managed by the Lister Institute) and the SNBTS have not been satisfactory over the years.

**23.281** Professor Cash told the Inquiry that:

[A]t CSA, the Department of Health level, major efforts were made by some well meaning people to get these organisations together at a supramanagement, strategic level; frankly we failed. With the one exception, and that is when DHSS decreed that BPL were to go up to Scotland to get the virus inactivation validation studies done. That was the only occasion.<sup>487</sup>

**23.282** The Inquiry explored whether, in the absence of any other structural links, the CBLA Central Committee on Research and Development in Blood Transfusion, which first met in 1983, might have provided a more formal route for the exchange of information.

**23.283** Professor Cash knew about the Central Committee On Research and Development: it was never going to bridge the gap between the SNBTS and the BPL/PFL because, in his view, it did not enjoy the support of the DHSS or the SHHD.<sup>488</sup> Dr McClelland, who was a member of the committee, 'was under the impression that this was essentially an English committee ... set up to advise the CBLA'.<sup>489</sup>

**23.284** For his part, Dr Perry's recollection was that the committee 'was never recognised as a UK committee and certainly never exercised any formal influence over the activities of the SNBTS – although the SNBTS took account of its actions and recommendations in its own planning processes'.<sup>490</sup> His impression was that the committee's role was 'primarily observational and reactive in relation to ... decisions taken elsewhere'. Dr Foster had not been aware of the Committee and did not believe that PFC representation on it would have led to the earlier introduction of Z8.<sup>491</sup>

**23.285** As far as personal contacts and communications were concerned, the Inquiry heard evidence that the relationship between senior managers at PFC and BPL had sometimes been difficult, whether from personal differences or from disagreements about strategy.<sup>492</sup>

---

<sup>485</sup> Professor Cash's statement on viral inactivation from 1985 to 1987 [PEN.017.1085] at 1091; See also Professor Cash – Day 57, page 145

<sup>486</sup> Professor Cash – Day 57, page 138

<sup>487</sup> Professor Cash – Day 57, page 137

<sup>488</sup> Professor Cash – Day 57, pages 143–144

<sup>489</sup> Dr McClelland's statement on viral inactivation from 1985 to 1987 [PEN.017.0003]

<sup>490</sup> Dr Perry's statement on viral inactivation from 1985 to 1987 [PEN.017.1219] at 1227

<sup>491</sup> Dr Foster's statement on viral inactivation to [PEN.017.1556] at 1568–69. Z8 was a PFC Factor VIII concentrate, heated at 80°C for 72 hours, introduced in 1987.

<sup>492</sup> Meeting between CSA and CBLA, 20 January 1984: Background notes for Chairman [SNB.006.5138] at 5140; Dr Perry's statement on viral inactivation from 1985 to 1987 [PEN.017.1219] at 1227; Professor Cash – Day 43, page 22; Dr Cuthbertson – Day 46, pages 45–46, Dr Foster – Day 57, pages 4–5

**23.286** In spite of this, and in spite of the absence of formal links between the organisations, there was real and substantial collaboration between them at the level of the scientific officers engaged with research. The close working relationships that existed between scientific staff at the PFC and the BPL have already been discussed at paragraph 23.75 above.

**23.287** For his part, Dr Foster resisted the suggestion that organisational problems affected relationships between the scientific officers. He had no personal experience of difficulties. He said:

[W]henever I met Dr Lane, it was always a very pleasant experience and I have to say I didn't meet him that often and I was always encouraged by Mr Watt to interact with colleagues at BPL and at PFL quite freely, and that was, to my knowledge, always reciprocated and I was never ordered to disengage this liaison at any time. I was aware that Mr Watt and Dr Lane had different views and that's understandable, that they were – at this time people did have different views but Mr Watt was very much trying to take forward the plan that English plasma be processed in Scotland and I don't think Dr Lane saw things the same way. So there was a point there, where they clearly disagreed and that's conceivable that that might have led to some friction but that's really all I can talk to. That's all I'm aware of.

Q. From your position as head of research and development at PFC, how were your relations with your counterpart or counterparts down south?

A They were always excellent ... shortly after I joined PFC, I was given a task by Mr Watt to lead a delegation from PFC to BPL to help people to meet their counterparts, and there were maybe 10 or 12 people from PFC went down to BPL, they met their counterparts, that was reciprocated by visits from BPL, and we always encouraged our staff to communicate with their counterparts and that was always the situation and remained the situation [throughout] my employment.

Q. So there was communication, not only between yourself and Dr Smith but also the staff beneath you as well?

A. Yes, very much so. All of my staff were encouraged to deal with their counterparts because we saw ourselves in the wider sense part of the same organisation. We all worked for the NHS and we were in an area where it's really highly specialised. So to find somebody who is dealing with the same problems and same issues is not something that happens every day. So to have, if you like, another branch of the same organisation where you can talk to somebody was really a very good thing to have. So we did encourage that and I think that happened at BPL as well. And I'm not aware of anybody saying, 'Please stop doing this,' either at BPL or PFC.

**23.288** Dr Foster was asked about Professor Cash's attempts to institute more formal relations. He said:

I can understand why Professor Cash perhaps was seeking something more formal because the relationships that we had were to a large extent informal and it did depend on the individual personalities, and if I had left or Dr Smith

had left and someone else had come [along], things might have been different. So Dr Cash might have wanted something more formal to have a structure in place. So I can understand that but from my perspective it wasn't necessary, but if Dr Cash had said, 'Please do this more formally,' we would have done.

Q. So certainly we saw the use of the words 'formal relationships' in Dr Cash's briefing notes and he did recognise in the notes that there was communication, dialogue and liaison between yourself and Dr Smith.

A. Yes, and if we had been asked to do it more formally then we would have had no difficulty with that.<sup>493</sup>

The exchange provides a clear indication of the approach adopted by Dr Foster to collaboration, as well as illustrating the balanced views he held about relationships in a wider context. There is no basis for apprehension that the apparent inability of senior management to develop formal structural arrangements for the exchange of information had any impact on scientific research and development at this stage.

**23.289** Indeed, Professor Cash accepted, in relation to the development of Z8, that given the relationships between Dr Foster and Dr Smith in particular, there was not a wide gap between the SNBTS and the BPL/PFL.<sup>494</sup> Their personal liaison was the best opportunity for exchange of information in the circumstances.<sup>495</sup>

**23.290** Dr Foster acknowledged that there were two occasions on which the CBLA's interest in the protection of intellectual property rights might have inhibited the exchange of information temporarily.<sup>496</sup> The PFC may have withheld information for similar reasons. Dr Foster said:

I did apply for a patent application for the method of thawing plasma, which I had designed, and that patent was awarded and so it's conceivable that that information wasn't given to BPL immediately but it was published shortly thereafter. The only other example I can think of is when we were working with Dr Johnson and, of course, we had to sign confidentiality arrangements with him and we weren't allowed to discuss that with anyone else.<sup>497</sup>

**23.291** The advice he had received from patent lawyers was that one should not breathe a word about an invention to anyone before filing because of the risk of prior disclosure undermining the application. Dr Smith received similar advice.<sup>498</sup> He commented that proprietary information released under a confidentiality agreement never featured in exchanges between the PFC and the PFL.<sup>499</sup>

**23.292** The UK as a whole, and for present purposes Scotland in particular, were fortunate indeed in benefiting from the relationships among the scientists engaged in their respective research projects in virus inactivation, despite the lack of formal structures. The active collaboration that resulted made good the lack of formal structures and met the needs of this period.

---

<sup>493</sup> Dr Foster – Day 57, pages 5–7

<sup>494</sup> Professor Cash – Day 57, page 144

<sup>495</sup> Professor Cash's statement on viral inactivation from 1985–87 [PEN.017.1085] at 1090; See also Professor Cash – Day 57, page 145

<sup>496</sup> Dr Foster's statement on viral inactivation 1985–87 [PEN.017.1093] at 1106; See also Dr Foster – Day 57, page 9

<sup>497</sup> Dr Foster – Day 57, page 10

<sup>498</sup> Dr Smith – Day 59, pages 84–85

<sup>499</sup> Dr Smith's statement on viral inactivation to 1985 [PEN.012.1551] at 1560; See also Dr Smith – Day 59, page 82

*Would closer collaboration, and UK-wide policy guidance, have avoided the services in Scotland and England pursuing different courses and have been more effective?*

**23.293** Any answer to this question must be speculative to a degree. It is impossible to know how UK policy would have been developed, or how policymakers would have obtained the information required to instruct policy, or how policy would have been formulated. More particularly, since there would inevitably have been competing priorities, it is impossible to know how such issues would have been resolved, or what the outcome would have been. Pooling of knowledge and thought, such as Professor Cash envisaged, might have added intellectual mass to the single project and accelerated progress. Alternatively, if the two services had been compelled to limit their researches to one common approach, the distinctive contributions of each might have been lost. Avoiding the pursuit of different courses would not necessarily, or obviously, have been to the advantage of the UK as a whole or Scotland in particular.

**23.294** So far as the second aspect of the question is concerned, it is possible to be more positive. It was the ability of Scottish scientists to pursue their own research that resulted in the development of effective heat inactivation at the end of 1984, enabling the SNBTS to provide the first comprehensive national supply of heat-treated Factor VIII in the world. At that stage, the Oxford and Elstree facilities were not carrying out model virus studies. Scotland was able to validate the effectiveness of the processes. While it is impossible to say where a fully integrated joint research programme would have reached by this stage, there is no basis in evidence for a view that a UK policy decision directing collaboration between the two services would have resulted in more effective research progress than was achieved in Scotland.

*Did the Protein Fractionation Centre have sufficient resources, including staff, and access to information and academic research for its viral inactivation programme?*

**23.295** Research links with the universities were not explored in detail in oral evidence, since there was no suggestion that there were barriers on the side of the public facilities that prevented access. In the mid-1980s there were close links between the SNBTS and Heriot-Watt University which were referred to in evidence. Professor Charles Brown conducted a research programme in biochemistry. One of his students was Dr Valerie Hornsey. The supervisors of her PhD studies on monoclonal antibodies, completed in 1988, included Dr Prowse and Dr Pepper. Dr Hornsey went on to join the SNBTS. Interaction of this kind with higher education institutions was not, and is not, uncommon in Scotland. However, as noted in Chapter 20 *Haemophilia Therapy – The Period up to the Early 1980s*, at paragraph 20.73, Dr Foster failed in his attempts to encourage research groups at a number of UK universities to undertake fundamental research into ways of eliminating the risk of coagulation factor concentrates transmitting hepatitis. Collaboration requires both parties to be convinced of the value of the research proposed.

**23.296** Whether access to academic research was sufficient might theoretically have been an issue, but it did not arise for extended examination on the evidence available to the Inquiry. Given the published research output of SNBTS scientists, there is good ground for the view that they were themselves at the forefront of academic research. The fact that SNBTS scientists were invited to provide supervision of academic research projects supports that view.

**23.297** Human and other resources are, almost as a matter of tradition, stretched in the public service. Professor Cash would no doubt have been willing at any time to invest more had the funds been made available. Questions were to arise later about resources, in connection with the development of products effectively heated to kill Hepatitis C. So far as this period is concerned, the evidence of Dr Foster and Dr Perry (paragraph 23.125) was that lack of resources did not delay research. Dr Foster's characteristic view was that it was not an issue for him and his research colleagues: it could be left to Mr Watt and Professor Cash to sort out.

**23.298** The answer to the question, at the end of the day, is that the work was done, it was done effectively, and it was done with remarkable expedition. Additional resources would no doubt have been welcome, but lack of resources did not inhibit progress.

*Should commercial heat-treated products have been adopted in advance of locally produced products or could/should the Protein Fractionation Centre have bought in a commercial heat-treated process instead of developing its own?*<sup>500</sup>

**23.299** It is necessary to define a time-frame for this question. Licences for heat-treated factor concentrates began to be issued in the USA in 1983, as set out in paragraphs 23.28 to 23.30 above and Appendix I to this chapter. The products licensed in the USA that have to be considered were:

- Baxter/Hyland's Hemofil T, licensed in March 1983
- Armour's HT Factorate, licensed in January 1984
- Alpha Therapeutic's Profilate HT, licensed in February 1984
- Cutter's Koate HT, licensed in February 1984

**23.300** Commercial heat-treated products were not licensed by the UK Medicines Control Agency for release in the UK until February 1985. Before that date, Scottish Haemophilia Centres purchased and infused heat-treated commercial products on a named patient basis. Assuming that the products used after licensing in the USA were heat-treated, Edinburgh used Factorate in 1984. Glasgow Royal Infirmary used Hemofil in 1984. Yorkhill used Factorate in 1984. None of these regions used any commercial product in 1985 and 1986. Aberdeen, Dundee and Inverness did not use commercial products over the material period. Haemophilia clinicians were not excluded from the commercial market. Indeed in England and Wales commercial purchases accounted for the majority of Factor VIII used at this period. The PFC's first heat-treated Factor VIII concentrate was issued in December 1984.

**23.301** The question can only relate to the general adoption of imported heat-treated products, and necessarily assumes that UK licensing might have occurred earlier than February 1985. There is no basis on the evidence for a finding that the UK licensing process at this time was other than in accordance with normal practice, or unduly delayed.

**23.302** There were other factors in the short period between US licensing and the production of the PFC's heat-treated product. As noted in paragraph 23.28, Behring's product, Haemate P, was available in small quantities from 1980 in Germany and some other places. It was not licensed and was not available in the UK. Initial chimpanzee

---

<sup>500</sup> See Dr Smith's statement on viral inactivation to 1985 [PEN.012.1551] at 1573 for a very brief mention of this point.

studies of Baxter/Hyland's product Hemofil T suggested that it was effective in preventing transmission of NANB Hepatitis but not HIV. In human recipients, the opposite outcome was eventually reported.

**23.303** Some at least of the procedures that were developed by commercial companies were protected by patents and, in the nature of things, prior publication of the inventive steps in the processes developed was most unlikely to have occurred at all and, if it happened, even more unlikely to have been comprehensive. Publication of a final specification would almost invariably take a period of years from filing of the original application.

**23.304** Dr Foster's paper following the Congress of the International Society of Haematology/International Society of Blood Transfusion in Budapest in August 1982 reported that there was at that time no final proof that the Behring product was free from NANB Hepatitis. The method of heat treatment of Hemofil T was not disclosed at the Congress. When, months later, Dr Prowse heard that the process involved dry heat treatment at 60°C, the methodology employed was not disclosed and to Dr Foster's knowledge has never been disclosed. Clinical trials of Hemofil T in 1982–83, including trials at St Thomas' Hospital in London, had shown that the product was less effective in inactivating virus than pasteurisation. That information was circulating informally within the industry, and within UK Government circles, in 1983 and 1984 (see paragraph 23.100). In October 1984, Professor Mannucci disclosed that, as far as AIDS was concerned, no patients treated with the product had apparently seroconverted after one year from treatment with Hemofil T (see paragraph 23.169). This was the first time that there was any evidence that dry heating inactivated, or might inactivate, the HIV virus. Events moved swiftly from then. By December 1984, dry heat treatment was operational in Scotland.

**23.305** In order to have advanced the provision of effectively heat-treated products so as to have ensured their supply in Scotland before the end of December 1984 as a matter of general prescription, the SNBTS would have required to be satisfied that the products were safe and effective to a degree that indicated that domestic research should be suspended or discontinued. The evidence has not disclosed any rational basis on which that could have been decided. Nor could one form or express any view on the likely reaction of the regulatory agencies if a licence application had been made.

*In general, was the approach taken to viral inactivation at the Protein Fractionation Centre in the period 1980–84 reasonable? In general, was the degree of priority accorded to viral inactivation by the Protein Fractionation Centre during this period reasonable?*

**23.306** These two questions relate to the work of the scientists explored in the evidence narrated in this chapter. They can be answered unequivocally in the affirmative.

## Appendix 1

### Commercial heat-treated coagulation factor products 1983–1991

#### Factor VIII

<u>ARMOUR PHARMACEUTICAL COMPANY</u>				
Product	FDA licence	Method	Temp	Time
HTFactorate	January 1984	Dry Heat	60°C	36 hours
HTFactorate Generation II	1984	Dry Heat	60°C	36 hours
Haemate-P <sup>501</sup>	May 1986	Pasteurised	60°C	10 hours
Monoclote	1987	Dry Heat	60°C	36 hours
Moncloate-P	1990	Pasteurised	60°C	10 hours

<u>ALPHA THERAPEUTIC CORPORATION</u>				
Product	FDA licence	Method	Temp	Time
Profilate HT	February 1984	Dry Heat <sup>502</sup>	60°C	24 hours
HT-Profilate	September 1985	Dry Heat	60°C	24 hours
Profilate HT HP	May 1988	Dry Heat	60°C	24 hours
Profilate SD	July 1989	Dry Heat	60°C	24 hours
Moncloate-P	1990	Pasteurised	60°C	10 hours

<u>BAXTER, HYLAND</u>				
Product	FDA licence	Method	Temp	Time
Hemofil T	March 1983	Dry Heat	60°C	72 hours
Hemofil CT	October 1985	Dry Heat	60°C	72 hours

<u>CUTTER BIOLOGICAL, MILES Inc</u>				
Product	FDA licence	Method	Temp	Time
Koate HT	February 1984	Dry Heat	60°C	72 hours
Koate HS	April 1986	Pasteurised	60°C	10 hours

<u>IMMUNO AG</u>				
Product	FDA licence	Method	Temp	Time
Kryobulin TIM	N/A	Dry Heat under steam pressure	60°C	10 hours

<sup>501</sup> Manufactured by Behringwerke, Marburg, Germany.

<sup>502</sup> Dr Foster – Day 41, pages 69–70; Sometimes described as a wet process, the Factor VIII was suspended in liquid, and not dissolved: it was properly a dry process.

**Factor IX**

<u>ALPHA THERAPEUTIC CORPORATION</u>				
<b>Product</b>	<b>FDA licence</b>	<b>Method</b>	<b>Temp</b>	<b>Time</b>
Profilnine HT	October 1984	Dry Heat	60°C	20 hours
AlphaNine	December 1990	Dry Heat	60°C	20 hours

<u>BAXTER, HYLAND</u>				
<b>Product</b>	<b>FDA licence</b>	<b>Method</b>	<b>Temp</b>	<b>Time</b>
Proplex SX-T	October 1984	Dry Heat	60°C	144 hours
Proplex T	January 1986	Dry Heat	60°C	144 hours

<u>CUTTER BIOLOGICAL, MILES Inc</u>				
<b>Product</b>	<b>FDA licence</b>	<b>Method</b>	<b>Temp</b>	<b>Time</b>
Konyne HT	October 1984	Dry Heat	68°C	72 hours
Konyne 80	April 1991	Dry Heat	80°C	72 hours



## CHAPTER 24

### VIRAL INACTIVATION OF BLOOD PRODUCTS FOR HAEMOPHILIA THERAPY 1985–1987

#### Introduction

**24.1** This chapter considers the steps undertaken at the Protein Fractionation Centre, Edinburgh (PFC) between 1985 and 1991 to inactivate virus in blood products so as to prevent transmission of non-A, non-B Hepatitis (NANB Hepatitis)/the Hepatitis C virus (HCV).

#### The international context

**24.2** As discussed in Chapter 23, *Viral Inactivation of Blood Products for Haemophilia Therapy up to 1985*, developments in factor concentrate technology in Scotland at the end of 1984 and in 1985 were focused on an immediate response to the discovery of HIV infection in Scottish patients treated with SNBTS Factor VIII concentrate, particularly in the group of patients that came to be known as the Edinburgh Cohort. The experimental work that led to heat treatment of intermediate Factor VIII concentrate to inactivate that virus was prompted by information obtained at the Groningen Conference at the beginning of November 1984. Research and development do not, and did not, take place within hermetically sealed national boundaries.

**24.3** The international context provides an important focus for discussing developments in viral inactivation in the period covered by this chapter. In Appendix 1 to Chapter 23, *Viral Inactivation of Blood Products for Haemophilia Therapy up to 1985*, early developments in commercial heat-treated products were summarised without comment on their effectiveness. For the purposes of this chapter, the effectiveness of commercial production methods to inactivate viruses, and in particular NANB Hepatitis/HCV, is relevant. It is also material to identify, so far as possible, the dates when commercial manufacturers of blood products, who tended to have greater resources for research and development than state fractionators, were able to produce Factor VIII and IX concentrates that were sufficiently virally inactivated to prevent transmission of NANB Hepatitis/HCV.

**24.4** Dr Peter Foster led the necessary research in Scotland at the PFC. He gave evidence to the Inquiry that, over time, three methods of virus inactivation became accepted as being effective in inactivating NANB Hepatitis/HCV, namely (1) pasteurisation at 60°C for 10 hours, (2) solvent detergent treatment, and (3) dry heat treatment at 80°C for 72 hours (albeit pasteurisation and solvent detergent treatment have been associated with occasional transmission of virus, including Hepatitis C).<sup>1</sup> The Factor VIII and IX products which were accepted as safe from the transmission of NANB Hepatitis/HCV, together with such information as was available about the licensing and availability of the products in the UK are set out in Tables 24.1 and 24.2:<sup>2</sup>

---

<sup>1</sup> Dr Foster's statement on Heat Treatment, 1985–87 [PEN.017.1556] at 1586

<sup>2</sup> Dr Foster's statement on Heat Treatment, 1985–87 [PEN.017.1556] at 1584–85

**Table 24.1: Factor VIII products effective in inactivating NANB Hepatitis/HCV**

<b>Manufacturer</b>	<b>Product name</b>	<b>Virus Inactivation Method</b>	<b>FDA licence</b>	<b>UK licence</b>
Armour Pharmaceutical (manufactured in Germany by Beringwerke)	Humate-P	Pasteurisation at 60°C for 10 hours	May 1986	March 1984, but not generally available in the UK due to low product yield and very low level of exports from Germany
Armour Pharmaceutical (manufactured in the USA) <sup>3</sup>	Monoclote-P	Pasteurisation at 60°C for 10 hours	1990	December 1989 <sup>4</sup>
Alpha Therapeutic Company	Profilate SD	Solvent/detergent	July 1989	Not known if available in UK
Alpha Therapeutic Company	Profilate OSD	Solvent/detergent	May 1990	Not known if available in UK
Alpha Therapeutic Company	Alpha-8	Solvent/detergent	Pending as at November 1992	Uncertain, but supply in the UK would appear from a patient information sheet to be from December 1992
Baxter (Hyland Division)	Hemofil M	Solvent/detergent	February 1988	June 1994
Cutter Biological, Miles Inc.	Koate HS	Pasteurisation at 60°C for 10 hours	April 1986	To the best of Dr Foster's knowledge, not available in the UK
Cutter Biological, Miles Inc.	Koate HP	Solvent/detergent	March 1989	June 1994

**Table 24.2: Factor IX products effective in inactivating NANB Hepatitis/HCV**

<b>Manufacturer</b>	<b>Product name</b>	<b>Virus Inactivation Method</b>	<b>FDA licence</b>	<b>UK licence</b>
Armour Pharmaceutical	Mononine	Treated with sodium thiocyanate	August 1992	February 1993
Alpha Therapeutic Company	AlphaNine SD	Solvent/detergent	August 1992	October 1993
Cutter Biological, Miles Inc.	Konyne 80	Dry heat at 80°C for 72 hours	April 1991	Not known to Dr Foster if this product was available in the UK

<sup>3</sup> Dr Foster – Day 57, page 24<sup>4</sup> Dr Foster's statement on Heat Treatment, 1985–87 refers to a date of 1999. However, this date was corrected to 1989 during the Oral Hearing – see Dr Foster – Day 57, page 24

**24.5** The list was based on information contained in an article by Kasper and others, published by the journal *Transfusion* in 1993.<sup>5</sup> While Dr Foster did not know precisely when the production or supply of the products in the list took place in the UK, he considered that the dates when the products were available in this country would be close to either: (a) the earlier of the date on which a USA FDA licence or a UK licence was granted for the manufacture of the product; or (b) the date that a UK licence was granted for supply of the product in the UK.<sup>6</sup>

**24.6** During the Oral Hearings reference was also made to a product known as NYBC/Melville Biologics Coagulation Factor VIII-SD (a solvent-detergent product using Tri-n-butyl-phosphate and sodium chloride) which was referred to in table 5 of the 1993 Kasper paper. The product was licensed in the USA in 1985. Dr Foster said that Melville Biologics was the name of a facility operated by the New York Blood Centre which manufactured the product. He said that while it appeared in due course that the product would have been safe from Hepatitis C, it was not available in the UK.<sup>7</sup>

**24.7** Within the UK, the Plasma Fractionation Laboratory and the Blood Products Laboratory (PFL/BPL) were able to supply Factor VIII concentrate (8Y) to England, Wales and Northern Ireland from September 1985. Over time, the product was found to be safe from transmission of NANB Hepatitis/HCV. It can be seen from the above tables that, with the exception of the Behringwerke pasteurised product (which resulted in low product yields and was not generally available in the UK), the PFL/BPL were the first fractionators able to produce a Factor VIII product that events were to show did not transmit NANB Hepatitis/HCV (albeit, as discussed at 24.22 below, they were not able to produce sufficient product to meet the needs of all haemophilia patients in England and Wales).

**24.8** In Scotland, the PFC was able to make available for clinical trial in December 1986 a Factor VIII concentrate (Z8) which, over time, was found not to transmit NANB Hepatitis/HCV. That product was available for use from April 1987. That date compares favourably with the achievements of commercial manufacturers in providing safe products, as shown in Table 24.1. In addition, unlike the position in England, PFC were able to supply a sufficient quantity of product to meet the needs of all Haemophilia A patients in Scotland.

**24.9** Both the PFC and the PFL/BPL were able to supply a Factor IX concentrate (respectively, DEFIX and 9A) to meet demand from Haemophilia B patients from October 1985. These products were also found, over time, to be safe from the transmission of NANB Hepatitis/HCV. Table 24.2 indicates that a safe NHS product was available many years before commercial manufacturers supplied Factor IX concentrates that were safe from the transmission of NANB Hepatitis/HCV.

---

<sup>5</sup> Kasper et al, 'Recent evolution of clotting factor concentrates for Hemophilia A and B', *Transfusion*, 1993; 33:422–434 [SGH.002.1947]

<sup>6</sup> Dr Foster's statement on Heat Treatment, 1985–87 [PEN.017.1556] at 1584. The dates the UK licence was granted for a product are, to the best of Dr Foster's knowledge, based on information provided by the UK Medicines and Healthcare Products Regulatory Agency (MHRA)

<sup>7</sup> Dr Foster – Day 57, pages 27–28

## Events in England

**24.10** As explained by Dr Jim Smith, Head of Research and Development at the PFL and the BPL, in 1984 the PFL was investigating, on a very small scale, the PFC's zinc/heparin precipitation process.<sup>8</sup> The aim of this process was to create a purer Factor VIII product by precipitating out (removing) the proteins fibrinogen and fibronectin.<sup>9</sup> There were two main reasons for seeking higher purity – firstly, to create a product which would dissolve more readily<sup>10</sup> and which could be administered to patients in smaller quantities of higher potency, and, secondly, to reduce the overall volume of product to be pasteurised, thus making it more straightforward to heat.<sup>11</sup>

**24.11** Dr Smith said that, when carrying out an experiment into this process, a PFL technician accidentally used a far greater quantity of heparin than was specified and, surprisingly, found an unusually heavy precipitate of fibrinogen and a high Factor VIII recovery.<sup>12</sup> Further research at the PFL showed that even better results could be obtained using heparin alone at much higher concentrations than had been used in the PFC's original zinc/heparin process.<sup>13</sup>

**24.12** This serendipitous discovery proved to be a key point in the development of 8Y and further work was carried out during 1984 to refine the steps in the process. Dr Smith explained that the heparin step allowed the PFL to:

[E]liminate a fiddly adsorption step in our current scheme and, after adding another precipitation method<sup>14</sup> conveniently emerging from our front-end work at the time, a ten-fold purification over the current product was achieved.<sup>15</sup>

**24.13** He added:

It often takes a long time to develop formulation and drying of a new concentrate, but we were fortunate to find a simple formulation which freeze-dried using the cycle applied to the current product. This very dry concentrate could then be heated at quite high temperatures without loss of solubility and with an acceptable loss of Factor VIII.<sup>16</sup>

**24.14** Although the PFL had conducted experiments on both wet and dry heating in the course of 1984,<sup>17</sup> the decision was taken in England, as in Scotland, to introduce immediate dry heating of the PFL/BPL's existing Factor VIII product upon hearing the news in November 1984 from the conference in Groningen that HIV could be inactivated by being dry heated to 68°C for one hour. Dr Smith explained that on his return from the meeting in Groningen, a small informal group at the PFL decided that the small, high-precision oven at the PFL would be used to heat retrospectively all batches of the current Factor VIII held in stock at the PFL and the BPL, at 70°C for 24 hours (or, if that proved unsatisfactory, 60°C for 72 hours).

<sup>8</sup> Dr Smith's statement on Viral Inactivation to 1985 [PEN.012.1551] at 1571

<sup>9</sup> See Dr Smith – Day 60, pages 20–21 and Dr McIntosh – Day 61, page 9

<sup>10</sup> For more details on the benefits of increased solubility see also Dr Smith – Day 60, pages 47–49

<sup>11</sup> See Dr Smith – Day 60, page 24. Dr Smith indicated that heat transfer, the control of temperature, and the removal of stabiliser and other impurities are all more straightforward with a smaller volume of liquid.

<sup>12</sup> Dr Smith's statement on Viral Inactivation to 1985 [PEN.012.1551] at 1571

<sup>13</sup> Ibid [PEN.012.1551] at 1572

<sup>14</sup> This was precipitation using glycine and sodium chloride which further concentrated the Factor VIII whilst removing some heparin and leading to a further fourfold reduction in fibrinogen and fibronectin. See Dr Smith – Day 60, page 24

<sup>15</sup> Dr Smith's statement on Viral Inactivation to 1985 [PEN.012.1551] at 1572

<sup>16</sup> Ibid [PEN.012.1551] at 1572

<sup>17</sup> See for example Dr Smith's statement on Viral Inactivation to 1985 [PEN.012.1551] at 1571; Dr Smith's supplementary statement [PEN.017.2198]; and Dr Smith – Day 60, pages 24–25

**24.15** The references to heating all batches of current PFL/BPL Factor VIII at 70°C for 24 hours and 60°C for 72 hours related to the existing English dry heat-treated intermediate purity products known as 8CRV (produced at the PFL) and HL (produced at the BPL), which were broadly equivalent to the PFC’s intermediate purity product, NY.<sup>18</sup> Batches which withstood heating at 60°C for 24 hours were known as HT1 and batches which survived heating to 70°C for 72 hours were known as HT2.<sup>19</sup> Dr Smith said that HT1 and HT2 were issued for general use in January 1985.<sup>20</sup> He indicated that the rationale for releasing HT1 and HT2 before 8Y was to try to protect haemophiliacs from HIV in the period up until 8Y could be released.<sup>21</sup>

**24.16** Dr Smith said that the BPL did not recall Factor VIII products that had already been issued in order to heat them. He stated:

[W]e did not do what some of the commercial companies did, which was to recover stocks of product from the haemophilia centre and even, I believe, from the fridges of haemophiliacs, their home treatment supply. I don’t believe we ever went that far or we even went back to the transfusion centres, which distributed our material. I believe we only retroheated the stocks in our own holding rooms.<sup>22</sup>

**24.17** As well as deciding in November 1984 to heat the existing intermediate purity Factor VIII product at 70°C for 24 hours, a decision was also taken at the PFL to complete the scale-up of production of the new high purity 8Y Factor VIII concentrate. It was further decided to prepare batches, dry heated at 80°C for 72 hours, for clinical trials with the intention that, if successful, production of 8Y would be transferred to the BPL. This would enable sufficient quantities of the product to be produced to supersede the existing intermediate purity product, heated at a lower temperature.<sup>23</sup>

**24.18** Dr Smith was asked at the public hearing whether the decision in November 1984 to proceed with the high purity 8Y product that could be heated at 80°C was taken with a view to inactivating HIV or NANB Hepatitis. He said it was certainly done to put HIV kill beyond all reasonable doubt. It was hoped that the product ‘could do a bit more damage to non-A non-B’, but he had ‘no hopes, to tell the truth, that this would deal with non-A non-B Hepatitis’.<sup>24</sup>

**24.19** The first pilot-scale production batch of the high purity 8Y product (80°C for 72 hours) was manufactured in November 1984. The product was rapidly scaled-up by the PFL from one litre in November 1984 to 300 litres by the end of January 1985, at which point there was sufficient material to begin clinical trials.<sup>25</sup> Dr Smith’s recollection was that Phase 1 clinical trials of the PFL product for safety and efficacy were carried out in March 1985, with Phase 2 clinical trials for virus safety starting in April 1985.<sup>26</sup> Once the BPL had successfully produced its first batches of 8Y, trials followed with its product.<sup>27</sup>

---

<sup>18</sup> See Dr Smith’s supplementary statement [PEN.017.2198] at 2198 – notwithstanding the different names, these products were virtually the same.

<sup>19</sup> Dr Smith’s supplementary statement [PEN.017.2198] at 2198

<sup>20</sup> Ibid [PEN.017.2198] at 2199

<sup>21</sup> Dr Smith – Day 60, page 25

<sup>22</sup> Dr Smith – Day 60, page 26

<sup>23</sup> Dr Smith’s statement on Viral Inactivation to 1985 [PEN.012.1551] at 1572

<sup>24</sup> Dr Smith – Day 60, page 27

<sup>25</sup> See Dr Smith – Day 60, pages 28–29

<sup>26</sup> Dr Smith’s supplementary statement [PEN.017.2198] at 2199 and Dr Smith – Day 60, page 29

<sup>27</sup> Dr Smith – Day 60, page 30

**24.20** Full-scale production of 8Y commenced at the BPL in April 1985<sup>28</sup> with general release of the product to Regional Transfusion Centres in England in September 1985.<sup>29</sup>

**24.21** Factor VIII concentrate had never before been able to be heated at such high temperatures and the ability of Dr Smith's team to do so was a considerable achievement. Research facilities at the PFL were relatively 'basic' when compared with commercial producers (or, indeed, when compared with facilities at the PFC) and Dr Smith pithily explained, there was:

[A]mazement ... that two men and a boy working in a dustbin under socialised medicine could have come up with a solution before large pharmaceutical companies.<sup>30</sup>

**24.22** During the Inquiry hearings, Dr Smith's attention was drawn to a letter dated 24 July 1985 from Dr Richard Lane, the Director of the BPL, to Haemophilia and Regional Transfusion Directors in England and Wales, and to a passage stating that BPL's output of 8Y at that time could only meet about one third of demand for Factor VIII.<sup>31</sup> Dr Smith indicated that he did not have the information to make such a calculation.<sup>32</sup> However, he agreed that there was not enough 8Y in September 1985 to meet the total demand for Factor VIII in England and Wales for treatment of all haemophilia patients if 'total demand' included potential demand from patients using commercial products.<sup>33</sup>

**24.23** Dr Lane's letter contained a suggestion that the 8Y heat treatment process might be effective against NANB Hepatitis, indicating that:

Clinical trials at six Haemophilia Centres are in progress to gain evidence of reduction or elimination of viral transmission, and several patients have safely passed the point at which first evidence of NANBH virus transmission would normally occur with unheated Factor VIII.<sup>34</sup>

**24.24** Over time, further reports became available which gave increasing reassurance that 8Y might not transmit NANB Hepatitis.

**24.25** On 9 May 1986, Dr Smith presented a paper to an international symposium in Melbourne, Australia, giving interim results for 33 patients in England who had received 8Y and who had been followed up with regular liver function tests.<sup>35</sup> The paper expressed a degree of optimism that the product did not transmit NANB Hepatitis, noting that:

Although these are only interim results on a limited number of batches, we think we are justified in thinking that the severe heating has been more effective in preventing transmission of NANBH than the milder heating accorded to the Hyland and Armour products in studies published last year.<sup>36</sup>

---

<sup>28</sup> Dr Smith – Day 60, page 29

<sup>29</sup> Dr Smith's supplementary statement [PEN.017.2198] at 2199. Note that, according to Dr Smith's supplementary statement, it appears that previously untreated patients (PUPs) in England may have had access to 8Y from March 1985 until general release in September 1985 – see [PEN.017.2198] at 2200

<sup>30</sup> Dr Smith – Day 60, page 42

<sup>31</sup> Dr Lane's letter of 24 July 1985 [DHF.003.0476]

<sup>32</sup> Dr Smith – Day 60, page 32

<sup>33</sup> Dr Smith – Day 60, page 33

<sup>34</sup> Dr Lane's letter of 24 July 1985 [DHF.003.0476]

<sup>35</sup> Smith et al, 'Interim results of surveillance for NANBH in patients receiving heated concentrates produced in England', *Developments in Biological Standardization* 1987; 67:323–325 [PEN.017.1264] and Dr Foster's statement on Heat Treatment, 1985–1987 [PEN.017.1556] at 1559

<sup>36</sup> *Ibid* [PEN.017.1264] at 1266

**24.26** The paper also advocated caution, however, by noting that:

It is too early to know whether NANBH transmission has been eliminated by severe dry heating or whether we may see transmission by only a few batches  
....<sup>37</sup>

**24.27** On 30 September 1986, Dr Smith provided further clinical results on the routine use of 8Y and 9A in England. The results were contained in an interim report, *Surveillance of previously untreated patients for possible virus transmission by BPL Factor VIII and Factor IX concentrates, 8Y and 9A*, prepared for a meeting of the UK Haemophilia Centre Directors Organisation (UKHCDO) in Edinburgh on 10 October 1986.<sup>38</sup> The report explained that in the spring of 1985 all Haemophilia Centre Directors in England were issued with a protocol for the detection of NANB Hepatitis, Hepatitis B and HIV in susceptible patients receiving BPL 8Y and 9A and were invited to collect data on this basis.<sup>39</sup> The summary of the results Dr Smith provided was restricted to patients who had no previous history of treatment with large-pool concentrates. It indicated that: (i) none of the patients ‘had any ALT or AST above 2.5 times the upper limit of the normal range’; (ii) no case of HIV seroconversion had been reported; and (iii) no evidence of infection with Hepatitis B had been seen.<sup>40</sup> The report concluded:

These data, showing no clinical or laboratory events attributable to transmission of the three main blood-borne viruses, may further encourage HCDs to use 8Y and 9A in previously untreated patients.<sup>41</sup>

**24.28** In his written evidence to the Inquiry Dr Smith indicated that these results were reason to be, ‘a little more upbeat, but not much’, explaining that the data in question were criticised throughout 1986–87 and that ‘using the only product “which hasn’t failed yet” does not necessarily denote confidence that it is going to be 100% successful’.<sup>42</sup>

**24.29** Dr Smith further explained that ‘the number of clean follow-ups at the end of 1986 was too small to either support or disprove the proposition that 8Y was statistically significantly safer from NANB Hepatitis transmission than commercial concentrates heated less severely’.<sup>43</sup> He ‘came to believe in the next few years that 8Y was probably safe, by sheer weight of good follow-ups and in particular the exposure of many batches of widely different provenance’ but he considered that liver enzyme tests (ie ALT tests) were unreliable and would not have vouched for 8Y’s safety ‘until application of the highly specific anti-HCV test’ in 1993.<sup>44</sup>

**24.30** Dr Foster advised the Inquiry that he was given a copy of the interim report by Dr Smith on 9 October 1986<sup>45</sup> and confirmed that this was the first occasion on which he saw written data on 8Y’s evaluation.<sup>46</sup> However, asked when it seemed to him to be likely

<sup>37</sup> Ibid [PEN.017.1264] at 1266

<sup>38</sup> Dr Smith’s report [SNF.001.1123]

<sup>39</sup> Dr Smith’s report [SNF.001.1123] at 1124. The original protocol accepted patients who had very little previous treatment with concentrates.

<sup>40</sup> Dr Smith’s report [SNF.001.1123] at 1124–25

<sup>41</sup> Dr Smith’s report [SNF.001.1123] at 1125

<sup>42</sup> Dr Smith’s statement on Viral Inactivation, 1985–1987 [PEN.017.1130] at 1133

<sup>43</sup> Dr Smith’s supplementary statement on Viral Inactivation, 1985–1987 [PEN.018.1408]

<sup>44</sup> Ibid [PEN.018.1408] at 1409

<sup>45</sup> Dr Foster’s statement on Heat Treatment, 1985–87 [PEN.017.1556] at 1559. For Dr Foster’s diary note confirming this meeting see [PEN.017.1435]. See also the SNBTS’s response to an Inquiry letter requesting certain documents [PEN.017.1662] at 1667 (question 26/27).

<sup>46</sup> Dr Foster – Day 56, page 69

that 8Y was free from NANB Hepatitis, Dr Foster said he had doubts whether the data could be used to say that 8Y was 'likely' to be free from NANB Hepatitis at this time.<sup>47</sup> He explained that in science one tends not to use words such as 'likely' and that products were either safe or unsafe. Dr Foster accepted, however, that safety could be measured statistically.<sup>48</sup>

**24.31** Dr Robert Perry was also asked when he thought that it seemed likely that 8Y was free from NANB Hepatitis. He advised that it was not until Dr Smith's report in September 1986 that 8Y's freedom from NANB Hepatitis would have been described as likely. He added the caveat, however, that 'even at this stage such a conclusion would have been regarded as cautionary and unconfirmed'.<sup>49</sup>

**24.32** Dr Bruce Cuthbertson also shared this view, stating in his written evidence that:

The letter from Dr Smith ... is the first evidence that I am aware of that 8Y could be potentially effective in significantly reducing the risk of NANBH .... The data available in Dr Smith's letter of September 1986 clearly showed a reduction in infectivity with NANBH, but was not yet conclusive of a lack of infectivity.<sup>50</sup>

**24.33** Asked to expand on his views, Dr Cuthbertson explained:

[C]learly there is a difference between the product which has a reduced risk from one which is absolutely free of evidence of infectivity. I think that's the point I was trying to get over in this text, that from the early work, it was clear that the risk of non-A non-B Hepatitis from the product was substantially less than from conventional unheated products. The infection rate with them was close to 100 per cent, whereas from the early evidence, a number of patients had not developed clinical evidence of non-A non-B Hepatitis. But to actually demonstrate freedom from infectivity is a very difficult process and takes time – or certainly took time then, when we were relying on indirect biochemical tests as a means of assessing infectivity.<sup>51</sup>

**24.34** On 16 September 1987 Dr Smith drew up a report for a UKHCDO AGM on 25 September 1987.<sup>52</sup> The report indicated that a two-year study, which was 'stricter' than the previous study, had shown a 'near zero' incidence of NANB Hepatitis transmission by 8Y or BPL's dry-heated Factor IX product, 9A.<sup>53</sup> Even at that stage, however, Dr Smith remained of the view that the effectiveness of severe dry heating in inactivating NANB Hepatitis had not been established. His report concluded:

It is not possible to determine the true incidence of transmission of NANBH by 8Y and 9A from this imperfect evidence, but the apparent near-zero incidence justifies the inclusion of a further series of patients in a more formally controlled prospective trial, to be co-ordinated by Dr Rizza and Dr Kernoff.<sup>54</sup>

<sup>47</sup> Dr Foster's statement on Heat Treatment, 1985–87 [PEN.017.1556] at 1559

<sup>48</sup> Dr Foster – Day 56, pages 55–57

<sup>49</sup> Dr Perry's statement on Viral Inactivation, 1985–87 [PEN.017.1219] at 1220

<sup>50</sup> Dr Cuthbertson's statement on Viral Inactivation, 1985–87 [PEN.017.1200] at 1201

<sup>51</sup> Dr Cuthbertson – Day 57, page 44

<sup>52</sup> See the Appendix to Professor Ludlam's witness statement [PEN.017.1625] at 1645

<sup>53</sup> Dr Smith's report for UKHCDO meeting, 25 September 1987 [SNF.001.1138]

<sup>54</sup> Ibid [SNF.001.1138] at 1141



**24.35** By 1988 further evidence was accumulating that 8Y was free from NANB Hepatitis. In particular, a paper by Dr Brian Colvin and others published in *The Lancet* in October 1988 reported that 32 patients who had been treated with 8Y had not developed NANB Hepatitis. The paper indicated that an additional, more rigorous, study was necessary, but noted that these data demonstrated that '80°C is highly effective in inactivating NANBH in coagulation factor concentrates'.<sup>55</sup>

**24.36** In 1993, once more sensitive and specific tests for HCV were available, a paper by Rizza and others reported that 27 previously untreated patients (PUPs) in England had received 24 batches of 8Y and that no evidence of infection by Hepatitis C, Hepatitis B or HIV had been found following these transfusions, thus finally confirming that 8Y was free from these viruses.<sup>56</sup>

## Developments in Scotland

1985

### The development of a high purity Factor VIII product and pasteurisation

**24.37** As indicated in Chapter 23, *Viral Inactivation of Blood Products for Haemophilia Therapy up to 1985*, (paragraphs 23.185 to 23.203) at the end of 1984 the PFC dry-heated stocks of its existing intermediate purity NY Factor VIII product at 68°C for two hours in an attempt to inactivate HIV, in response to the report from Groningen that HIV could be inactivated by dry heating at 68°C for one hour. This was regarded as an interim measure, which, in view of the extreme urgency brought about by the discovery that HIV had been transmitted by SNBTS Factor VIII concentrate, could be implemented immediately.

**24.38** Production of new batches of Factor VIII by the PFC had largely been suspended between October 1984 and January 1985 to allow for improvements required by the Medicines Inspectorate to be carried out at the plant.<sup>57</sup> The PFC's policy (and therefore the policy for Scotland) at the beginning of the year was intimated formally in a letter by Dr Perry to Dr Duncan Thomas, from the National Institute for Biological Standards and Control (NIBSC), dated 8 January:<sup>58</sup>

- All FVIII issued from PFC had been heat-treated since mid-December 1984;
- PFC would recall all existing regional stocks of non-heat treated FVIII for heating and reissue;
- The heating conditions applicable at that date were 68°C for 2 hours in the dry state. Those conditions were the best that could be achieved with the existing product without compromising solubility, and in the knowledge that a joint CDC/Cutter study had suggested that they might provide 4–5 logs inactivation of HTLV III virus;
- Analytical specification and *in vivo* characteristics were identical to the unheated precursor;
- There was no significant deterioration as a result of the changes;

<sup>55</sup> Colvin et al, Study Group of the UKHCDO on Surveillance of Virus Transmission by Concentrates, 'Effect of dry heating of coagulation factor concentrates at 80°C for 72 hours on the transmission of non-A, non-B Hepatitis', *The Lancet*, 8 October 1988: 814 [LIT.001.0330]

<sup>56</sup> Rizza et al, 'Confirmation of viral safety of dry heated Factor VIII concentrate (8Y) prepared by Bio Products Laboratory (BPL): a report on behalf of UK Haemophilia Centre Directors', *British Journal of Haematology*, 1993; 84:269–272 [SNB.004.5996]

<sup>57</sup> SNBTS Briefing Paper on the development of heat treatment, November 2010 [PEN.013.1309] at 1346

<sup>58</sup> Dr Perry's letter to Dr Thomas of 8 January 1985 [SNB.007.4734]

- Plans were well advanced for the manufacture of a new product, with a modest reformulation involving the addition of carbohydrate, which would be subjected to more extreme conditions of temperature and time.

**24.39** Developments were in hand on the last point. When the PFC recommenced production on 20 January 1985, sucrose was added to all intermediate purity Factor VIII to enable heating at 68°C for 24 hours with the objective of achieving a greater margin of safety against HIV. It was correctly thought, however, that the 68°C/24 hours product was unlikely to be free from risk of transmitting NANB Hepatitis.<sup>59</sup>

**24.40** Despite the introduction of dry heat treatment of the existing intermediate purity Factor VIII product in an attempt to inactivate HIV, a progress report produced by Dr Foster for the meeting of the SNBTS Factor VIII Study Group in February 1985 commented that the development of a high purity product that could be pasteurised ‘would seem to be still the preferred option’.<sup>60</sup>

**24.41** Dr Foster’s progress report explained that the aim at that stage had been to apply pasteurisation to the high-purity Factor VIII product under development in collaboration with Dr Alan Johnson of New York University (NYU). PFC had been sufficiently impressed with the NYU process that in October 1984 a decision had been taken to shelve further research into the existing zinc heat-treated method (ZHT) ‘so that maximum effort could be given to the newer method’.<sup>61</sup>

**24.42** When asked to explain the attractions of the NYU process and pasteurisation, Dr Foster said:

[T]he objective was to have a product that was safe from non-A non-B Hepatitis, and at that time pasteurisation was the front runner in terms of the knowledge that existed, in terms of what might be safe, and in order to make that process work in our production operation, I wanted to increase the degree of purification so that I could reduce the volume of pasteurisation by maybe 50- or 100-fold, and the Johnson process would allow me to do that and that’s why we gave priority to that at that time.<sup>62</sup>

**24.43** Dr Foster explained that the NYU product was significantly more pure than the PFC’s existing intermediate Factor VIII product NY, pointing out that, ‘[for] the NYU product, we were looking for an increased purification of the order of 100- to 200-fold’.<sup>63</sup>

**24.44** While expressing a preference for wet heat treatment (pasteurisation), the progress report commented that ‘recent information concerning HTLV-III’ had led to dry heating of the existing product. It commented that ‘severe heating of the freeze dried powder may be possible (Smith, unpublished results)’.<sup>64</sup> The mention of ‘severe heating’ in the report was a reference to the work by the PFL/BPL on 8Y discussed above. The impression given at that stage, however, was that resort to dry heat treatment of the PFC’s product was a temporary measure.

<sup>59</sup> SNBTS Briefing Paper on the development of heat treatment, November 2010 [PEN.013.1309] at 1346–47

<sup>60</sup> *Progress Report for Factor VIII Study Group*, Foster, PR, February 1985 [SNB.007.4867] at 4874

<sup>61</sup> *Ibid* [SNB.007.4867] at 4874

<sup>62</sup> Dr Foster – Day 56, page 44

<sup>63</sup> Dr Foster – Day 56, page 6

<sup>64</sup> *Progress Report for Factor VIII Study Group*, Foster, PR, February 1985 [SNB.007.4867] at 4874

**24.45** Dr Ronald McIntosh, a biochemist at the PFC during the relevant period, also gave evidence to the Inquiry as to the rationale for the move, in late 1984, from developing the ZHT process to developing the NYU process. He explained that there were significant problems with the ZHT process, including: the need to add large percentages (20–40%) of carbohydrate stabilisers to allow for satisfactory Factor VIII recovery (resulting in a solution with a large volume that was very viscous and hence difficult and time-consuming to process); the precipitation step (where Factor VIII was recovered from the high concentration of stabilisers) was difficult to control; and lower yields for ZHT than the existing intermediate Factor VIII product (which would have had a negative impact on the PFC's policy of self-sufficiency).<sup>65</sup>

**24.46** Dr McIntosh was asked whether it would have been practical to ramp up the ZHT process to achieve full production. Dr McIntosh replied:

It would not have been feasible. The difficulties in processing such large volumes of viscous solution and also adding additional processing steps to fit into the available working schedule in production, would have made it very difficult to do.<sup>66</sup>

**24.47** In contrast to the problems with ZHT, the NYU process appeared more promising. Dr McIntosh indicated in his oral evidence that the NYU process 'would allow us to get the purification that was needed to aid pasteurisation, without compromising yield'.<sup>67</sup> He explained in more detail the initial research carried out on the NYU process between late 1984 and the middle of 1985, indicating that various changes were made to the process with the aim of making it compatible with the requirements for Factor VIII production at PFC.<sup>68</sup> These included: the addition of a zinc heparin precipitation step derived from the ZHT process to filter out unwanted fibrinogen and fibronectin; the use of an ion exchange gel different from the gel used by Dr Johnson; the substitution of calcium with other salt combinations which were physiologically more acceptable; and the development of a more stable formulation.<sup>69</sup>

**24.48** Although pasteurisation was, in principle, still the PFC's preferred option for viral inactivation at the start of 1985, the PFC appears to have carried out relatively little pasteurisation work in the first few months of the year. In that regard, another report for the meeting of the SNBTS Factor VIII Study Group on 7 February 1985, *Update Paper on Viricidal Action Since Last Meeting One Year Ago*, indicated that the PFC's work on pasteurisation was 'in abeyance' at this time.<sup>70</sup> This was apparently due to the shelving of the ZHT project (see above) and because of pressure on the PFC to complete dry heat treatment of all existing intermediate purity NY Factor VIII batches (ie the interim measure to inactivate HIV introduced at the end of 1984 as an emergency response to the infection of Edinburgh patients with HIV which temporarily diverted attention from NANB Hepatitis).<sup>71</sup>

---

<sup>65</sup> Dr McIntosh – Day 61, pages 4–6

<sup>66</sup> Dr McIntosh – Day 61, page 6. For further details of the problems with the ZHT process see Dr McIntosh – Day 61, pages 4–6

<sup>67</sup> Dr McIntosh – Day 61, page 8

<sup>68</sup> Dr McIntosh – Day 61, pages 7–14

<sup>69</sup> Dr McIntosh – Day 61, pages 7–14

<sup>70</sup> Factor VIII Study Group update paper [SNB.007.4911]

<sup>71</sup> Factor VIII Study Group update paper [SNB.007.4911]

**24.49** The February 1985 *Update Paper* noted that a ‘watching brief’ would be kept on detergents and organic solvents as potential methods of viral inactivation. Dr Foster said that the PFC was aware of the research being carried out elsewhere into the use of solvent detergent as a method of viral inactivation.<sup>72</sup> He explained, however, that this method was only effective against viruses that had ‘lipid envelopes’, and that given that the structure of the NANB Hepatitis virus or viruses was not clear at the time, the solvent detergent method was less obviously attractive than heat treatment. Dr Foster also noted that an additional downside to the solvent detergent method was that it involved adding and then removing toxic chemicals from the product, which at the time could not readily be applied to the PFC’s manufacturing processes.

**24.50** Another report for the February 1985 meeting of the Factor VIII Study Group, prepared by Professor John Cash, noted that preliminary clinical evaluation studies (bioacceptability, clinical efficacy and residual infectivity) were planned for SNBTS Factor VIII products, both pasteurised (60°C for 10 hours and an additional period at 70°C) and dry heated (68°C for 24 hours), and outlined the PFC’s rationale for examining both wet and dry heat treatments. The report commented that:

The need to assess both dry and wet heat arises because the former is less costly and subject to lower yield penalties. However the wet heat is likely to be more virucidally effective.<sup>73</sup>

**24.51** At this time, research into the heat treatment of Factor IX was also continuing. These studies were carried out in collaboration with the BPL.<sup>74</sup> Difficulties had been encountered in arranging animal model studies using dogs, which were needed to test for thrombogenicity. According to a report by Professor Cash in March 1985:

Despite considerable efforts over the last 2 years it has only very recently been possible to make arrangements for animal model (thrombogenicity) testing. These were recently begun and provided all goes well it is anticipated that a heat treated product will be available for preliminary clinical evaluation by late Spring of 1985. The product currently the candidate for heat treatment is DEFIX.<sup>75</sup>

**24.52** A meeting of the SNBTS and Haemophilia Directors took place on 7 March 1985.<sup>76</sup> A paper drawn up for this meeting by Professor Cash summarised the position as regards heat treatment of Factor VIII by PFC. It explained that the current product was a reaction to AIDS. The period from November 1984 to March 1985 had been difficult. Professor Cash reported:

It has been a period in which disaster struck in Australia and in which both UK transfusion services were implicated in the transmission of HTLV-III viruses.<sup>77</sup>

**24.53** The standard routine SNBTS issue, Dry (Intermediate) HT (68°C for two hours) involved the dry heat treatment of the existing intermediate product without the addition

<sup>72</sup> Dr Foster – Day 57, page 28. Dr Foster noted, however that, in 1991, once more information became available on the effectiveness of the solvent detergent method PFC started to treat high purity Factor VIII with a solvent detergent method.

<sup>73</sup> SNBTS Heat Treated Factor VIII: Preliminary Clinical Evaluation Studies, February 1985 [SNF.001.3176]

<sup>74</sup> For more details of the animal studies with BPL see SNBTS Briefing Paper on the development of heat treatment, November 2010 [PEN.013.1309] at 1338–39

<sup>75</sup> Notes for Scottish Health Service Haemophilia Centre/Transfusion Service Directors’ Meeting: March 1985 [SNB.001.5357] at 5368

<sup>76</sup> Minutes of meeting [SNF.001.0241]

<sup>77</sup> Notes for Scottish Health Service Haemophilia Centre/Transfusion Service Directors’ Meeting: March 1985 [SNB.001.5357] at 5362. The Australian incident appears to have related to the deaths of three babies in Brisbane from AIDS.

of stabilisers.<sup>78</sup> According to the paper, it was anticipated that this product would remain the standard SNBTS Factor VIII product until autumn 1985 and that preliminary clinical evaluations of the new dry-heated product (68°C for 24 hours with the addition of stabilisers) would be completed by the end of May 1985. The paper indicated that work on the high purity NYU product was ‘proceeding satisfactorily’ and that, ‘decisions have not yet been made with regard to the heat treatment regime but at the present time wet heat treatment is favoured’.<sup>79</sup>

**24.54** Dr Perry also drew up a paper for this meeting, which summarised progress in heat treatment work at the PFC.<sup>80</sup> Dr Perry’s paper indicated that current heat-treated material (68°C/2 hrs) was available for the treatment of all haemophilia patients in Scotland and Northern Ireland and that an ongoing programme was underway to subject all existing stocks (including those recalled from Regional Transfusion Centres) to these heating conditions, with stocks anticipated to last until autumn 1985.<sup>81</sup> The paper noted that clinical trials of the intermediate purity NY Factor VIII product, dry-heated at 68°C for 24 hours, should be planned and implemented so as to ensure continuity of product supply later in the year.<sup>82</sup> By this date, it had been established that this product could be heated in the dry state to 68°C for 24 hours without reducing solubility. On 4 March 1985, Dr Perry had written to Dr Frank Boulton intimating that two batches of this product would be available for clinical trials within two weeks.<sup>83</sup> One hundred vials of two separate batches were arranged to be sent on or around 13 March 1985.<sup>84</sup> At the meeting, Dr Perry informed members that the new intermediate Factor VIII concentrate, dry-heated at 68°C for 24 hours, was ready for clinical evaluation. It was remitted to a Working Group to facilitate clinical evaluations in Scottish centres. It was also proposed that the Working Group should look into involving hospital Ethical Committees in evaluation proposals.<sup>85</sup>

**24.55** By late March 1985 a degree of progress had been made as regards the clinical trials mentioned in Dr Perry’s paper. On 2 April 1985, Professor Cash wrote to Professor Arthur Bloom with arrangements for trials of the latest product heat-treated at 68°C for 24 hours.<sup>86</sup> Professor Bloom, who had been hesitant about committing resources to the Scottish project earlier in the year,<sup>87</sup> responded with proposals on 10 April 1985.<sup>88</sup>

**24.56** However, the plan to proceed to clinical trials of safety and efficacy in Scotland led to some disquiet among haemophilia clinicians in the absence of compensation arrangements for participants in the trial.<sup>89</sup> In response to a request from Dr Boulton to test the 68°C/24 hours material, Professor Christopher Ludlam indicated in a letter dated 19 March 1985 that if compensation arrangements were not put in place he would have to seek ethical approval before continuing with the trial (Professor Ludlam’s letter noted that it would take some time to gain such approval).<sup>90</sup> There also appears to have been a degree of reluctance from the Glasgow Royal Infirmary in undertaking clinical trials.<sup>91</sup>

<sup>78</sup> Notes for Scottish Health Service Haemophilia Centre/Transfusion Service Directors’ Meeting: March 1985 [SNB.001.5357] at 5363

<sup>79</sup> *Ibid* [SNB.001.5357] at 5364

<sup>80</sup> PFC Report for SHS Haemophilia/SNBTS Directors Meeting (March 1985) [SNB.001.5376]

<sup>81</sup> PFC Report for SHS Haemophilia/SNBTS Directors Meeting (March 1985) [SNB.001.5376] at 5379

<sup>82</sup> PFC Report for SHS Haemophilia/SNBTS Directors Meeting (March 1985) [SNB.001.5376] at 5379

<sup>83</sup> Dr Perry’s letter to Dr Boulton of 4 March 1985 [SNB.007.5001]

<sup>84</sup> Dr Perry’s letter to Dr Boulton of 13 March 1985 [SNB.007.5021]

<sup>85</sup> Minutes of meeting [SNF.001.0241], pages 0242 and 0244

<sup>86</sup> Professor Cash’s letter to Professor Bloom of 2 April 1985 [SNB.007.5055]

<sup>87</sup> Professor Bloom’s letter to Professor Cash of 15 February 1985 [SNB.007.4932]

<sup>88</sup> Professor Bloom’s letter to Professor Cash of 10 April 1985 [SNB.007.5064]

<sup>89</sup> The background to the issue of compensation in this context is discussed more fully at paragraph 24.138 below.

<sup>90</sup> Professor Ludlam’s letter to Dr Boulton of 19 March 1985 [SNB.005.7320]

<sup>91</sup> Professor Cash’s letter to Dr Forbes of 11 March 1985 [SNB.007.5036]

**24.57** The discussions in March 1985 highlight a feature of SNBTS policy in relation to the rolling out of new products reflecting technological developments. All existing stocks, heat-treated at 68°C for two hours were to be used until exhausted in the autumn. The new formulation, prepared for heating at 68°C for 24 hours, would be held unheated pending trials of the preliminary batches, and issued (after dry heat treatment) in July or August when sufficient clinical experience of the product had accumulated. The policy of exhausting existing supplies before new (and, theoretically, superior) products were released was to become a recurrent theme.

**24.58** Professor Cash wrote to Professor Ludlam on 22 March 1985, expressing concern that his decision on trial of the product was likely to impact on progress, and commenting on the risk that delay could affect supplies of Factor VIII in mid-1985.<sup>92</sup> Professor Ludlam replied on 4 April 1985 expanding on his position as regards compensation arrangements and indicating that he was prepared to assist once he had received the full product specification.<sup>93</sup> However, the letter notes that Professor Ludlam would be, 'looking for concrete guidance from the Department' (that is, guidance from the SHHD on compensation arrangements).<sup>94</sup> Dr Boulton reacted to these developments in a letter to Professor Cash dated 19 April 1985. In his letter Dr Boulton queried Professor Ludlam's version of events, but indicated that he would contact Professor Ludlam once he had full details of the product, so as to come up with a 'mutually acceptable protocol'.<sup>95</sup> There appears to have been some progress thereafter. On 29 April, Professor Ludlam wrote to Professor Cash that he had sought ethical approval and was arranging for four haemophilia patients to 'come up' in the very near future.<sup>96</sup>

**24.59** On 15 May 1985 a meeting of the Haemophilia and Blood Transfusion Working Group took place.<sup>97</sup> Dr Perry reported that the PFC continued to manufacture FVIII, including 2% sorbitol, dry-heated at 68°C for 24 hours. Preliminary clinical evaluation studies had been good, and he said that the PFC could now proceed to heat all unheated stocks of FVIII. Meantime, as noted above at paragraph 24.15, the PFL and the BPL had already proceeded with production and release for general use of HT1 and HT2 in January 1985. At the Edinburgh meeting of the British Society for Haemostasis and Thrombosis on 26 March 1985 progress with the BPL's product prepared by heating freeze-dried concentrate at 60°C for 72 hours was reported, together with information on the outcome of trials.<sup>98</sup> Prospective studies on three surgical patients had shown no evidence of transmission of NANB Hepatitis. Development work proceeded at PFL on 8Y. From December 1984, the PFL had scaled up 8Y for clinical trial for safety and efficacy. Trials were conducted satisfactorily in February 1985 by which time 8Y had become the sole Factor VIII product manufactured at the PFL. Haemophilia Directors were informed in March 1985 that 8Y was available for clinical trial. The BPL followed through with manufacture of 8Y in May 1985.<sup>99</sup> The English Factor VIII development programme was now clearly ahead of Scottish work on dry heat treatment of FVIII.

<sup>92</sup> Professor Cash's letter to Professor Ludlam of 22 March 1985 [SGH.003.1967]

<sup>93</sup> Professor Ludlam's letter to Professor Cash of 4 April 1985 [SNB.005.7332]

<sup>94</sup> *Ibid* [SNB.005.7332] at 7333

<sup>95</sup> Dr Boulton's letter to Professor Cash of 19 April 1985 [SNB.005.7329]

<sup>96</sup> Professor Ludlam's letter to Professor Cash of 29 April 1985 [SNB.005.8646]

<sup>97</sup> Minutes of meeting [SNB.001.5352]

<sup>98</sup> Presentation abstract for British Society for Haemostasis and Thrombosis meeting, 26 March 1985 [SNB.007.5022]

<sup>99</sup> Dr Smith's statement on Viral Inactivation to 1985 [PEN.012.1551] at 1574

**24.60** On 15 May, there was further discussion of heat treatment of Factor IX. It had been reported in February that dog studies of thrombogenicity had been instructed.<sup>100</sup> The minutes of 15 May disclose that Dr Perry informed the meeting that:

[T]he heat treatment of Factor IX was a high priority project and that dog tests were underway at Cambridge. PFC expected initial clinical evaluation studies to begin in 2/3 months' time. Dr Cash was pleased to inform members that the first results received from Cambridge looked promising and tests had shown no trace of DIC in the heat treated product.<sup>101</sup>

**24.61** However, progress had not been sufficient to satisfy demand for Factor IX. In May 1985, when the SNBTS stopped supplying its unheated Factor IX, Haemophilia Directors purchased heated commercial Factor IX from the USA.<sup>102</sup>

**24.62** On 4 July 1985, results from Professor Bloom, added to results from Edinburgh, indicated excellent validation of the biological efficacy of the PFC's 'latest batch' of heat-treated Factor VIII.<sup>103</sup> The product would have been dry-heated for 24 hours at 68°C (the 'second generation' Factor VIII<sup>104</sup>) in May 1985, if it was the same as the Edinburgh test material.

**24.63** On 15 July 1985 Dr Perry sent a letter to Dr Lane, Director of BPL, which indicated that both the PFC and the BPL were involved in the clinical evaluation of their respective heat-treated Factor VIII products and noted that, as regards PFC's 68°C/24 hours product, the PFC was 'primarily concerned with half-life and recovery since it is unlikely that we will achieve freedom from NANB'.<sup>105</sup> The letter also included a copy of the PFC's heating protocol with the explanation that:

[S]ince we anticipate future trials of a product subjected to more substantial conditions of viral inactivation, I believe it would be helpful if we exchanged our respective trial protocols with a view to achieving commonality wherever possible.<sup>106</sup>

**24.64** Over the summer of 1985, further research continued. It was not expected that Factor VIII heated at 68°C for 24 hours would clear the product of NANB Hepatitis. New equipment had been ordered to achieve higher temperatures in the production process. The first heat treatment cabinet commissioned for the purpose was received and commissioned by the SNBTS in July 1985.<sup>107</sup> It was used thereafter for the dry heat treatment of Factor VIII concentrate at 68°C and Factor IX concentrate at 80°C. This equipment made it possible to proceed to more effective heat treatment.

**24.65** On 16 August 1985, at a meeting of the PFC Heads of Department/Section Managers, Dr Perry reported that heat-treated Factor IX product, DEFIX (dry heat treated at 80°C for 72 hours) 'had now been issued for routine use at Edinburgh Centre and further

---

<sup>100</sup> See paragraph 24.51 above

<sup>101</sup> Minutes of meeting [SNB.001.5352] at 5353

<sup>102</sup> Events concerning the safety of blood and blood products with special reference to the treatment of haemophilia, SNBTS, October 2009 [PEN.013.0220]

<sup>103</sup> Dr Boulton's letter to Dr Perry of 4 July 1985 [SNB.007.5176]

<sup>104</sup> Dr Perry's letter to Dr Boulton of 11 July 1985 [SNB.007.5200]

<sup>105</sup> Dr Perry's letter to Dr Lane of 15 July 1985 [SNB.007.5202]

<sup>106</sup> Ibid [SNB.007.5202]

<sup>107</sup> Investigation Concerning Events Surrounding the Introduction of Heat Treatment for Blood Products in the Mid 1980s – Additional Information Requested by the Scottish Executive, SNBTS, February 2000 [SGF.001.1439] at 1448

issues would be made to remaining centres in September/October 1985'.<sup>108</sup> On 26 August 1985, he wrote to the Scottish Transfusion Directors and NIBTS Director intimating that the PFC had almost exhausted their stocks of the original heat-treated product (68°C for two hours) and that the 'new' product would be issued within the next two months.<sup>109</sup>

**24.66** On 4 September 1985 the PFC commenced routine issue of its intermediate purity NY Factor VIII, dry heated at 68°C for 24 hours.<sup>110</sup> The 68°C/2 hours product continued to be released until 13 September 1985 after which it was recalled.<sup>111</sup>

**24.67** By October 1985, the PFC's heated Factor IX product (HT DEFIX), dry heat-treated at 80°C for 72 hours, was routinely distributed to all centres.<sup>112</sup> Existing stocks of unheated Factor IX were subsequently recalled and destroyed.<sup>113</sup>

**24.68** Over the second half of 1985, there were several technological developments at the PFC. Where necessary these will be described in some detail. In addition to the need for new ovens, they included new equipment for purification, specified in October 1985, and delivered by Pharmacia, the manufacturer, in mid-1986;<sup>114</sup> and the development of innovative freeze-drying procedures and associated equipment arising from study of the BPL's production methods for 8Y.<sup>115</sup> The implementation of developments in scientific research required sophisticated hardware.

**24.69** The lead time from discovery to full production was unavoidably long in some cases. In this, as other areas of research and development, laboratory scale experiments with small quantities of material might provide proof of principle, but scaling up to routine production of hundreds of litres of material safe for therapeutic application in patients required proof of practicability and effectiveness at each successive stage in the production process. And the equipment required for novel manufacturing processes often had to be custom-designed and made.

### Dr McIntosh's discovery

**24.70** By October 1985 there was sufficient volume of the NYU high purity Factor VIII product being developed by the PFC for work to progress to freeze-drying experiments.<sup>116</sup> Initial experiments were carried out on the high purity product using the established process for freeze-drying the PFC's intermediate purity NY Factor VIII.<sup>117</sup> However, this freeze-drying process led to the destruction of the high purity NYU product.<sup>118</sup> Dr McIntosh

<sup>108</sup> Minutes of meeting [SNB.010.3401]

<sup>109</sup> Dr Perry's letter of 26 August 1985 [SNB.007.5243]

<sup>110</sup> SNBTS Briefing Paper on the development of heat treatment, November 2010 [PEN.013.1309] at 1350. See also *PFC Report for SHS Haemophilia/SNBTS Directors Meeting (March 1986)* dated 10 January 1986 [SNB.001.5469] at 5472

<sup>111</sup> SNBTS Briefing Paper on the development of heat treatment, November 2010 [PEN.013.1309] at 1350. Recall was due to reports from Dr Prince that HIV was less susceptible to heat than was previously thought: Dr Perry's letter to Dr McClelland of 25 November 1985 [SNB.007.5358] and *PFC Report for SHS Haemophilia/SNBTS Directors Meeting (March 1986)* dated 10 January 1986 [SNB.001.5469] at 5472

<sup>112</sup> Dr Cuthbertson's letter to Professor Cash of 14 March 1988 summarising the key events in the PFC's response to the emergence of AIDS [SNF.001.0445] at 0447 and SNBTS Briefing Paper on the development of heat treatment, November 2010 [PEN.013.1309] at 1360

<sup>113</sup> SNBTS Briefing Paper on the development of heat treatment, November 2010 [PEN.013.1309] at 1360

<sup>114</sup> Investigation Concerning Events Surrounding the Introduction of Heat Treatment for Blood Products in the Mid 1980s – Additional Information Requested by the Scottish Executive, SNBTS, February 2000 [SGF.001.1439] at 1446

<sup>115</sup> The Development of Hepatitis-Safe Factor VIII Concentrate by the Scottish National Blood Transfusion Service, SNBTS, December 1999 [SNB.001.6647] at 6655–56

<sup>116</sup> *Ibid* [SNB.001.6647] at 6655

<sup>117</sup> *The Development of Hepatitis-Safe Factor VIII Concentrate by the Scottish National Blood Transfusion Service*, SNBTS, December 1999 [SNB.001.6647] at 6655. See also Dr McIntosh's statement on Viral Inactivation 1985–1987 [PEN.017.1234] at 1235. For a detailed overview of the workings of the PFC's established freeze drying process see Dr McIntosh – Day 61, pages 38–40.

<sup>118</sup> SNBTS Briefing Paper on the development of heat treatment, November 2010 [PEN.013.1309] at 1350. See also Dr Foster – Day 56, pages 87–88



explained that freeze-drying using the standard production cycle ‘completely failed’ and that ‘the primary drying conditions were much too warm, so the product literally boiled instead of sublimation occurring’.<sup>119</sup>

**24.71** As a result of this failure, the PFC was forced to design a new freeze-drying process from first principles in order to freeze-dry the high purity NYU product.<sup>120</sup> The key features of the re-designed freeze-drying process were: (i) a much lower primary drying temperature and a longer primary drying phase and (ii) a defined time and temperature in the secondary drying phase (as opposed to removing product when it was judged that it had dried sufficiently<sup>121</sup> under the existing ‘pressure hold test’).<sup>122</sup>

**24.72** On 21 October 1985, Dr McIntosh conducted a freeze-drying and heat treatment experiment based on this new process on a sample of high purity NYU Factor VIII prepared in the PFC’s research laboratory.<sup>123</sup> A sample from a standard vial of intermediate purity Factor VIII was also included as an experimental control.<sup>124</sup> Although the high purity product tolerated the new freeze-drying process, it failed to withstand dry heat treatment at 80°C.<sup>125</sup> In contrast, the intermediate purity product was found to have withstood both the freeze-drying process and dry heat treatment at 80°C.<sup>126</sup> Dr Foster included a description of the experiment in a memo to Dr McIntosh dated 22 October 1985.<sup>127</sup> This memo did not mention the experimental control,<sup>128</sup> but indicated that the heated NYU high purity product ‘looked overheated’, did not re-dissolve properly and had no Factor VIII activity. A list of possible areas to research was set out.<sup>129</sup> Dr Foster explained that the result of the experiment was ‘very surprising’ as he had ‘expected the high purity product to be able to withstand dry heating at 80 and even to be able to withstand heating beyond 80’.<sup>130</sup> There had been no expectation that the intermediate purity product would be able to withstand heating to that temperature. The expectation until that point was that increased purity was the key to heating at higher temperatures.

**24.73** In the following weeks, the PFC conducted further investigations into the reasons for the unexpected result of the experiment and the possibilities regarding dry heat treatment. The initial experiment was repeated,<sup>131</sup> and on 11 November 1985 Dr Foster drew up handwritten laboratory notes detailing further dry heat treatment experiments (80°C/72 hours) involving the PFC’s existing intermediate purity Factor VIII (referred to by its product code NY 776) and the high purity product (product code NYU 195), and took photographs of the results.<sup>132</sup> On 21 November 1985, Dr McIntosh carried out

<sup>119</sup> Dr McIntosh – Day 61, pages 40–41. Sublimation is the process of transformation directly from the solid phase to the gas phase without passing through an intermediate liquid phase.

<sup>120</sup> SNBTS Briefing Paper on the development of heat treatment, November 2010 [PEN.013.1309] at 1350 and Dr McIntosh – Day 61, page 41. For a general overview of how freeze-drying works (and the three stages of: freezing, preliminary drying and secondary drying) see Dr McIntosh – Day 61, pages 24–28

<sup>121</sup> For a brief description of the new process see Dr McIntosh – Day 61, pages 22, 40 and 45

<sup>122</sup> For a description of the ‘pressure hold test’ see Dr McIntosh – Day 61, page 39

<sup>123</sup> SNBTS Briefing Paper on the development of heat treatment, November 2010 [PEN.013.1309] at 1350 and Dr Foster’s statement on Heat Treatment, 1985–1987 [PEN.017.1556] at 1560

<sup>124</sup> Dr Foster’s statement on Heat Treatment, 1985–1987 [PEN.017.1556] at 1560. See also Dr Foster – Day 56, page 89. For more information on the experimental control see Dr McIntosh – Day 61, pages 20–21 and 42–43.

<sup>125</sup> SNBTS Briefing Paper on the development of heat treatment, November 2010 [PEN.013.1309] at 1350

<sup>126</sup> *Ibid* [PEN.013.1309] at 1350

<sup>127</sup> Dr Foster’s memo to Dr McIntosh of 22 October 1985 [PEN.017.1376]. According to Dr Foster the reason why he wrote to Dr McIntosh and not the other way round was because Dr McIntosh had given him the results in order that Dr Foster could reflect on them – see Dr Foster – Day 56, page 91.

<sup>128</sup> See Dr McIntosh – Day 61, page 35 for confirmation

<sup>129</sup> Dr Foster’s memo to Dr McIntosh of 22 October 1985 [PEN.017.1376]

<sup>130</sup> Dr Foster – Day 56, page 89

<sup>131</sup> See Dr Foster – Day 56, page 92. The Inquiry does not, however, have a record of this having occurred.

<sup>132</sup> Dr Foster’s notes dated 11 November 1985 [PEN.017.1378] and Dr Foster – Day 56, pages 105–106

an experiment to examine the feasibility of dry heating intermediate Factor VIII at high temperatures (ie the ZHT product purified using zinc/heparin precipitation).<sup>133</sup> Notes of these experiments were made on an existing method sheet for the ZHT product, with the elements related to the pasteurisation step deleted by hand.<sup>134</sup> When asked during the Inquiry hearings to explain what this experiment involved Dr McIntosh said:

[T]his is one of the early experiments ... taking the – as I call, front end of the ZHT process and not carrying on into pasteurisation but freeze-drying that material, preparing that material for freeze-drying in such a way that it could be terminally dry heat-treated.<sup>135</sup>

**24.74** Dr McIntosh confirmed in oral evidence that these experiments were the first laboratory scale experiments on the product that would, in due course, become known as Z8.<sup>136</sup>

**24.75** Meanwhile, on 13 November 1985 Dr Foster wrote to Dr Smith at the BPL enclosing some recent PFC publications. He also said:

One question I've been meaning to ask you; what are the freeze drying conditions for your new FVIII concentrate (especially during primary drying). We have some preliminary data that suggests that drying conditions may be particularly critical for the subsequent sensitivity of both protein and virus components to heating (not unexpected).<sup>137</sup>

**24.76** Dr Foster said that this question about the freeze-drying procedure for 8Y, which was known to tolerate dry heat treatment at 80°C/72 hours, arose from Dr McIntosh's discovery in the laboratory scale experiment that intermediate purity Factor VIII tolerated dry heat treatment at 80°C/72 hours.<sup>138</sup> This discovery led Dr Foster to consider that the freeze-drying process might be important in relation to the ability of Factor VIII to tolerate dry heat treatment.<sup>139</sup> Although Dr McIntosh's discovery was surprising at the time, Dr Foster indicated during the Inquiry hearings that once he had had the opportunity to consider it further he came to the conclusion that, on reflection, it was not entirely surprising that the freeze-drying procedure might influence the subsequent heat treatment step given that it was not unusual in fractionation for the success of a manufacturing step to be influenced by a preceding step or steps.<sup>140</sup>

**24.77** Dr Smith responded to Dr Foster in a letter of 11 December 1985 which included details of the freeze-drying conditions at the BPL for 8Y.<sup>141</sup> Dr Foster said that the information supplied by Dr Smith 'confirmed that the new freeze drying cycle devised at the PFC was similar in design to that being used to freeze dry 8Y, consistent with this being the key aspect of the 8Y process, rather than the degree of purification'.<sup>142</sup>

---

<sup>133</sup> Method Sheets dated 21 November 1985 and 2 December 1985 [PEN.017.1379] and SNBTS Briefing Paper on the development of heat treatment, November 2010 [PEN.013.1309] at 1341

<sup>134</sup> Method Sheets dated 21 November 1985 and 2 December 1985 [PEN.017.1379]

<sup>135</sup> Dr McIntosh – Day 61, page 34

<sup>136</sup> Dr McIntosh – Day 61, page 34. See also Dr Foster – Day 56, page 106

<sup>137</sup> Dr Foster's letter to Dr Smith of 13 November 1985 [SNB.007.5355]

<sup>138</sup> Dr Foster – Day 56, page 92

<sup>139</sup> Dr Foster's letter to Dr Smith of 13 November 1985 [SNB.007.5355]

<sup>140</sup> Dr Foster – Day 56, page 93

<sup>141</sup> Dr Smith's letter to Dr Foster of 11 December 1985 [SNB.007.5458]

<sup>142</sup> SNBTS Briefing Paper on the development of heat treatment, November 2010 [PEN.013.1309] at 1350

## Change of direction

**24.78** By late 1985 work at the PFC had progressed far enough that it was possible to re-assess the various options regarding heat treating Factor VIII. In particular, on 18 December 1985 Dr Foster sent a memorandum entitled *FVIII Progress and Options* to Dr Perry. The memorandum explained that it was ‘a brief summary of where we are at with the NYU [high purity] FVIII project and the various options that are available to us to achieve a product heated at 80°C for 72 hours’.<sup>143</sup>

**24.79** The NYU project was summarised first and it was explained that the latest attempt at heating the product on 17 December 1985 had given a negative result (the speculative suggestion was that this was due to a problem with the product’s ‘ionic strength’).<sup>144</sup> Three options for the NYU project were set out:<sup>145</sup>

- Option 1.1. Heat material at high ionic strength but with lysine added to provide extra stabilisation.
- Option 1.2. Reduce the ionic strength to a subcritical level (with or without lysine).
- Option 1.3. Recover the whole FVIII molecule instead of FVIIIc. It was noted that this would entail a loss of purity of 25%–50% and that it would be an ‘ideological’ step backwards.

**24.80** The memorandum also set out three options for the development of PFC’s existing intermediate purity NY Factor VIII product.<sup>146</sup> These options were:

- Option 2.1. Heating the existing product at 80°C for three days, which apparently could be achieved by using a more conservative freeze-drying regime.<sup>147</sup>
- Option 2.2. Purifying the existing product a little further so that the solution could be concentrated by ultra-filtration so as to reduce fill volume and hence the freeze-drying time (this could apparently be achieved by zinc precipitation of cryoprecipitate).
- Option 2.3 Copying the BPL method. It was noted, however, that, ‘a fair amount of work would be needed to finish this project off and it is not an attractive proposition for transfer to production’.<sup>148</sup>

**24.81** The memorandum indicated that, ‘unfortunately all of these options compete for resources, particularly FVIII assays, still the rate limiting factor’,<sup>149</sup> and concluded with the recommendation to:

[G]ive options 1.1 and 1.2 top priority but to continue on 1.3 and 2.2 so that we can either change tack on the NYU project if progress is slow or produce a modification of our existing product if pressure on heat inactivation demands it.<sup>150</sup>

<sup>143</sup> Dr Foster’s memo to Dr Perry of 18 December 1985 [SNB.013.6680]. See also Dr Foster – Day 56, pages 101–103

<sup>144</sup> Dr Foster’s memo to Dr Perry of 18 December 1985 [SNB.013.6680]

<sup>145</sup> Dr Foster’s memo to Dr Perry of 18 December 1985 [SNB.013.6680] and also Dr Foster – Day 56, page 103

<sup>146</sup> Dr Foster’s memo to Dr Perry of 18 December 1985 [SNB.013.6680] at 6681

<sup>147</sup> Dr Foster’s memo to Dr Perry of 18 December 1985 [SNB.013.6680] at 6681. According to Dr Foster’s oral evidence, the reference to a ‘conservative freeze drying regime’ means a slower, more gentle freeze drying process – see Dr Foster – Day 56, pages 103–104

<sup>148</sup> Dr Foster’s memo to Dr Perry of 18 December 1985 [SNB.013.6680] at 6681

<sup>149</sup> For details on why access to assays, by definition, limited the rate of research and development see: Dr Foster – Day 56, page 108–109 and Dr Foster’s statement on Heat Treatment, 1985–1987 [PEN.017.1556] at 1582–83

<sup>150</sup> Dr Foster’s memo to Dr Perry of 18 December 1985 [SNB.013.6680] at 6681

**24.82** Dr Foster was asked during the Inquiry hearings whether his preference at the time was to continue to give priority to the NYU high purity project, but to have option 2.2 (further purification of the intermediate product) as a back-up plan. He confirmed that this was the case and explained that, in his view, pasteurisation was still his preference for the high purity product as there ‘was more evidence to support it in terms of achieving a safe product’.<sup>151</sup> In addition, however, a high purity product would also be compatible with alternative viral inactivation techniques such as dry heat treatment or solvent detergent.<sup>152</sup> He added:

[O]ne of the factors in my thinking at this time was the knowledge that the haemophilia directors were very keen on having higher purity products and they were concerned about the possibility that there might be some immune disturbance in patients as a result of the lower purity products. So that was an added aspect to consider with this higher purity material.<sup>153</sup>

**24.83** Dr Foster indicated that the statement, ‘if pressure on heat inactivation demands it’, was a reference to work carried out by Dr Alfred Prince in the USA which had questioned the effectiveness of dry heat treatment against HIV<sup>154</sup> and pointed out that for the PFC this was a potential concern, explaining that, ‘looking back now, we kind of see non-A non-B as equal or even perhaps of more concern but at this point in time it was HIV that was driving everyone’s thinking’.<sup>155</sup>

**24.84** The question of which option or options to proceed with was discussed at a meeting between Drs Foster, McIntosh, Perry and Cuthbertson on 23 December 1985.<sup>156</sup> Other than a brief diary entry by Dr Foster on this date, which simply refers to ‘FVIII meeting’, there was no formal record of the meeting.<sup>157</sup>

**24.85** During the Inquiry hearings, Drs Foster, McIntosh, Perry and Cuthbertson were each asked for their recollections of this important meeting.<sup>158</sup> All indicated that the purpose of the meeting was to discuss Dr Foster’s memo of 18 December and the two main heat treatment options – ie continuing with the high purity NYU process or moving to severe dry heat treatment of the PFC’s intermediate Factor VIII product.<sup>159</sup> There appears to have been a degree of urgency in holding this meeting as it was scheduled immediately before the Christmas holidays when the PFC would not have been in production (a non-urgent meeting would normally have been left until the New Year).<sup>160</sup>

**24.86** Dr Foster explained that his view before the meeting had been that the PFC should continue to prioritise the high purity NYU process, whilst exploring alternatives.<sup>161</sup> In contrast, Dr McIntosh was of the opinion that the PFC should pursue severe dry heat

<sup>151</sup> Dr Foster – Day 56, page 112

<sup>152</sup> *Ibid*

<sup>153</sup> Dr Foster – Day 56, page 110. ‘Antigen overload’, the theory that immune disturbance was related to repeated infusions of ‘impure’ factor products is discussed in Chapter 11, *HIV/AIDS Aetiology*. The SNBTS had a Neoantigen Study Group examining the problem from May 1985: Notes of Neoantigen Study Group meeting 9 May 1985 [SNB.007.5113]

<sup>154</sup> SNBTS became aware of Dr Prince’s work as of late October/early November 1985. See letter from Dr Perry to Dr McClelland dated 5 November 1985 [SNB.007.5358] and pre-print of Dr Prince’s paper [SNB.007.5360]

<sup>155</sup> Dr Foster – Day 56, page 111. See also Dr Foster’s statement on Heat Treatment, 1985–1987 [PEN.017.1556] at 1583

<sup>156</sup> Dr Foster’s statement on Heat Treatment, 1985–1987 [PEN.017.1556] at 1573 and Dr Foster – Day 56, page 113

<sup>157</sup> Extract from Dr Foster’s diary [PEN.017.1383] and Dr Foster, Day 56 – page 113

<sup>158</sup> For their responses see: Dr Foster – Day 56, pages 113–118; Dr Cuthbertson – Day 57, pages 50–53; Dr Perry – Day 58, pages 15–23 and pages 33–34; and Dr McIntosh – Day 61, pages 48–52

<sup>159</sup> See Dr Perry – Day 58, page 16; Dr Cuthbertson – Day 57, page 51; Dr McIntosh – Day 61, page 48; and Dr Foster – Day 56, pages 113–115.

<sup>160</sup> See Dr Foster – Day 56, pages 113–114 and see Dr Perry – Day 58, page 16

<sup>161</sup> See Dr Foster – Day 56, pages 115–116

treatment (80°C/72hours) of the PFC's intermediate purity NY product (purified a little further) on the grounds that: (i) laboratory experiments had shown that the product could be freeze-dried and heated at high temperatures; and (ii) dry heating would be more straightforward than pasteurisation (both in terms of equipment and staffing) and could be fitted into the PFC's current manufacturing and staffing processes more easily.<sup>162</sup> Dr Cuthbertson shared Dr McIntosh's view for similar reasons, but also on the basis that dry heat treatment would take place in the final sealed container which would reduce the risk of cross-contamination.<sup>163</sup> Dr Cuthbertson also indicated that 8Y's apparent success in England was another factor in favour of dry heat treatment.<sup>164</sup> For his part, Dr Perry went into the meeting with an open mind. While dry heat treatment was likely to be the simpler route, he was conscious of the 'presentational issue' that early commercial dry-heated products, heated at lower temperatures, had not turned out to be safe. The dry heat treatment process had the potential to be discredited due to previous failures.<sup>165</sup>

**24.87** At the end of the meeting a decision was made to recommend the prioritisation of the severe dry heat treatment of PFC's intermediate purity product.<sup>166</sup> Dr McIntosh was to lead the development of the project and Dr Perry would inform Professor Cash, as head of the SNBTS, of the group's recommendation.<sup>167</sup>

**24.88** In his written evidence to the Inquiry, Dr Foster summarised the reasons for the PFC changing its Factor VIII strategy as follows:

- a pre-publication report from the USA [the Prince report noted above] which found HIV to be more resistant to dry heat treatment than earlier experiments had indicated ... leading to uncertainty over the margin of safety being provided by the current SNBTS dry heat treated Factor VIII concentrate,
- a problem of instability that had been identified on the scale-up of SNBTS high purity NYU Factor VIII product, which required to be solved,<sup>168</sup>
- difficulty in dry heating high purity Factor VIII product at 80°C,
- recognition that the sophisticated equipment required for the production of high purity Factor VIII could not be obtained quickly<sup>169</sup> and that its operation would require revised staffing arrangements, the establishment of which was uncertain,<sup>170</sup>
- that full scale production of 8Y had been achieved successfully at the BPL,
- that the 8Y produced at the BPL had been found to be satisfactory in terms of clinical efficacy and tolerability.<sup>171</sup>

<sup>162</sup> Dr McIntosh – Day 61, pages 49–51

<sup>163</sup> Dr Cuthbertson – Day 57, page 52. See also Dr Foster – Day 56, pages 115–116 who mentions that Dr McIntosh also made this argument, and that he considered it persuasive.

<sup>164</sup> Dr Cuthbertson – Day 57, pages 52–53

<sup>165</sup> See Dr Perry – Day 58, page 18; and, for a discussion of the 'presentational issue' pages 20–21. Dr Perry was also attracted to the fact that dry heat treatment would take place in the final container – see Dr Perry – Day 58, page 34

<sup>166</sup> See Dr Foster – Day 56, pages 116–117; Cuthbertson – Day 57, page 51; Dr Perry – Day 58, page 22 and Dr McIntosh – Day 61, pages 48–49

<sup>167</sup> Dr Foster – Day 56, page 117. It would appear that any such meeting would have had to have taken place in 1986 (see discussion of the events of 1986 below and Dr Perry – Day 58, page 22).

<sup>168</sup> The product became unstable when around 100 litres of plasma was used. This problem had not been solved by the time of the meeting on 23 December 1985. Dr Foster – Day 56, pages 96–97

<sup>169</sup> A delay of 6–9 months was likely: Dr Foster – Day 56, pages 97–98

<sup>170</sup> Shift-working: Dr Foster – Day 56, pages 97–98

<sup>171</sup> SNBTS Briefing Paper on the development of heat treatment, November 2010 [PEN.013.1309] at 1351

1986

### Research on Z8 prioritised

**24.89** Although it appears to have been understood that Dr Perry and Professor Cash would meet in early 1986 to discuss the proposed new heat treatment strategy, the Inquiry has been unable to find any record of such a meeting and neither witness could recall such a meeting having taken place.<sup>172</sup> Despite that, in their evidence to the Inquiry, both Dr Perry and Professor Cash were of the view that such a meeting must have taken place some time at the start of 1986. Professor Cash indicated that the PFC would have required to discuss its proposed change of strategy with him as he was the ‘ultimate decision maker’ for the SNBTS.<sup>173</sup> Although there is a degree of uncertainty as to exactly when and how Professor Cash approved the proposed change of direction at the PFC, it seems highly likely that at some point in early 1986 Professor Cash must have approved the new strategy to develop an intermediate purity Factor VIII product that could be severely dry- heated.

**24.90** Dr Perry drew up a report for a meeting of the Haemophilia Directors in March 1986.<sup>174</sup> The report, dated 10 January 1986, mentioned the BPL’s 8Y product, indicating that, ‘preliminary clinical data indicates that this material is non-infective with respect to HTLV III, NANB and Hepatitis B’.<sup>175</sup> The report referred to the PFC’s NYU high purity product and noted that, ‘[A] programme of in-vitro characterisation and animal studies has been initiated and it is likely that the product will be ready for Phase I clinical studies in April 1986’.<sup>176</sup>

**24.91** No mention was made in Dr Perry’s report, however, of the decision made at the meeting on 23 December to prioritise the development of an intermediate purity Factor VIII product that could be severely dry-heated.

**24.92** When asked during the public hearings why the report did not mention that important change in strategy, Dr Perry suggested that the report may have been drawn up before he had had a chance to speak to Professor Cash, or that Professor Cash may have been away in January of 1986.<sup>177</sup> He considered it equally possible that the report was drafted in late 1985, before the meeting on 23 December had taken place.<sup>178</sup> Dr Perry further explained that the reference in his report to the high purity NYU product being ready for Phase I clinical trials in April 1986 was ‘perhaps an over-optimistic statement’ and that, in any event, any trials would have been of a pilot production scale product rather than a full production scale product.<sup>179</sup>

**24.93** It appears likely that Dr Perry was correct in speculating that his report was drafted before the meeting on 23 December 1985 and, because of the Christmas break, was not typed up until 10 January 1986.<sup>180</sup> In any event, the outcome of the meeting on 23 December

---

<sup>172</sup> Dr Perry – Day 58, page 22; Professor Cash – Day 57, pages 92–94

<sup>173</sup> Professor Cash – Day 57, pages 92–94

<sup>174</sup> Dr Perry’s report [SNB.001.5469]. The report was attached as Appendix VI to notes [SNB.001.5454] drawn up by Professor Cash in February 1986 for this meeting.

<sup>175</sup> Dr Perry’s report [SNB.001.5469] at 5472

<sup>176</sup> Dr Perry’s report [SNB.001.5469] at 5473

<sup>177</sup> Dr Perry – Day 58, pages 22–27

<sup>178</sup> Dr Perry – Day 58, page 24

<sup>179</sup> Dr Perry – Day 58, pages 32–33

<sup>180</sup> The report comments that it was unlikely that the current PFC Factor VIII product could be treated successfully at 80°C for 72 hours, a view Dr Perry was unlikely to have expressed after the meeting: Dr Perry’s report [SNB.001.5469] at 5472

was reflected in an addendum produced by Dr Perry to his report.<sup>181</sup> While the addendum is undated, it appears to have been sent to Professor Cash on either 25 January 1986 or 18 February 1986.<sup>182</sup> The addendum indicated that research had shown that the PFC's intermediate purity product could tolerate severe heat treatment and that:

This information will enable a non-infective product to be achieved using intermediate-purity material without compromising the development of the very high purity product ....<sup>183</sup>

**24.94** Various advantages of the new strategy were mentioned in the addendum including that it would allow: (i) non-infective product to be introduced more quickly and (ii) the high purity product to be properly assessed and phased in without undue haste (the implication being that work on the high purity product had not been completely abandoned).<sup>184</sup> It was also noted that it was likely that the intermediate dry heated product, 'will be available for evaluation in April 1986'.<sup>185</sup> When asked about this projection, Dr Perry said that it could have only been in relation to a product 'somewhere between laboratory and pilot scale manufacture' and that he must have written the addendum relatively early in 1986 as 'if [he] had been writing it in March' then his April estimate 'would have been wildly off course'.<sup>186</sup> Dr Foster also commented on the issue of the April 1986 evaluation date in his written statement to the Inquiry.<sup>187</sup> He advised that he had suggested this date to Dr Perry, but that it was incorrect because he had assumed that pilot scale material would be used for clinical trials as this had been the approach previously taken with the pasteurised ZHT product. However, in the event, trials were not carried out until full-scale production Z8 was available.<sup>188</sup> In addition, various unexpected problems occurred in the development and production of Z8 (as discussed at paragraph 24.125 below).<sup>189</sup>

**24.95** Although it is unclear when exactly a final management decision was taken to prioritise the severe dry heat treatment of the PFC's intermediate purity product, it is clear that the PFC continued research, led by Dr McIntosh, into this process at the start of 1986. The Inquiry recovered handwritten notes of experiments undertaken by him during January and February 1986.<sup>190</sup> A significant development was the introduction of ultra-filtration (in substitution for size-exclusion chromatography) in formulating the supernatant from the zinc-precipitated material to become a finished product.<sup>191</sup> The development of full scale ultra-filtration equipment for manufacturing purposes and the sequencing of production processes had occupied time and resources in 1985.<sup>192</sup> Freeze-drying equipment and procedures also presented difficulties.<sup>193</sup>

<sup>181</sup> Addendum to Dr Perry's report [SNB.001.5484]. The addendum appears intended to replace the Factor VIII information in the 'Development of New Products in 1986/7' section of the original 10 January 1986 report – ie [SNB.001.5469] at 5472

<sup>182</sup> See letter from Dr Perry to Professor Cash attaching report dated 25 January 1986 [SNB.001.5485] and a similar letter also attaching a report dated 18 February 1986 [SNB.001.5442]. Although this is unclear, it may be that the initial letter in January contained the first report [SNB.001.5469] and the letter in February the addendum.

<sup>183</sup> Addendum to Dr Perry's report [SNB.001.5484]

<sup>184</sup> Addendum to Dr Perry's report [SNB.001.5484]

<sup>185</sup> Ibid [SNB.001.5484]

<sup>186</sup> Dr Perry – Day 58, pages 38–39

<sup>187</sup> Dr Foster's statement on Heat Treatment, 1985–1987 [PEN.017.1556] at 1563

<sup>188</sup> For Dr Cuthbertson's explanation as to why the PFC may have waited until full-scale production to carry out trials see Dr Cuthbertson – Day 57, pages 56–58

<sup>189</sup> Dr Cuthbertson – Day 57, pages 56–58. For details of the 'unexpected problems' see Dr Foster's statement on Heat Treatment, 1985–1987 [PEN.017.1556] at 1562

<sup>190</sup> Dr McIntosh's notes [PEN.017.1384]

<sup>191</sup> Dr McIntosh – Day 61, page 56

<sup>192</sup> Dr McIntosh – Day 61, pages 56–58. It would have been necessary to purchase and install new equipment for large-scale size-exclusion chromatography, and PFC already had experience of ultra-filtration from work on ZHT: SNBTS Briefing Paper on the development of heat treatment, November 2010 [PEN.013.1309] at 1352

<sup>193</sup> Dr McIntosh – Day 61, pages 58–59

**24.96** From February 1986 the change of direction at the PFC began to be recorded in contemporaneous documents. In his notes for the March 1986 meeting of the Haemophilia Directors and Transfusion Directors, for example, which were drawn up in February 1986, Professor Cash indicated that difficulties had arisen as regards the heat treatment of the high purity product and that:

As a consequence it is anticipated that there will be some delay in it reaching phase 1 (recovery and ½ [life]) studies. Accordingly, a decision has been taken to introduce an interim solution: a product which is only 2–3 times purer than the existing intermediate VIII but which can be dry heated at 80°C for 72 hours.<sup>194</sup>

**24.97** While this document is further evidence that work on the high purity product had not been abandoned completely, Dr Foster said that at this time Dr McIntosh was focusing almost entirely on severe dry heat treatment, rather than high purity work.<sup>195</sup> Dr Cuthbertson echoed this point. He said that the high purity process had been put ‘on the backburner’ and that even if there had been a desire to develop the high purity project rapidly there was insufficient assay capacity in his testing laboratory to focus on two research and development projects simultaneously in addition to routine testing of manufactured products for quality control.<sup>196</sup>

**24.98** During this period, contact with the PFL in England continued and, on 26 February 1986, Dr Smith wrote to Dr Duncan Pepper with details on what he described as ‘the last significant stage of 8Y’ as well as his thoughts on ‘very fast freezing’.<sup>197</sup> Freeze-drying was also discussed during a meeting of the SNBTS Coagulation Factor Study Group on 27 February 1986 in which mention was made by Dr Perry of plans for ‘improved freezing’ and improved freeze-drying of the intermediate purity product which was to be heated at 80°C for 72 hours.<sup>198</sup>

**24.99** At the meeting of Haemophilia Directors and SNBTS Directors on 5 March 1986, the switch to developing severe heat treatment of the intermediate purity product was discussed with the Haemophilia Directors.<sup>199</sup> It was at this stage, following a memorandum sent by Dr Foster to Dr Perry and Dr McIntosh dated 5 March 1986 that ‘Z8’ was selected as the name for the product (intended to be heated at 80°C for 72 hours).<sup>200</sup> Dr Foster had become concerned that the multiplicity of PFC Factor VIII products under consideration might cause confusion outside the PFC. He listed two ZHT products heated at 68°C, the 80°C product that was named Z8, and a fourth ‘PFC, NYU FVIII’, the high purity product on the ZHT base, which he proposed should be named ‘REAL 8’.

### Spring 1986 – work on Z8 continues

**24.100** Further work relating to the development of Z8 continued throughout the spring of 1986. A meeting took place at the PFC between individuals from the BPL and the SNBTS on 17 March 1986 at which the two organisations exchanged information about

<sup>194</sup> Professor Cash’s notes for meeting in March 1986 [SNB.001.5454] at 5459

<sup>195</sup> Dr Foster – Day 56, page 121

<sup>196</sup> Dr Cuthbertson – Day 57, page 55

<sup>197</sup> Dr Smith’s letter to Dr Pepper of 26 February 1986 [SNB.007.5606]

<sup>198</sup> Minutes of Coagulation Factor Study Group meeting, 27 February 1986 [SNB.007.5596] at 5598 – this group was formerly known at the ‘Factor VIII Study Group’.

<sup>199</sup> Minutes of SNBTS and Haemophilia Directors meeting, 5 March 1986 [SNB.001.5448] at 5450

<sup>200</sup> Dr Foster’s memorandum of 5 March 1986 [SNB.007.5608]



progress in research and development and agreed further collaboration.<sup>201</sup> Discussion was summarised by Dr Perry in a note dated 24 March 1986.<sup>202</sup> During this meeting virus inactivation studies were discussed and it was agreed that the BPL would send samples of 8Y to the PFC, which had more specialist facilities, to carry out studies into levels of virus inactivation.<sup>203</sup> At the meeting Dr Smith outlined clinical trial results for 8Y. It was noted by Dr Perry that:

While results cannot be considered conclusive at this stage ... no cases of virus infection have occurred (attributable to 8Y material) after 12 months experience of 8Y in virgin haemophiliacs.<sup>204</sup>

**24.101** At the Inquiry's public hearings Dr Smith said that by March 1986 there was evidence that heating Factor VIII at 80°C instead of 60°C was beneficial as regards HIV.<sup>205</sup> However, as regards NANB Hepatitis he said that he considered that Dr Perry's summary of the March meeting relating to the perceived safety of 8Y was based probably on a very brief review of the facts and that it was too optimistic.<sup>206</sup> Dr Smith accepted that, logically, the preliminary results reported gave what he called 'a slightly larger margin of safety'. However he stressed that he was not of the view at the time that this could be viewed as significant statistically or that there was a 'high probability of the product being safe'.<sup>207</sup> While initial results from its use suggested that 8Y had a greater margin of safety in respect of the transmission of NANB Hepatitis, Dr Smith was of the opinion that there was insufficient evidence of freedom from infection in 1986 to enable any robust scientific conclusions to be made.<sup>208</sup>

**24.102** Dr Foster was asked about his knowledge of the clinical results for 8Y at this period.<sup>209</sup> He said that he was aware of the general view that the clinical trial of 8Y was proceeding well,<sup>210</sup> but that he was not specifically kept up to date with the emerging clinical data available from the routine use of 8Y. He would have expected Dr Smith to inform him of any bad news, and the lack of any such news was reason for cautious optimism.<sup>211</sup>

**24.103** At the BPL/SNBTS meeting on 17 March 1986 mentioned above, there was also discussion of the likelihood that freeze-drying conditions might affect the efficacy of heat treatment.<sup>212</sup> On 24 March 1986 Dr Foster received further details of the freeze-drying cycles for BPL's Factor VIII and Factor IX products as requested.<sup>213</sup>

<sup>201</sup> The Advisory Committee on the Virological Aspects of the Safety of Blood Products had recommended on 7 February 1986 that a working group should be established between the BPL, Elstree, the PFC, Edinburgh and NIBSC, which would meet periodically and provide a forum for the exchange of technical and scientific information pertaining to the safety of blood and blood products, especially in relation to virus contamination and the evaluation of manufacturing procedures to inactivate or eliminate viruses: Minutes of 7 February 1986 meeting [SNB.005.1495] at 1508.

<sup>202</sup> Dr Perry's note of the 17 March 1986 meeting [SNB.007.5664]

<sup>203</sup> Ibid [SNB.007.5664] at 5665

<sup>204</sup> Ibid [SNB.007.5664] at 5666

<sup>205</sup> Dr Smith – Day 60, page 109

<sup>206</sup> Dr Smith – Day 60, page 107

<sup>207</sup> Dr Smith – Day 60, page 109–110

<sup>208</sup> Dr Smith's comments applied equally to Dr Perry's statement in his report of 10 January 1986 [SNB.001.5469] at 5472 that, as regards 8Y, 'preliminary clinical data indicates that this material is non-infective with respect to HTLV III, NANB and Hepatitis B' – see Dr Smith – Day 60, page 105

<sup>209</sup> Dr Foster – Day 56, pages 62–67

<sup>210</sup> ie as briefly outlined in Dr Perry's note of the 17 March 1986 meeting [SNB.007.5664] and in Dr Perry's report providing background for the meeting of the Haemophilia Directors of 5 March 1986 [SNB.001.5469] at 5472

<sup>211</sup> Dr Foster – Day 56, page 66

<sup>212</sup> Dr Perry's note of the 17 March 1986 meeting [SNB.007.5664] at 5665

<sup>213</sup> Letter from Mr Kinnarney (BPL) to Dr Foster, dated 19 March 1986, received at PFC on 24 March 1986 [PEN.017.1399]

**24.104** Between March and May 1986 work on developing Z8 continued. Dr McIntosh indicated that during this period the PFC was involved in ‘further work on freeze-drying and on the formulation of the ultra-filtered material’.<sup>214</sup> The scale-up of the ultra-filtration stage in preparation for Z8 manufacture was a large part of this work and would have involved familiarising staff with new ultra-filtration equipment.<sup>215</sup> On 25 April 1986, the first virus inactivation experiments were performed on samples of Z8 produced in the research laboratory and dry-heated at 80°C.<sup>216</sup>

**24.105** Steps were also underway at the PFC to carry out virus inactivation experiments on 8Y on behalf of the BPL. On 9 May 1986, for example, Dr Cuthbertson sent Dr Lane of the BPL an outline of the protocol (using model viruses) which the PFC intended to use in evaluating virus kill in 8Y.<sup>217</sup>

**24.106** In May 1986, Drs Cuthbertson, McIntosh and Foster of the PFC presented a paper at an international conference in Sydney, Australia. A summary of the paper emphasised the importance of freeze-drying for successful heat treatment, noting that:

During heating in the freeze dried state we have noted that the stability of FVIII and FIX concentrates is influenced profoundly by changes to freeze drying conditions and product formulation. Unfortunately these parameters have been omitted from publications concerning virus inactivation, making it impossible to properly interpret results and their relevance to manufacturing procedures.<sup>218</sup>

#### Pilot-scale production of Z8 and plans for clinical trials

**24.107** On 23 June 1986 the first pilot scale production of Z8 (80°C for 72 hours) was carried out at the PFC using around 200 litres of plasma.<sup>219</sup>

**24.108** At this time, efforts were also under way in relation to setting up clinical trials and planning for the introduction of new heat-treated products as they became available. On 27 June 1986 Dr Boulton wrote to Professor Cash indicating that:

I have again spoken to Christopher Ludlam who continues to assert his willingness to participate in studies of new factor VIII materials for patients, both virgin and multi-transfused.

Apparently a few weeks ago he was asking Brian McClelland if VIIIY<sup>220</sup> could be made available in the event of a ‘virgin’ haemophiliac being presented. He tells me that he would be happy to treat such patients with a product prepared by the SNBTS that has been subjected to an ‘equivalent’ heat-treatment regime.<sup>221</sup>

<sup>214</sup> Dr McIntosh – Day 61, page 55

<sup>215</sup> Dr McIntosh – Day 61, pages 56–57

<sup>216</sup> SNBTS Briefing Paper on the development of heat treatment, November 2010 [PEN.013.1309] at 1370, the SNBTS’s response to an Inquiry letter requesting certain documents [PEN.017.1662] at 1666 (question 17) and the summary of the experiments [PEN.017.1407]

<sup>217</sup> Dr Cuthbertson’s letter to Dr Lane of 9 May 1986 [SNB.007.5799]. Outline of protocol [SNB.007.5801]. See also Dr Smith – Day 60, pages 111–114.

<sup>218</sup> Cuthbertson et al, ‘Virus inactivation in plasma derivatives’, Abstract of paper presented at the XXI Congress of the International Society of Haematology and XIX Congress of the International Society of Blood Transfusion, May 1986 [SNB.008.5850] at 5851

<sup>219</sup> SNBTS notes on preparation of intermediate purity Factor VIII [PEN.017.1411] and Dr Foster – Day 56, page 136

<sup>220</sup> ‘VIIIY’ refers to the English product 8Y.

<sup>221</sup> Dr Boulton’s letter to Professor Cash of 27 June 1986 [SNB.007.5869]

**24.109** Professor Cash responded to Dr Boulton's letter on 1 July 1986, explaining that:

You may be under some misunderstanding with regard to the type of studies we require. I can best emphasise the point by stating that we have already agreed that until such times as we have a product which is to be the definitive product for at least 5 years we won't consider further the awesome task of a NANB study on virgin haemophiliacs. In the meantime we will require to consider ½ life and in vivo recovery studies (on small numbers of non-virgin patients) ....<sup>222</sup>

**24.110** On 2 July 1986, Dr Perry wrote to Dr Boulton intimating that the PFC was poised to launch another Factor VIII product, heated at 80°C for 72 hours (Z8), which, he said, 'should therefore be comparable to 8Y' and better than anything available commercially. The comment was clearly intended to respond to Dr Boulton's letter dated 27 June (paragraph 24.108). Dr Perry suggested that virgin haemophilia patients might have access to this product before the stocks of existing products were exhausted, though that had not been formally agreed.<sup>223</sup> Dr Boulton was prompted to ask about PFC's plans, and a telephone conversation ensued.

**24.111** On 4 July 1986 Dr Boulton wrote to Dr Perry enclosing notes of the projected production sequence as he understood it from the telephone conversation between them.<sup>224</sup> Dr Perry responded to Dr Boulton's letter on 7 July 1986, adjusting some of the detail recorded.<sup>225</sup> Full scale production of Z8 was expected to begin in September 1986. Half life and recovery studies on 'non virgin' haemophilia patients would be required between September and December 1986. It was planned to begin production of the PFC's high purity NYU product (which Dr Foster proposed to name 'REAL 8') in January 1987 with supply in September 1987 after stocks of Z8 had been used up. On this projection there would be no PFC product virucidally comparable to the BPL's 8Y until September 1986. Dr Perry intended to supply Z8 for 'virgin' patients from September 1986, removing the need to 'go south' for such patients. In the immediate future, until September 1986, he thought that they could probably get supplies of 8Y for special cases, and expressed the view that it would be preferable to obtain and supply English material through the PFC. At this stage production of Z8 was still seen as an interim measure with the development of a high purity Factor VIII product continuing as the eventual aim.

**24.112** On 28 July 1986 production of the second pilot scale preparation of Z8 was carried out.<sup>226</sup>

**24.113** On 30 July 1986 a meeting of a steering group, 'New FVIII Product Manufacture', took place which decided that no further 'old-style FVIII' (ie the 68°C/24 hours product) would be made for the time being and noted that a large-scale production run of the new Z8 product had been approved to take place on 4 August 1986.<sup>227</sup> The cessation of 68°C/24 hours production and the date for the first large-scale run of Z8 were both a little earlier than Dr Perry had forecast in his discussion with Dr Boulton.

---

<sup>222</sup> Professor Cash's letter to Dr Boulton of 1 July 1986 [SNB.005.1522]

<sup>223</sup> Dr Perry's letter to Dr Boulton of 2 July 1986 [SNB.007.5909]

<sup>224</sup> Dr Boulton's letter to Dr Perry of 4 July 1986 [SNB.007.5910] and his note of their telephone conversation [SNB.007.5911]

<sup>225</sup> Dr Perry's letter to Dr Boulton of 7 July 1986 [SNB.007.5913]

<sup>226</sup> Preparation of Improved Intermediate Purity FVIII (Z8) – Batch No: Z8-5-002 [SNB.007.9049]

<sup>227</sup> Notes of New FVIII Product Manufacture Steering Group meeting, 30 July 1986 [SNB.007.9072]

**24.114** Dr Perry said that the routine manufacture of NYFVIII (68°C/24hr) was discontinued in July 1986 to allow the the PFC to focus its development and manufacturing resources on the final development stages of Z8 with a view to building up working stocks of Z8 for distribution through the batch dedication system. At this point it was estimated that sufficient stocks of NYFVIII were available to meet planned requirements until the spring of 1987, which was therefore the estimated date for the transition from NYFVIII to Z8.<sup>228</sup>

**24.115** In his briefing paper on the development of heat treatment, Dr Foster stated that:

By July 1986, progress in the pilot studies was encouraging and there were good stocks of existing 68°/24-hour heat-treated Factor VIII concentrate available. It was therefore decided to cease production of the existing product to release production staff and facilities in order to fast track the development of Z8 at large scale. Preparation of the first production trial batch of Z8 was begun in August 1986.<sup>229</sup>

**24.116** Dr Perry explained that PFC's production strategy was based on a phased development plan involving the progressive development and introduction of heated products, without interruption of supply. The strategy required that the PFC should continue to routinely manufacture NYFVIII (68°C/24hr) until the Z8 product had been developed, validated at scale, transferred to routine production, and safe working stocks established.<sup>230</sup>

**24.117** Dr Perry further explained the rationale behind the switch to Z8 production in the summer of 1986 indicating that, 'we had a high level of confidence that we were on the right track. We had a very high level of expectation that the development would be successful within the sort of timescales that we had established'.<sup>231</sup>

**24.118** At the Inquiry hearings these comments were echoed by Dr McIntosh who said that, 'production of the previous product, NY [heated at 68°C for 24 hours], had been suspended or halted, to give us full access to production, and a decision was made to prepare material [ie Z8] at as large a scale as possible but for experimental purposes'.<sup>232</sup>

**24.119** In mid-1986, therefore, the SNBTS's priority project was the production of Z8, considered to be 'virucidally equivalent' to the BPL's 8Y, as an interim solution to the transmission of virus infection, retaining the longer term objective of developing a superior pasteurised product. It was implicit in the development process that trials would be required of successive products, at least for half-life and in vivo recovery. Apart from the difficulties inherent in the development and production of effective products, there was growing resistance from haemophilia clinicians to exposing their patients to trials without adequate insurance against adverse reactions. It is important to set Scottish experience at this time in a wider context.

---

<sup>228</sup> Dr Perry's statement on Viral Inactivation, 1985–87 [PEN.017.1219] at 1223

<sup>229</sup> SNBTS Briefing Paper on the development of heat treatment, November 2010 [PEN.013.1309] at 1353

<sup>230</sup> Dr Perry's statement on Viral Inactivation, 1985–87 [PEN.017.1219] at 1223. Dr Perry admitted during the Oral Hearing that, as the 68°C/24hr product was stopped in July 1986 when Z8 was only at the pilot scale, this statement was not completely correct – see Dr Perry – Day 58, page 44

<sup>231</sup> Dr Perry – Day 58, page 45

<sup>232</sup> Dr McIntosh – Day 61, page 57

**24.120** In June 1986, the World Hemophilia Federation Conference was held in Milan. Dr Smith attended and produced notes. A copy was available in Scotland.<sup>233</sup> Reports of the discussions of a range of products underlined doubt about their effectiveness. Armour's product Factorate, issued before January 1986, was withdrawn in July 1986. Other heat-treated products such as Travenol (60°C for 72 hours) and Cutter (68°C for 72 hours) were not withdrawn, but were gradually replaced in the period after 1 January 1987. It seems likely that this development was prompted primarily by the search for a form of viral inactivation effective against the risk of transmission of NANB Hepatitis, although general misgivings about the effectiveness against the risk of transmission of HIV of dry heat treatments at temperatures in the region of 60°C may have contributed to the development.

**24.121** Pasteurised products began to appear. Alpha Profilate was a heat-treated, wet method product, heated at 60°C for 20 hours. Armour were licensed in the USA to market Haemate P, the pasteurised heat-treated Factor VIII developed by Behringwerke. Cutter was licensed to manufacture Koate HS, a heat-treated pasteurised product. The wider, worldwide, market appeared to have been moving towards pasteurised products at this time, though further change was imminent. On 21 July 1986, Immuno distributed a circular intimating that dry-heated products had been discontinued: all products would be subject to steam treatment for the future, and that included FEIBA. This was a period of considerable uncertainty worldwide. Developments in Scotland have to be seen in that light. Retaining the option of pasteurisation while prioritising dry heat treatment was not out of line with international developments.

**24.122** As approved on 30 July (paragraph 24.113), the first large-scale production run of PFC Z8 took place on 4 August 1986.<sup>234</sup> On 7 August 1986 satisfactory viral inactivation studies were carried out comparing the effects of heating Z8 at 75°C and 80°C on model viruses.<sup>235</sup> On the same day Dr Perry wrote to Dr Boulton indicating that two batches of Z8 (the pilot-scale batches, prepared in June and July 1986)<sup>236</sup> had been successfully manufactured and noting that, 'assuming all is well on the QA front, we are well on target to make product available for clinical trial end of August/beginning of September'.<sup>237</sup> He said that discussions could start with Professor Ludlam regarding clinical trials of Z8. In the event, as noted below at paragraph 24.131, early production batches could not stand heating at 80°C and were heated at 75°C until January 1987 and released for use.<sup>238</sup> Around this time Dr Smith passed to Dr Foster a memo outlining changes to the freeze-drying regime for 8Y.<sup>239</sup>

**24.123** On 20 August 1986 a meeting of the CSA Blood Transfusion Service Sub-Committee took place at which the issue of 'compensation of volunteers' was discussed.<sup>240</sup> The minutes of the meeting noted that the National Medical Director (Professor Cash)

<sup>233</sup> Dr Smith's report on XVIII Congress of the World Federation of Hemophilia, 1986 [SNB.007.5955]. The document is contained in contemporaneous SNBTS files. It was probably provided to Dr Foster in accordance with their practice of exchanging reports of conferences: See Chapter 23, *Viral Inactivation of Blood Products for Haemophilia Therapy up to 1985*, paragraph 23.80

<sup>234</sup> Preparation of Improved Intermediate Purity FVIII (Z8) – Batch No: Z8-5-002 [SNB.007.9049]

<sup>235</sup> SNBTS report summarising data from dry-heating experiments, 15 September 1986 [PEN.017.1429] at 1433. See also the SNBTS's response to an Inquiry letter requesting certain documents [PEN.017.1662] at 1667 (question 23).

<sup>236</sup> For confirmation that the batches in question were pilot-scale batches see Dr Foster – Day 56, page 138

<sup>237</sup> Dr Perry's letter to Dr Boulton of 7 August 1986 [SNB.007.6048]

<sup>238</sup> Dr Foster – Day 56, page 159

<sup>239</sup> [PEN.017.1426]. See also the SNBTS's response to an Inquiry letter requesting certain documents [PEN.017.1662] at 1667 (question 22).

<sup>240</sup> Minutes of CSA Blood Transfusion Service Sub-Committee, 20 August 1986 [SGH.002.0455] at 0456

had had ‘a useful dialogue with the Legal Adviser concerning arrangements for the compensation of volunteers and agreed that the General Manager [of the CSA] should now pursue the bringing forward of firm proposals’.<sup>241</sup>

**24.124** On 22 August Dr Boulton wrote to Dr Perry enquiring as to the availability of the Z8 product and wondering how to approach Professor Ludlam to conduct in vivo half-life and survival studies.<sup>242</sup>

### An eleventh-hour problem

**24.125** Dr Perry responded to Dr Boulton’s letter on 29 August 1986, explaining that:

While we now have material which can be used for trial (beginning September) in Dr Ludlam’s patients, I am not, at this stage, convinced that it has a proper GMP [Good Manufacturing Practice] pedigree or that it represents our definitive process. We have recently encountered an eleventh hour problem with freeze-drying which we are now addressing with some considerable urgency. The result of this is that we will not be able to meet the target dates of early September for clinical trials.<sup>243</sup>

**24.126** In his briefing paper Dr Foster explained that the ‘eleventh hour problem’ resulted from the switch from pilot-scale production to full-scale production. While only a small number of vials of Z8 had been produced in each pilot batch, the number of vials produced by full-scale production completely filled the freeze-dryer. That affected the conditions in the freeze-dryer with the result that a significant number of vials failed to withstand 80°C dry heating.<sup>244</sup>

**24.127** It was observed that vials with frozen plugs of a uniform, fine crystal structure could withstand dry heating to 80°C, whereas those with larger crystals or a mixture of fine and large crystals did not withstand heating to that temperature.<sup>245</sup> Dr Foster explained that as differences in crystal structure are determined by the rate of freezing it was postulated that the uniform formation of fine crystals in the vials which had survived heating might be the result of ‘super-cooling’, a condition at which the vial contents remain liquid below the freezing point of the solution. In this situation a small disturbance in the fluid is sufficient to cause instantaneous crystal formation resulting in fine crystals.<sup>246</sup>

**24.128** On 25 September 1986 Dr McIntosh carried out further experiments using a production-scale dryer in order to investigate the super-cooling hypothesis, following which he concluded that super-cooling had, indeed, occurred.<sup>247</sup> Efforts then followed to develop a freeze-drying cycle which, in the words of Dr McIntosh, ‘would induce supercooling ... in a reproducible way and in a uniform way across the batch’.<sup>248</sup> This was reported in a meeting of the PFC Development Review Group of 15 October 1986 where

<sup>241</sup> Ibid [SGH.002.0455] at 0456

<sup>242</sup> Dr Boulton’s letter to Dr Perry of 22 August 1986 [SNB.007.6078]. For a description of half-life and recovery studies see Professor Ludlam – Day 58, pages 118–121

<sup>243</sup> Dr Perry’s letter to Dr Boulton of 29 August 1986 [SNB.007.6080]

<sup>244</sup> SNBTS Briefing Paper on the development of heat treatment, November 2010 [PEN.013.1309] at 1353–5 and Dr Foster – Day 56, pages 138–146

<sup>245</sup> SNBTS Briefing Paper on the development of heat treatment, November 2010 [PEN.013.1309] at 1353–55 (includes photographs illustrating this at 1354). For confirmation of this point, and the experiments carried out, see also the notes of the Z8 Meeting held on 26 September 1986 [SNB.007.9092] and [SNB.007.9094] and Dr McIntosh – Day 61, pages 61–62

<sup>246</sup> SNBTS Briefing Paper on the development of heat treatment, November 2010 [PEN.013.1309] at 1354

<sup>247</sup> SNBTS Briefing Paper on the development of heat treatment, November 2010 [PEN.013.1309] at 1354; Dr McIntosh – Day 61, pages 61–62; and Dr Foster – Day 56, page 141. For the notes of these experiments see [PEN.017.1434].

<sup>248</sup> Dr McIntosh – Day 61, page 61

it was noted that the Z8 process 'requires further developments in formulation and freeze drying to enable heating at 80°C/72hr to be achieved reproducibly'.<sup>249</sup>

**24.129** On 14 October 1986 a further meeting of the SNBTS Coagulation Factor Study Group took place. The minutes of the meeting included an update on Z8 and a summary of steps taken in respect of its 'Introduction to Routine Production'.<sup>250</sup> The summary explained that heating to 80°C/72 hours of various lots of Factor VIII in a full-scale, large-production dryer had resulted in losses of Factor VIII activity ranging from 30% to 70%. It was noted that:

Failure at full scale production was due to varying performance of the freeze drier and a change in product composition .... In an effort to overcome these problems work was continuing in the following areas:

1. Modifications to procedure to improve extraction.
2. Establishment of freeze drying parameters to cope with 'worst case scenario.'
3. Reduction of weight of cryo/L plasma to 1984 levels.<sup>251</sup>

**24.130** Dr Foster reviewed the Z8 studies undertaken, including the efforts made to overcome the difficulties with the performance of the freeze dryer. Heating at 75°C for 72 hours was reported. It was thought that there were difficulties in the production and issue of a product heated to 75°C/72 hours and it was agreed that Professor Cash would write to Dr Boulton seeking the co-operation of the Haemophilia Directors in undertaking a small study of recovery and half-life of this product.<sup>252</sup>

**24.131** In the light of this meeting, Professor Cash indicated to Dr Perry in a letter dated 15 October 1986 that it was appropriate for the PFC to commence production of a 75°C/72 hours dry-heated product, while continuing to work on the development of an 80°C/72 hours product.<sup>253</sup> According to Dr McIntosh, the decision to try to release a product heated to 75°C first was due to the fact that the PFC had not yet been able to develop a product with a crystalline structure which could tolerate heating at 80°C.<sup>254</sup> Given this, the PFC was of the view that heating to 75°C (which was achievable) would be a suitable interim solution and was an improvement on the existing 68°C/24 hours dry-heated Factor VIII.<sup>255</sup>

**24.132** On 13 November 1986 Professor Cash wrote to Dr Boulton explaining the plan to commence production of 'a new factor VIII concentrate which will be called Z8' and which 'will be dry heat treated at 75°C for 72 hours'.<sup>256</sup> The letter asked Dr Boulton to 'liaise with Chris Ludlam, Charles Forbes and Elizabeth Mayne with a view to obtaining t/2 and % recovery data on the product'.<sup>257</sup> This was followed by a letter from Dr Cuthbertson to

<sup>249</sup> Notes for Development Review Group meeting, 15 October 1986 [SNB.006.7564] at 7564. According to Dr McIntosh – Day 61, page 63 – the reference to 'developments in formulation' refers primarily to increasing the 'ionic strength' (ie salt content) of Z8.

<sup>250</sup> Minutes of Coagulation Factor Study Group meeting on 14 October 1986 [SNB.007.6144] at 6147

<sup>251</sup> Minutes of Coagulation Factor Study Group meeting on 14 October 1986 [SNB.007.6144] at 6148

<sup>252</sup> Ibid at 6148

<sup>253</sup> Professor Cash's letter to Dr Perry of 15 October 1986 [SNB.006.0335]

<sup>254</sup> Dr McIntosh – Day 61, page 67

<sup>255</sup> Ibid

<sup>256</sup> Professor Cash's letter to Dr Boulton of 13 November 1986 [SNB.007.6241]

<sup>257</sup> Professor Cash's letter to Dr Boulton of 13 November 1986 [SNB.007.6241]. Professor Ludlam was the Haemophilia Director in Edinburgh. Dr Forbes and Dr Mayne were his counterparts in Glasgow and Belfast respectively (see: Dr Cuthbertson – Day 57, page 59).

Dr Boulton on 26 November 1986 enclosing a copy of the draft specification for Z8.<sup>258</sup> On 1 December 1986 Dr Perry noted, during a Clinical Trial Review meeting, that the 75°C/72 hours product was now available for half-life and recovery studies in Edinburgh, Glasgow and Northern Ireland and that Dr Boulton was coordinating this study.<sup>259</sup> On 1 December Dr Boulton wrote to Dr Perry, acknowledging receipt of Professor Cash's letter and the Z8 specification; and explaining that he wished to supply Professor Forbes in Glasgow directly with the product rather than following the usual course of sending the product via Law BTS.<sup>260</sup> On 12 December 1986 Dr Crawford of the Glasgow and West of Scotland Blood Transfusion Service (Law Hospital) wrote to Dr Perry expressing a degree of disquiet as regards the possible direct transfer and asking Dr Perry to contact Dr John Davidson (Glasgow Royal Infirmary, haematology laboratory)<sup>261</sup> with a note of any Z8 supplied to Professor Forbes.<sup>262</sup> Dr Perry passed on this message to Dr Boulton in a letter dated 23 December 1987 and asked Dr Boulton to contact Dr Davidson 'with a note of that material which will be issued to Charles Forbes ... when you know how much to send to Dr Forbes'.<sup>263</sup>

**24.133** According to PFC records, the first clinical grade batch of the 75°C/72 hours product was 'placed at issue' (ie certified as fit for clinical use)<sup>264</sup> on 2 December 1986,<sup>265</sup> the batch in question having been manufactured in October 1986 and then having undergone standard quality control procedures.

**24.134** Towards the end of 1986 research was continuing at the PFC into improving freeze-drying techniques. On 16 December 1986 Dr Foster wrote to Dr Smith indicating that the PFC had been involved in 'intensive work on freezing and freeze drying over the last 3 months' and that two problems had arisen when scaling up the Z8 process, namely: (i) the large production dryer performed differently to the small production and pilot dryers; and (ii) variations in final product total protein had arisen which had led to major batch-to-batch differences in solubility.<sup>266</sup> There were also substantial differences within batches when product was heated to 80°C. The letter explained that the PFC believed that they had now overcome all of these problems by means of a special freezing technique and by designing the freeze-drying cycle more carefully. The technological solution, which involved super-cooling to ensure an amorphous crystalline structure, was a so-called '2-stage freezing process'.<sup>267</sup>

**24.135** On 8 December 1986, Dr Smith sent Dr Foster, on a confidential basis, a paper on the effects of plasma conditioning on subsequent cryoprecipitation and cryoextraction.<sup>268</sup>

<sup>258</sup> Dr Cuthbertson's letter to Dr Boulton of 26 November 1986 [SNB.007.6268]

<sup>259</sup> Note of Clinical Trial Review meeting, 1 December 1986 [SGH.001.6672] at 6675

<sup>260</sup> Dr Boulton's letter to Dr Perry of 1 December 1986 [SNB.007.6270]. See also Dr Cuthbertson – Day 57, pages 60–61 for a description of the usual method of supply to Glasgow via Law BTS and Dr Perry – Day 58, pages 83–85 for further discussion as regards this letter.

<sup>261</sup> See Dr Cuthbertson – Day 57, page 67 for confirmation of John Davidson's position.

<sup>262</sup> Dr Crawford's letter to Dr Perry of 12 December 1986 [SNB.007.6298]. For discussion of this letter see Dr Perry – Day 58, page 79; and Dr Cuthbertson – Day 57, pages 66–67

<sup>263</sup> Dr Perry's letter to Dr Boulton of 23 December 1986 [SNB.007.6312]

<sup>264</sup> For more details on the meaning of 'placed at issue' see Dr Cuthbertson – Day 57, pages 62–63

<sup>265</sup> Batch issue history document [PEN.017.1437]; and Dr McIntosh – Day 61, pages 68–69 and Dr Cuthbertson – Day 57, page 62 (Drs McIntosh and Cuthbertson confirmed that PFC Factor VIII had an expiry date two years from the date of filling and that therefore the reference to a expiry date of October 1988 meant that manufacture must have been in October 1986).

<sup>266</sup> Dr Foster's letter to Dr Smith of 16 December 1986 [SNB.007.6296]

<sup>267</sup> According to Dr Foster's letter, this involved the following process, '[P]re-cool the shelf to -10°C; load the drier then leave the vials with the shelf controlled at -10°C for 1 hour (the Z8 product supercools to about -6°C within 30 minutes) ... then drop the shelf to -50°C 1 hour after loading and proceed as usual': Dr Foster's letter to Dr Smith of 16 December 1986 [SNB.007.6296] at 6297. See also SNBTS Briefing Paper on the development of heat treatment, November 2010 [PEN.013.1309] at 1354

<sup>268</sup> Dr Smith's letter to Dr Foster of 8 December 1986 [SNB.007.6275] and paper on plasma conditioning [SNB.007.6276]



He explained that the 8Y process reflected know-how not yet 'sewn up' by patent. The studies based on information from empirical observations by Scottish scientists now had a measure of analytical support and theoretical underpinning. Dr Foster said as much in a reply dated 16 December 1986.<sup>269</sup>

**24.136** By the end of December 1986 the 75°C/72 hours product was released to Dr Boulton for distribution to centres participating in the clinical trial. On 22 December Dr Perry sent a memorandum to Dr Cuthbertson headed 'Z8 for clinical trial', in which he asked Dr Cuthbertson to 'send 200 vials of the selected batch to Dr Boulton who will subsequently distribute it to participating Centres'.<sup>270</sup> Twenty units of the product were issued on 22 December 1986, and a further 180 units were released on 24 December.<sup>271</sup>

**24.137** At a meeting of the Z8 steering group on 22 December 1986 it was noted that 'all batches manufactured in 1986 will be heated at 75°C/72 hours with 20 vials from each batch being heated at 80°C/72 hours'.<sup>272</sup> At this point, the two-stage freezing process had also been used successfully to manufacture certain batches of Z8 at 80°C/72 hours. There was a partial release for clinical trial of a batch of 80°C/72 hours product, manufactured in December 1986,<sup>273</sup> in February 1987.<sup>274</sup>

### Compensation for clinical trials

**24.138** On 5 December 1986 Dr Boulton wrote to Professor Cash noting that he had received the specifications of Z8 and had discussed the situation with Professor Ludlam who 'still has some reservations'. Professor Ludlam was concerned about patients who suffered as a result of being infused with the trial material and Dr Boulton felt he would be unwilling to agree to trials without a specific commitment by the SHHD to compensate them.<sup>275</sup> This was followed by a letter from Professor Ludlam to Professor Cash on 11 December 1986 which indicated that Professor Ludlam had 'obtained ethical approval to undertake recovery and survival studies in haemophiliacs' but was 'awaiting an appropriate commitment from either the PFC, the SHHD or the DHSS concerning the question of indemnity'.<sup>276</sup> The letter also commented that Professor Ludlam had 'raised this a long time ago with the SHHD and there [had] been no response' and that there was 'great disquiet' about this issue among colleagues at other Haemophilia Centres.<sup>277</sup> On 30 December 1986 Professor Cash telephoned Dr Archibald McIntyre of the SHHD and followed this up with a letter in which he stated that he would very much appreciate a formal response from the SHHD that patients receiving coagulation factor concentrates as part of a trial would receive compensation in the same way as 'blood donors who undergo immunisation/boosting for the procurement of anti-Rh (D) immune plasma'.<sup>278</sup>

<sup>269</sup> Dr Foster's letter to Dr Smith of 16 December 1986 [SNB.007.6296]

<sup>270</sup> Dr Cuthbertson's memo to Dr Perry of 22 December 1986 [SNB.009.4073]

<sup>271</sup> Batch issue history document [PEN.017.1437] and Dr Cuthbertson – Day 57, page 64

<sup>272</sup> Notes of Z8 Steering Group meeting, 18 December 1986 [SNB.007.9130] at 9130

<sup>273</sup> Batch issue history document [PEN.017.1470]; Dr McIntosh – Day 61, page 69; Dr Cuthbertson – Day 57, page 69. The reference to an expiry date of December 1988 meant that manufacture must have been in December 1986.

<sup>274</sup> Batch issue history document [PEN.017.1470] refers to the release of 50 units of product to Edinburgh on 11 February 1987; and Dr Cuthbertson – Day 57, pages 69–70

<sup>275</sup> Dr Boulton's letter to Professor Cash of 5 December 1986 [SNB.007.6274]

<sup>276</sup> Professor Ludlam's letter to Professor Cash of 11 December 1986 [SNB.005.8711]. Professor Ludlam confirmed in his oral testimony that the term 'indemnity' was misleading and that the real issue was one of compensation for patients, not an indemnity for clinicians should a patient be harmed by a clinical trial. See Professor Ludlam – Day 58, pages 107–108

<sup>277</sup> Professor Ludlam's letter to Professor Cash of 11 December 1986 [SNB.005.8711]

<sup>278</sup> Professor Cash's letter to Dr McIntyre of 30 December 1986 [SGH.003.1919]. See also internal minute dated 30 December 1986 to Mr Murray [SGH.003.1920]. The reference to 'anti-Rh (D) immune plasma' refers to a group of 12 blood donors in Inverness whose blood was used to produce Anti-D for rhesus negative mothers in Scotland whose babies could be susceptible to Rhesus D Haemolytic Disease of the Newborn (ie Rh disease). See Professor Cash – Day 57, pages 108–109

1987

**24.139** The issue of compensation for clinical trials of Z8 continued into 1987. On 5 January Professor Ludlam wrote to Professor Cash explaining that he was ‘unwilling to test further blood products on patients’ until he received ‘written assurance that appropriate compensation will be available’.<sup>279</sup> The letter further noted that the SHHD had known of Professor Ludlam’s concerns since 1983; that ‘in such a serious matter more than verbal assurances are essential’; and that Professor Ludlam would be delighted to resume testing once he received ‘written assurance from an appropriate authority’.

**24.140** On 7 January 1987, Professor Cash sent a copy of Professor Ludlam’s letter to Dr McIntyre of the SHHD.<sup>280</sup> He also responded to Professor Ludlam directly, assuring Professor Ludlam of his ‘fullest support on this matter’, but emphasising that since existing Factor VIII (68°C/24 hours) would become exhausted ‘some time in February 1987’ it would be helpful for Professor Ludlam to respond to the following questions:

Given written (SHHD) assurance that appropriate compensation will be available to patients/relatives in the context of clinical assessment of Z8:

(a) Would you be prepared to use your best efforts to undertake recovery and t/2 life studies as quickly as possible, bearing in mind the PFC supply position?

(b) If Z8 proved to have acceptable recovery/t/2 life and there were no untoward (clinical) effects in the patients studied in (a) above would you be prepared to use Z8 immediately thereafter for routine clinical purposes?

(c) If time runs out on us (i.e. we can’t complete the Z8 in vivo recovery/t/2 studies before PFC stocks of factor VIII are exhausted) is it your intention to ask the Lothian Health Board to purchase product or would you prefer us to start up (if possible) the old intermediate (NY) factor VIII process again and thus maintain a no change position?<sup>281</sup>

**24.141** On the same date, Professor Cash wrote to the Scottish Haemophilia Centre Directors enclosing a copy of Professor Ludlam’s letter of 5 January 1987 and his response and asked them whether they were of the same view as Professor Ludlam.<sup>282</sup>

**24.142** Professor Ludlam responded to Professor Cash’s letter on 9 January 1987 explaining that given written assurance from the SHHD as regards compensation he ‘would be happy to organise immediately the appropriate infusion studies’ but that if Z8 was initially released on a ‘named patient basis’ he would require that the SHHD ‘extends its indemnity until a product licence is obtained’.<sup>283</sup> Professor Ludlam also indicated that if there was a delay in releasing Z8 before PFC stocks of Factor VIII ran out he would favour a return to ‘the old intermediate (NY) factor VIII’.<sup>284</sup>

**24.143** Meanwhile, an internal SHHD minute from Mr Alexander Murray dated 12 January 1987 explained that stocks of the existing Factor VIII product (NY) would

<sup>279</sup> Professor Ludlam’s letter to Professor Cash of 5 January 1987 [SGH.003.1911]

<sup>280</sup> Professor Cash’s letter to Dr McIntyre of 7 January 1987 [SGH.003.1907]. See also internal memo dated 7 January 1987 from Dr Forrester [SGH.003.1912] and the accompanying statement from Professor Cash [SGH.003.1913]

<sup>281</sup> Professor Cash’s letter to Professor Ludlam of 7 January 1987 [SGH.003.1980]

<sup>282</sup> Professor Cash’s letter to Scottish Haemophilia Directors of 7 January 1987 [SGH.003.1908]

<sup>283</sup> Professor Ludlam’s letter to Professor Cash of 9 January 1987 [SNF.001.3020]

<sup>284</sup> *Ibid* [SNF.001.3020]

shortly be exhausted, that a new Factor VIII product (Z8) had been developed but that the Haemophilia Directors had refused to carry out clinical trials on the new product unless suitable compensation arrangements were in place in respect of patients who suffered harm from the product.<sup>285</sup> Mr Murray explained that the DHSS faced a similar problem with the English Haemophilia Directors in respect of heat-treated Factor VIII produced by BPL. Mr Murray had alerted the Treasury (who would require to fund or agree to SHHD funding any compensation scheme) of the difficulties and to the fact that the SHHD would be making an approach to them. There then followed correspondence on the question of clinical trials between the SHHD, the DHSS and the Treasury.<sup>286</sup>

**24.144** On 13 January 1987, Drs Bruce Bennett and Audrey Dawson (Haemophilia Directors, Aberdeen Royal Infirmary) replied to Professor Cash's letter of 7 January indicating that they shared Professor Ludlam's view that the SHHD should give written assurance on compensation before the Z8 trial began.<sup>287</sup> Similarly, on 15 January 1987 Dr Heppleston phoned Professor Cash to indicate that the Haemophilia Directors in Dundee would also require SHHD assurance in respect of compensation.<sup>288</sup> Professor Ian Hann of the Royal Hospital for Sick Children (Yorkhill, Glasgow) responded to Professor Cash on 19 January 1987 noting that he agreed with Professor Ludlam that 'as usual the administrative process here has dragged on for too long' and that he believed strongly that children should not be used in the trials, 'especially as I do not know what Z8 is'.<sup>289</sup>

**24.145** Professor Ludlam's letter of 9 January appeared to have given Professor Cash some confidence as to the timeframe for the introduction of Z8 and on 13 January 1987 Professor Cash advised Professor Ludlam that:

Right now, assuming SHHD deliver the necessary assurances, we'll keep your team in reserve to test the 80°C/72 hours material which will very soon be with us. In the meantime Charles Forbes has agreed to look at the 75°C/72 hours product.

All being well we should just slip past the rocks I felt some days ago we were destined to founder on.<sup>290</sup>

**24.146** By letter dated 5 February 1987 the Treasury confirmed to the DHSS and the SHHD that it agreed that arrangements for compensation along the lines of the Association of the British Pharmaceutical Industry (ABPI) procedures could apply to clinical trials of heat-treated Factor VIII product.<sup>291</sup> Mr Murray advised Professor Cash of that by letter dated 6 February 1987.<sup>292</sup>

<sup>285</sup> Mr Murray's minute to Mr Kernohan of 12 January 1987 [SGH.003.1883]

<sup>286</sup> See DHSS letter to the Treasury dated 12 January 1987 [SGH.003.1891]; the Treasury's initial response dated 12 January 1987 [SGH.003.1890]; letter dated 14 January from SHHD to the Treasury [SGH.003.1881]; and letter dated 4 February 1987 from the Scottish Office Finance Division to the Treasury [SGH.003.1873].

<sup>287</sup> Drs Bennett and Dawson's letter to Professor Cash of 13 January 1987 [SNB.005.8713]

<sup>288</sup> Note of telephone conversation [SNF.001.3024] and Professor Cash – Day 57, page 113

<sup>289</sup> Dr Hann's letter to Professor Cash of 19 January 1987 [SNB.005.8712]

<sup>290</sup> Professor Cash's letter to Professor Ludlam of 13 January 1987 [SNF.001.3022]. In his oral evidence, Professor Cash confirmed that his reference to 'slipping past the rocks' related to fact that it appeared that the clinical evaluation and supply of Z8 would be possible before stocks of the 68°C/24 hours product ran out. See Professor Cash – Day 57, pages 111–112.

<sup>291</sup> Letter from Treasury to DHSS and SHHD, 5 February 1987 [SGH.003.1871]

<sup>292</sup> Mr Murray's letter to Professor Cash of 6 February 1987 [SGH.003.1870]

**24.147** On 11 February 1987 Professor Cash responded to Mr Murray's letter indicating that he was 'delighted with the news', but also noting that Mr Murray:

[M]ight also wish to consult with Duncan McNiven<sup>293</sup> [*sic*] as he will be aware of the particular point made by the haemophilia Directors, with regard to their perceived need for cover during the period a product is being made available for patient treatment on a named patient basis.<sup>294</sup>

**24.148** The mention of the Haemophilia Directors in Professor Cash's letter appears to relate to a meeting of the SNBTS and Haemophilia Directors which took place on 9 February 1987. According to the minutes of this meeting, Mr Duncan Macniven of the SHHD informed the meeting that:

The Department had consulted with Treasury, and ... a scheme similar to that already in force for the production of Anti-D would operate in the new factor VIII trials. Any claims would be considered by a 3 man panel and the ABPI guidelines<sup>295</sup> would apply.<sup>296</sup>

**24.149** However, it was also pointed out that, 'the new agreement would only apply to the initial trials of the new factor VIII' and not to its 'administration for therapeutic purposes'.<sup>297</sup> The minutes of the meeting also included a report from the SNBTS which noted that:

Plans are now well advanced for the introduction of a new factor VIII which is of higher purity and higher yielding. Further batches manufactured since January 1987 have been dry heated at 80°C for 72 hours to inactivate virus ... Dr Ludlam wished success to PFC's efforts to make a purer product still, and he and Dr Forbes agreed to accept the new product for trial.<sup>298</sup>

**24.150** According to Professor Ludlam's recollection, the minutes of this meeting (in particular the exclusion of compensation for therapeutic use) were not a correct record of the agreement which had been reached with the SHHD that cover would be granted from the first test infusion of a new Factor VIII product until the granting of a product licence.<sup>299</sup> In order to clarify this point, on 23 February 1987 Professor Ludlam wrote to Mr Murray querying what Mr Murray meant by 'clinical trial' and asking whether the SHHD interpreted this as meaning the period between the first test injection and the issuing of a full product licence.<sup>300</sup> On 26 February 1987 Dr Forrester minuted Mr Murray advising that:

I believe the answer to Dr Ludlam has to be that the Department is not yet in a position to follow the ABPI guidelines beyond the stage of where the injections begin to be given for treatment and not purely for reasons of testing. Furthermore, I understand that a full product licence may never be obtained from CSM, a body which is in any case not able to grant a licence at all. I told

---

<sup>293</sup> ie Duncan Macniven of the SHHD.

<sup>294</sup> Professor Cash's letter to Mr Murray of 11 February 1987 [SGH.003.1864]

<sup>295</sup> ABPI stands for the Association of the British Pharmaceutical Industries

<sup>296</sup> Minutes of meeting of SNBTS Directors and Haemophilia Directors on 9 February 1987 [SGF.001.2261] at 2261

<sup>297</sup> Ibid [SGF.001.2261] at 2262

<sup>298</sup> Ibid [SGF.001.2261] at 2262

<sup>299</sup> Appendix to Professor Ludlam's statement on Viral Inactivation, 1985–87 [PEN.017.1625] at 1637 and Professor Ludlam – Day 58, page 111

<sup>300</sup> Professor Ludlam's letter to Mr Murray of 23 February 1987 [SGH.003.1859]

Dr Ludlam informally recently of my doubts whether the full product licence procedure would ever go into action.

I understand today from Dr Perry that trials have already begun in any case.<sup>301</sup>

### Commencement of clinical trials

**24.151** Although Professor Ludlam still had queries about the precise scope of the compensation arrangements, clinical trials of Z8 were commenced in late February/early March 1987. These clinical trials, being Phase I trials, were to test the clotting and other properties of the product and could be completed in a few patients over a relatively short period. Phase II trials, which investigated whether the product was safe from the transmission of viruses, including NANB Hepatitis, would require to study use of the product by more patients over a far longer period.<sup>302</sup> It appears that it was initially intended that Phase I trials of Z8 would take place in Northern Ireland, Glasgow and Edinburgh. The Inquiry has, however, been unable to find any record of trials having taken place in Northern Ireland and there is no record of Z8 having been supplied to Northern Ireland for this purpose.<sup>303</sup> Although the evidence is not conclusive, it seems likely that clinical trials of Z8 took place in Glasgow in late February 1987. That is a reasonable inference from: (i) the Minutes of a Meeting of the Heads of Department/Section Managers of the PFC held on 17 February 1987 which refers to ‘the Glasgow Centre [having] received 75°C product for trial’;<sup>304</sup> (ii) a handwritten note dated 25 February 1987 from Dr Christopher Prowse of the Royal Infirmary of Edinburgh (RIE) to Dr Perry stating, as regards ‘the Z8-80 trial material’, that ‘I understand Glasgow have done 2 or 3 infusions successfully (from Dr Forbes). Your best contact there may be Dr Gordon Lowe’;<sup>305</sup> and (iii) a letter from Dr Perry to Professor Lowe of the Glasgow Royal Infirmary dated 30 March 1987 which appears to suggest that Professor Lowe had carried out infusions of Z8. The letter stated:

I understand that you have now infused this material into patients and that these infusions were uneventful.

I would be most grateful if you could provide me with a summary of this ‘trial’ (T½, recovery etc) so that I am in a position to release this new product for general use.<sup>306</sup>

**24.152** Dr Perry said that he was unable to find a reply to this request, the date(s) when the trial took place or the results of any trial.<sup>307</sup> The Inquiry has been unable to unearth any further details of the clinical trial of Z8 in Glasgow, including whether product for the trial was sent to Glasgow directly from the PFC or via Dr Boulton at the Edinburgh Regional Transfusion Centre.<sup>308</sup> Dr Boulton said that he was ‘unable to recall anything about the

<sup>301</sup> Dr Forrester’s minute to Mr Murray of 26 February 1987 [SGH.003.1853]

<sup>302</sup> For a discussion of the difference between Phase I and Phase II clinical trials see Professor Ludlam – Day 58, pages 118–121

<sup>303</sup> Dr Perry’s supplementary statement on Viral Inactivation, 1985–87 [PEN.017.2201] at 2202 and Dr Perry – Day 58, pages 78–82; and Appendix to Professor Ludlam’s statement on Viral Inactivation, 1985–87 [PEN.017.1625] at 1633

<sup>304</sup> Minutes of meeting of PFC Department and Section Managers, 17 February 1987 [SNB.010.3236] at 3237

<sup>305</sup> Dr Prowse’s memo to Dr Perry of 25 March 1987 [SNB.006.5619]

<sup>306</sup> Dr Perry’s letter to Dr Lowe of 30 March 1987 [PEN.017.2205]. See also Dr Perry’s supplementary statement on Viral Inactivation, 1985–87 [PEN.017.2201] at 2202

<sup>307</sup> Dr Perry’s supplementary statement on Viral Inactivation, 1985–87 [PEN.017.2201] at 2202. Dr Perry notes that given the date of his letter, ‘it seems likely ... that these trials took place after the trials which were eventually conducted by Professor Ludlam on 3<sup>rd</sup> March 1987’.

<sup>308</sup> Both Dr Cuthbertson and Dr Perry suggest that there is a possibility that Dr Boulton sent product directly to Dr Forbes. See Dr Cuthbertson – Day 57, page 67 and Dr Perry – Day 58, page 79

reported issue of any “Z8” from the Edinburgh and SE Scotland Transfusion Centre to any Scottish Haemophilia Centre’.<sup>309</sup>

**24.153** Clinical trials of Z8 took place in Edinburgh in February and March 1987. In his handwritten note dated 25 February 1987 to Dr Perry, Dr Prowse enclosed data on haemophilia patients infused with the ‘Z8-80 trial material’ and pointed out that Dr Susan Howe (RIE) could answer any queries on ‘clinical monitoring sheets’.<sup>310</sup> Dr Howe subsequently wrote to Dr Perry on 31 March 1987 enclosing the latest data on ‘haemophiliacs infused with Z8-80 trial material’ and indicated that ‘no further infusions are planned until Dr C Ludlam returns from holiday in three weeks time’, (ie at the end of April).<sup>311</sup>

### Z8 released for use

**24.154** By the end of March the issue of the precise scope of compensation for clinical trials of Z8 remained unresolved. On 12 March 1987 Professor Ludlam wrote to Dr John Forrester of the SHHD referring to the draft minutes of the SNBTS/Haemophilia Directors Meeting of 9 February 1987, reiterating his view that the compensation envisaged should apply to ‘all clinical trial infusions’ and asking Dr Forrester to clarify this matter ‘as it will be difficult to use the material therapeutically without this undertaking’.<sup>312</sup> On 25 March 1987 Dr Forrester circulated a minute within the SHHD, *Compensation Arrangements for Participants in Trials of PFC Products*.<sup>313</sup> The memorandum indicated that Dr Forrester had met Professor Ludlam on 24 March and explained that the SHHD’s position remained that participants who receive Factor VIII for ‘reasons of treatment as well as trial’ would not be covered by the compensation arrangements.

**24.155** At this point, the issue of the phasing out of the existing 68°C/24 hours product and the introduction of Z8 into the PFC’s batch dedication system came to the fore.<sup>314</sup> A report drawn up by Dr Perry for the SNBTS’s Supply and Demand meeting on 7 April 1987 noted that:

[T]here exists the need to phase out old product and phase in the new Z8. The following proposal is presented for consideration.

- (a) Batch dedication is maintained.
- (b) Residual NY and Z8 (75°/72 hrs) stocks are fed into the batch dedication system as normal.
- (c) An additional lane(s) is created at each RTC of Z8 (80°/72 hr) to make available material for special patient cohorts (eg virgins, elective surgery, mild haemophiliacs) prior to consumption of existing stocks of old material.

This will ensure equity of new product distribution whilst at the same time recognising the needs of special patient groups.<sup>315</sup>

<sup>309</sup> See [PEN.017.1825] for Dr Boulton’s response. Professor Cash was also unable to recall what occurred – see his supplementary statement [PEN.017.1874]

<sup>310</sup> Dr Prowse’s memo to Dr Perry of 25 March 1987 [SNB.006.5619]

<sup>311</sup> Dr Howe’s letter to Dr Perry of 31 March 1987 [SNB.006.5609].

<sup>312</sup> Professor Ludlam’s letter to Dr Forrester of 12 March 1987 [SGH.003.1849]

<sup>313</sup> Dr Forrester’s minute of 25 March 1987 [SGH.003.1847]

<sup>314</sup> The batch dedication system was introduced with a view to increasing patient safety. It enabled patients to be treated with product from the same manufacturing batch, thereby restricting the number of batches (and hence donors) a patient was exposed to. Professor Cash – Day 57, pages 120–123.

<sup>315</sup> Dr Perry’s report of March 1987 [SNB.004.0529]

**24.156** In other words, it was intended that there would be a phased introduction of Z8. Existing stocks of the 68°C/24 hours product (NY) would be exhausted under the PFC's standard batch dedication system before a switch to Z8 was made. It was also recognised, however, that certain patients (eg previously untreated patients) should receive Z8 at an earlier date.<sup>316</sup> Dr Perry's report noted that 'at present rates of demand it is estimated that Z8 will become available for all patients by July 1987'.<sup>317</sup>

**24.157** Around this time (April 1987), Phase I trials of Z8 had been successful and it was concluded that the product could be released for clinical use. In particular, on 10 April 1987 Professor Cash wrote to Dr Perry explaining that 'Dr Cuthbertson and I have reviewed the raw data from the Edinburgh patients and I am satisfied that PFC may now move to issue Z8 for routine clinical use'.<sup>318</sup> During the Inquiry hearings Dr Perry indicated that it was likely that Dr Boulton would have presented a report to Professor Cash on the studies and that Professor Cash, in his role as SNBTS National Medical Advisor, would have considered this report and authorised the release of Z8.<sup>319</sup> Professor Cash's letter was followed on 15 April 1987 by the release to Glasgow of 830 units of the 75°C/72 hours Z8 product for clinical use.<sup>320</sup> On 22 May 1987, 368 units of the 80°C/72 hours Z8 product were released to Glasgow.<sup>321</sup> The last issue of the existing 68°C/24 hours (NY) product was made on 13 May 1987.<sup>322</sup>

**24.158** The gradual introduction of Z8, in terms of the batch dedication scheme, followed in the period May–July 1987.

**24.159** Although reference was made to Z8 being released for 'routine' use, given that no product licence or clinical trial certificate had been issued, it appears that Z8 was prescribed to patients on the basis of the 'named patient' exemption in the Medicines Act 1968 (which applied to medicinal products 'specially prepared' for a doctor 'for administration to a particular patient').<sup>323</sup>

### Compensation arrangements extended

**24.160** The issue of compensation for trials of Z8 continued to be discussed. The minutes of a meeting of the SNBTS Directors on 10 June 1987 record that 'in Mr Murray's absence Dr Forrester explained that the SHHD had extended the Treasury Compensation Scheme to Z8' and that 'Miss Corrie and the CSA Secretary were working together on draft proposals for revision of the current compensation scheme'.<sup>324</sup> The minutes also noted that 'Dr Forrester recommended that the agency should get the ABPI guidelines extended to cover all SNBTS products for all trials involving volunteers of any product given for non-

<sup>316</sup> For more information on the phased introduction of Z8 see: Dr Perry's statement on Viral Inactivation, 1985–1987 [PEN.017.1219] at 1222–23; Dr Perry – Day 58, pages 94–95; and Professor Ludlam – Day 58, pages 128–129

<sup>317</sup> Dr Perry's report of March 1987 [SNB.004.0529]. Dr Perry clarified in his written statement that the July 1987 date was his best estimate at the time of when all product at issue would have been Z8 (ie when stocks of the existing 68°C/24 hours product would have been exhausted). See Dr Perry, Day 58, pages 94–95.

<sup>318</sup> Professor Cash's letter to Dr Perry of 10 April 1987 [PEN.017.1267]. (Dr Cash became a Professor in April 1987).

<sup>319</sup> Dr Perry – Day 58, pages 95–96

<sup>320</sup> Batch issue history document [PEN.017.1451]; Dr Cuthbertson confirmed during the Oral Hearing that this batch was released for clinical use – Day 57, page 71–72.

<sup>321</sup> Batch issue history document [PEN.017.1470]; the letter from the SNBTS to the Inquiry – [PEN.017.1662] at 1669; and Dr Foster's Briefing Paper [PEN.013.1309] at 1372. Dr Cuthbertson confirmed that, given the number of units supplied to Glasgow, the product for Glasgow was intended for clinical use and that the Edinburgh product was also available to be included in the clinical trial – see Dr Cuthbertson – Day 57, page 69.

<sup>322</sup> SNBTS Briefing Paper on the development of heat treatment, November 2010 [PEN.013.1309] at 1372

<sup>323</sup> Professor Ludlam – Day 58, pages 122–124. See also the Medicines Act 1968, sections 7, 9(1) and 31. In addition, there was an ongoing debate at the time as to whether the legal doctrine of Crown Immunity exempted the NHS and the PFC from the legal requirement to obtain manufacturers' and product licences in respect of products manufactured by them.

<sup>324</sup> Minutes of SNBTS Directors' meeting, 10 June 1987 [SGF.001.0127] at 0133

therapeutic reasons'. On 10 June 1987 Mr Murray, SHHD, wrote a letter to Mr Donald (the General Manager of the CSA) indicating that the Treasury had granted approval for a compensation scheme for Factor VIII trials in line with ABPI guidelines. The letter stated:

The Department has sought Treasury approval to appropriate arrangements for compensation in the event of injury during clinical trials of Factor VIII. We sought cover for those haemophilia patients participating in clinical trials to ascertain the quality and efficacy of new batches of Factor VIII which have been subjected to the improved heat-treatment process.

Treasury approval has now been received to a compensation scheme adhering to the guidelines recommended by the Association of the British Pharmaceutical Industries.<sup>325</sup>

**24.161** Professor Ludlam remained dissatisfied, however, that the compensation scheme was limited to use of the product during clinical trials and did not extend to its use in the period after trials had been concluded and before a product licence was obtained. On 11 June 1987 he wrote to Dr Forrester reiterating that he did not view the draft minutes of the meeting of Haemophilia/SNBTS Directors on 9 February 1987 as a correct record of the meeting and that he was of the view that Mr Macniven had given an undertaking that all infusions of Factor VIII would be covered by the compensation scheme.<sup>326</sup> Professor Ludlam also wrote to Dr Boulton on 11 June indicating that he had been led to believe that the issue of Z8 to patients had begun and expressed concern that that had taken place without 'a Product Licence from the CSM' or a 'Clinical Trials Exemption Certificate'.<sup>327</sup> Professor Ludlam's letter indicated that it was unclear 'who is responsible for any adverse side effects' and emphasised that in his view the minutes of the meeting of Haemophilia/SNBTS Directors on 9 February 1987 were incorrect and that the SHHD compensation arrangements should apply to all test infusions to assess clinical efficacy (ie Phase II trials) and not just half-life tests (ie Phase I trials).<sup>328</sup> The letter described the decision to introduce Z8 as a 'fait accompli' and Professor Ludlam indicated that he was forced 'either to accept the situation ... or to go over to the purchase of commercial factor VIII'.<sup>329</sup>

**24.162** In a letter of 25 June 1987 Professor Cash advised Professor Ludlam that he was in no doubt that the minutes of the meeting of Haemophilia/SNBTS Directors on 9 February 1987 were correct and that the SHHD's compensation scheme only included cover for half-life studies.<sup>330</sup> He also indicated that the reason for introducing Z8 was due to the shortage of the PFC's current 68°C/24 hours product, which was the result of 'the long delay in establishing the t/2 studies' and that Professor Ludlam's mention of giving patients the option of using commercial products was 'opening a Pandora's box'.<sup>331</sup> The letter closed by stating that, 'we're taking every possible step to expedite the licensing of Z8'.

**24.163** Professor Ludlam responded to Professor Cash's letter on 30 June 1987, outlining in more depth (albeit in a conciliatory manner) his concerns as regards compensation and the introduction of Z8 and stating that, 'as Z8 is under clinical trial I must reserve the right to use another product if the patient refuses to accept the trial material, but I need not

<sup>325</sup> Mr Murray's letter to Mr Donald of 10 June 1987 [SGH.003.1813]

<sup>326</sup> Professor Ludlam's letter to Dr Forrester of 11 June 1987 [SNF.001.3028]

<sup>327</sup> Professor Ludlam's letter to Dr Boulton of 11 June 1987 [SNB.001.5534]

<sup>328</sup> Ibid [SNB.001.5534]

<sup>329</sup> Ibid [SNB.001.5534]

<sup>330</sup> Professor Cash's letter to Professor Ludlam of 25 June 1987 [SGF.001.1356]

<sup>331</sup> Ibid [SGF.001.1356] at 1357



make this explicit'.<sup>332</sup> Professor Cash responded to this letter on 13 July 1987 suggesting that he and Professor Ludlam meet to discuss the various issues.<sup>333</sup>

**24.164** In the meantime, on 6 July 1987 Professor Ludlam wrote to the Medical Defence Union<sup>334</sup> and a contact (Dr Leonard) at the relevant Ethics Committee<sup>335</sup> outlining his (Professor Ludlam's) understanding that (i) the current issue of Z8 could be considered as a Phase II clinical trial to assess clinical efficacy; (ii) there was no clinical trial certificate; and (iii) that current SHHD compensation policy would not cover patients who experienced a severe reaction. Dr Leonard responded on 8 July 1986 indicating that Professor Ludlam should convey to the SHHD his misgivings about the use of Z8 when it 'has not received the appropriate ABPI cover'.<sup>336</sup>

**24.165** Shortly thereafter, the compensation arrangements were extended, as Professor Ludlam had wished, to cover the continued prescription of Z8 beyond the Phase I trial. On 8 July 1987, Professor Cash wrote to Mr Macniven noting that 'there is now a need for ... the creation of a new concept ... – compensation for products undergoing trials when the product is being given for therapeutic purposes (Type II)'.<sup>337</sup> On 9 November 1987, following further correspondence between the various parties,<sup>338</sup> Mr Macniven responded to Professor Cash explaining that the SHHD had reassessed its position and had concluded that the existing compensation arrangement should now also apply to therapeutic trials.<sup>339</sup> Professor Cash passed on Mr Macniven's news to Professor Ludlam who replied on 19 November indicating that he was 'delighted' that the SHHD had agreed to extend compensation to cover therapeutic trials of Factor VIII.<sup>340</sup> Although further discussion followed regarding the technicalities of the compensation scheme,<sup>341</sup> by November 1987 the underlying issue of compensation for the continued use of Z8 (and, indeed, other products manufactured by SNBTS) had finally been resolved.

### 1988 to 1991

#### Evidence of viral inactivation in Factor VIII concentrates heated to 80°C for 72 hours

**24.166** Although Z8, heated to 80°C for 72 hours, had been introduced from the middle of 1987 there was still work to be done in order to confirm the effectiveness of viral inactivation.

**24.167** A formal Phase II clinical trial for Z8 in 'virgin' patients was set up in 1988.<sup>342</sup> Professor Ludlam explained that the trial was:

[A] national study to monitor patients who received Z8 for the first time under the protocol laid down by the ISTH,<sup>343</sup> which was a very rigorous protocol – fortnightly blood samples for, I think, the first 16 weeks and then monthly for two months, looking at ALT levels.<sup>344</sup>

<sup>332</sup> Professor Ludlam's letter to Professor Cash of 30 June 1987 [SNB.005.8716]

<sup>333</sup> Professor Cash's letter to Professor Ludlam of 13 July 1987 [SNB.006.4605]

<sup>334</sup> Professor Ludlam's letter to the Medical Defence Union of 6 July 1987 [PEN.017.1651]

<sup>335</sup> Professor Ludlam's letter to Dr Leonard of 6 July 1987 [PEN.017.1653]

<sup>336</sup> Dr Leonard's letter to Professor Ludlam of 8 July 1987 [PEN.017.1653] at 1655

<sup>337</sup> Professor Cash's letter to Mr Macniven of 8 July 1987 [SNB.011.3839]

<sup>338</sup> For details of this correspondence see the Annex to Professor Ludlam's witness statement [PEN.017.1625] at 1643–46

<sup>339</sup> Mr Macniven's letter to Professor Cash of 9 November 1987 [SNF.001.3039]

<sup>340</sup> Professor Ludlam's letter to Professor Cash of 19 November 1987 [SNB.005.8727]

<sup>341</sup> For more information see the Annex to Professor Ludlam's witness statement [PEN.017.1625] at 1646–47

<sup>342</sup> Dr Cuthbertson – Day 57, page 84

<sup>343</sup> The International Society on Thrombosis and Haemostasis, an international blood organisation

<sup>344</sup> Professor Ludlam – Day 58, pages 130–131

**24.168** In 1989 Mrs Winkelman and others published on the method of manufacture of the BPL's 8Y Factor VIII (dry-heated at 80°C for 72 hours).<sup>345</sup> The key step in the new manufacturing process was said to be the use of heparin at temperatures above ambient to precipitate fibrinogen and fibronectin. Good results were reported.<sup>346</sup> In 1989 a paper by Pasi and others was published reporting that the BPL Factor VIII product 8Y appeared to have prevented transmission of HCV and HIV.<sup>347</sup>

**24.169** By November 1989 when Professor Ludlam provided his expert opinion to support the SNBTS's application for a product licence variation for Z8 he was able to report that:

Factor VIII Z8 has been the concentrate treatment of first choice for my patients since its introduction into routine use in 1987. This is consistent with the view of the UK Haemophilia Reference Centre Directors report ... which recognises FVIII products which have been dry heat-treated at 80°C for 72 hours as being amongst the safest available products with regards to the risk of virus transmission.<sup>348</sup>

**24.170** At this stage, publication was often some years after work was done. The paper by Mrs Winkelman and others referred to at paragraph 24.168 above, published in 1989, reflected work done three to four years earlier. Similarly, commercial products approved and marketed around 1989 were often the result of research and Phase I and II trials carried out several years earlier.

**24.171** The results of the Scottish and Northern Irish Phase II study were not published until 1993. The paper contained the following summary:

To assess the viral safety of the Scottish National Blood Transfusion Service (SNBTS) intermediate purity Factor VIII and IX concentrates, the liver function and viral status were assessed prospectively in 13 recipients. None developed hepatitis or seroconverted to HIV or HCV. This study provides additional evidence for the efficacy of dry heat treatment at 80°C for 72 h in preventing virus transmission by coagulation factor concentrates.<sup>349</sup>

### Regulatory framework for viral safety

**24.172** In the UK, the regulatory framework for ensuring viral safety was about to change. The first meeting of the Advisory Committee on the Virological Safety of Blood (the ACVSB) was held on 4 April 1989.<sup>350</sup> The ACVSB was expected to have a role in relation to regulation: the EC Directives on blood products could have a major impact on the UK. Products that had until this time been made under Crown privilege would have to be licensed. Blood would have to be harvested from donors selected according to the Directives and certain tests for virological conditions might be mandatory. It would also have regard to NANB Hepatitis, in respect of which it was recorded that the issue of

<sup>345</sup> Winkelman et al, 'Severely heated therapeutic factor VIII concentrate of high specific activity', *Vox Sanguinis*, 1989; 57:97–103 [LIT.001.0617]

<sup>346</sup> As more fully reported in 1988 by Colvin et al, Study Group of the UKHCD on Surveillance of Virus Transmission by Concentrates, 'Effect of dry heating of coagulation factor concentrates at 80°C for 72 hours on the transmission of non-A, non-B Hepatitis', *The Lancet*, 8 October 1998; 814 [LIT.001.0330]

<sup>347</sup> Pasi and Hill, 'Safety trial of heat treated Factor VIII concentrate (8Y)', *Archives of Disease in Childhood*, 1989; 64:1463–67 [LIT.001.1805]

<sup>348</sup> Professor Ludlam's Expert Report on the Clinical Documentation, received at PFC on 21 November 1989 [SNF.001.2914]

<sup>349</sup> Bennett et al, 'Study of viral safety of Scottish National Blood Transfusion Service Factor VIII/IX concentrate', *Transfusion Medicine*, 1993;3: 295–298 [LIT.001.0868].

<sup>350</sup> Minutes of first meeting of Advisory Committee on the Virological Safety of Blood, 4 April 1989 [SNF.001.1219]; Membership of ACVSB [SNB.001.9364]; Terms of Reference [SNB.001.9366]; Overview of issues for ACVSB [SNB.001.9368]

surrogate or direct testing for NANB Hepatitis was of some urgency. The activities of the ACVSB and the Advisory Committee on Transfusion-Transmitted Diseases (ACTTD) are examined elsewhere in relation to a number of topics of interest to the Inquiry and, in particular, surrogate testing and later HCV screening.

**24.173** At the second meeting of the ACVSB on 22 May 1989 the UKBTS/NIBSC Guidelines (Draft March 1989), Part 5, dealt with viral inactivation, and set out a specification for the validation of virus inactivation procedures to be used during the manufacture of clotting factor concentrates.<sup>351</sup>

#### Development of a higher purity product (S8) and clinicians' concerns about Z8

**24.174** Through this time SNBTS continued with research and development work for a high purity product, now designated S8. The 'S8 Group' met on 28 February 1989.<sup>352</sup> The date of the first full clinical trial production run was confirmed as 3 April 1989. However, a number of research and development issues remained to be resolved. A draft specification for the new product was prepared<sup>353</sup> and circulated with the notes of the S8 Group meeting held on 10 May 1989.<sup>354</sup> A forward programme was agreed.

**24.175** The report of the first meeting of the Scotland and Northern Ireland Factor VIII working party, dated April 1989, commented on the PFC's Z8 product.<sup>355</sup> It was thought that Z8 was not an optimal product. The working party strongly supported a project for a new higher purity concentrate (now designated S8), noting that development had progressed more slowly than originally anticipated. It was anticipated that the first infusions would occur in June and a formal Phase I study (of percentage recovery and half life) would take place at the premises of Drug Development (Scotland) Ltd in September. Thereafter a Phase II study would follow to demonstrate clinical efficiency. The report on viral safety of Z8 noted that there was no evidence to suggest the product would transmit HIV or NANB Hepatitis, and that there was substantial evidence to demonstrate HIV safety. There were said to be very few data positively to demonstrate NANB Hepatitis safety. However, the opinion of the group was that at that stage only heat treatment was preferable to a solvent detergent technique.

**24.176** Professor Ludlam presented the first report of the working party to a meeting of the SNBTS and Haemophilia Directors on 21 July 1989.<sup>356</sup> The new product S8 was discussed: the Haemophilia Directors expressed the hope that this product, which had the same purity as commercial products, would be available soon. Z8 had a low purity. Professor Ludlam said that there was an international movement towards high and very high purity products 'even though evidence of their value was lacking',<sup>357</sup> and that Directors were coming under pressure to use them. It was pointed out that purity did not equate with safety, and was associated with lower yield.

**24.177** The S8 group met on 10 November 1989.<sup>358</sup> It identified priority areas for action including additional plant, assay development, stabilisers and other specific matters related to the manufacturing process. Various options for development of the high purity

<sup>351</sup> Draft UKBTS/NIBSC Guidelines – viral inactivation [SNB.001.9437]

<sup>352</sup> Notes of (S)8 meeting held on 28 February 1989 [SNB.007.6846]

<sup>353</sup> Draft specification for (S)8 [SNB.007.6835]

<sup>354</sup> Note of (S)8 meeting held on 10 May 1989 [SNB.007.6833]

<sup>355</sup> First report of Scotland and Northern Ireland Factor VIII Working Party, April 1989 [SNB.001.5628]

<sup>356</sup> Note of SNBTS Directors and Haemophilia Directors meeting, 21 July 1989 [SGH.001.7491]

<sup>357</sup> Ibid [SGH.001.7491] at 7493

<sup>358</sup> Minutes of meeting held on 10 November 1989 [SNB.007.6933]

product were discussed, and in particular terminal heating (including both dry and wet heat and possibly solvent-detergent) as virucidal steps. It was agreed that there would be empirical and theoretical studies of variables. Existing and novel stabilisers were to be studied. Assays for detergents and solvents were to be set up. Work was to be done on viral inactivation of Hepatitis B (especially by wet heat treatment). A period of three years to clinical trials was thought to be a reasonable estimate of the time required. In relation to Hepatitis B, it was noted that a major area requiring discussion was how toxicology and safety should be tackled.

**24.178** On 30 November 1989, there was a 'Z8 trouble shooting' meeting.<sup>359</sup> Analysis had demonstrated increasing fibrinogen content in process cryoprecipitate resulting from coolant problems. The increase made the overall Z8 process less efficient, and led to a decline in solubility. The emerging complaint of the Haemophilia Directors about the usefulness of the product (related to its solubility) appeared to have been substantiated. Improvements were scheduled for research and development.

**24.179** In 1990 the approach to manufacture changed, with development involving collaboration with the Centre Régional de Transfusion Sanguine (CRTS), Lille, in the production of purer products. Dr Prowse of the SNBTS South East Regional Centre and Department of Transfusion Medicine reported to Professor Cash, Dr Foster and Dr Pepper on the results of heat treatment at 80°C for 72 hours of Lille concentrates, including High Purity FVIII. The appearance of the FVIII product following treatment was 'clear'. Dr Prowse concluded that it appeared that terminal heat treatment could be a valid option for 'high purity' products.<sup>360</sup>

**24.180** Dr Prowse prepared a development proposal for a virally inactivated FVIII concentrate in a paper for the SNBTS Product Development Group in April. The PFC's recurrent problems, in which he included the critical limits in terms of freeze drying for success in severe heat treatment, and advice from Dr Smith on the difficulty in achieving severe heat treatment of products under 10mg/ml, led him to conclude that the SNBTS would need to adopt established solvent detergent technology in due course. He commented:

However, recent in-house data on heat treatment of the Lille product ... suggests it may be possible to retain in excess of 70% VIII activity at a specific activity of 100u/mg. Thus we should not abandon terminal treatment, but should continue to work on this as a 'belt and braces' approach.<sup>361</sup>

**24.181** Among other proposals, and having regard to time constraints, he advocated sub-licensing an established technology such as that used by the CRTS Lille. He also proposed a collaborative effort with England and Wales.

**24.182** The need for a high purity product had been discussed by Professor Cash in a memorandum dated 22 May 1990.<sup>362</sup> In relation to viral inactivation, he thought that terminal dry heating should not lightly be abandoned but, because there was an open invitation to acquire the CRTS Lille technology, solvent detergent had to be considered seriously. By now, the vast majority of the world's fractionators had taken that route. He proposed that the PFC 'bite the bullet' and opt for the total Lille package.

---

<sup>359</sup> Notes of Z8 trouble shooting meeting, 30 November 1989 [SNB.007.6957]

<sup>360</sup> Dr Prowse's memorandum to Professor Cash and others of 2 February 1990 [SNB.007.7024]

<sup>361</sup> *Factor VIII Development Proposal*, Dr Prowse, April 1990 [SNB.007.7074]

<sup>362</sup> Professor Cash's memorandum on Factor VIII concentrates into the 1990s, dated 22 May 1990 [SNB.005.3141]

**24.183** Dr Foster and Dr McIntosh visited Lille on 9–11 July 1990 and prepared a report.<sup>363</sup> They had mixed impressions of the Lille operation. Some aspects of the plant impressed, but the general conclusion was that practice was not up to US or UK standards. The reporters thought that collaboration was required on a range of technical matters, and recommended a review of the SNBTS's strategy for development of a high purity Factor VIII.

**24.184** On 13 July 1990, it was reported that Dr Prowse was making progress in establishing a joint venture with the NIBSC on the immunosuppressive properties of Factor VIII concentrates.<sup>364</sup> This was of potential importance because there had been suggestions that, because of their lack of purity, Z8 and S8 might contain proteins which might lead to impaired immune response if administered chronically.

**24.185** Discussions with Lille continued, and regulatory requirements in France were progressed in October 1990.<sup>365</sup> On 30 October 1990, the SNBTS sent details of the PFC's methods for preparation of Factor VIII (S8) to Lille.<sup>366</sup> The CRTS had prepared documentation for licence purposes and arrangements were made for the SNBTS to have access to that documentation if it was decided to proceed with the Lille process.<sup>367</sup> This was the beginning of a new chapter in factor concentrates research and development.

**24.186** There was continuing contact with the New York Blood Centre relating to licensing of solvent/detergent technology. This was a necessary treatment step in the manufacture of the Lille product. Discussions with the New York Centre established the licensing arrangements and fees required for access to its solvent/detergent technology on 21 January 1991.<sup>368</sup>

**24.187** On 3 May 1991 a technology exchange agreement was signed between the French and the Scottish blood transfusion services to enable the SNBTS to produce a high purity Factor VIII using CRTS technology.<sup>369</sup>

**24.188** There continued to be wide-ranging research and development in Scottish laboratories in 1991 and beyond. Dr Foster wrote an interesting and typically perceptive article on the history of the Protein Fractionation Centre, tracing its final stages in particular, in 2008.<sup>370</sup> Chapter 11 of the Preliminary Report gave an account of some of that work.

**24.189** However, the developments bearing on the issues raised by the Terms of Reference had all taken place by the end of 1990 or early 1991. Transmission of infection with HIV and HCV by SNBTS products, now subject to effective terminal heat treatment, was no longer an issue and it is not appropriate to discuss at length the evolving history of the final years of PFC research, development and production of factor concentrates.

<sup>363</sup> Report of SNBTS visit to CRTS Lille, 9–11 July 1990 [SNB.007.7331]

<sup>364</sup> Professor Cash's letter to Mr McIntosh of 13 July 1990 [SNB.007.7404]

<sup>365</sup> M Goldé's letters to Professor Cash of 19 October 1990 [SNB.007.7448]; 23 October 1990 [SNB.007.7451]; and 23 October 1990 [SNB.007.7453]

<sup>366</sup> Dr Foster's letter to Dr Burnouf-Radesovich of 30 October 1990 [SNB.007.7456]

<sup>367</sup> Professor Cash's letter to Dr Prowse of 6 November 1990 [SNB.007.7462]

<sup>368</sup> Ms Watklevicz's letter to Dr Prowse of 21 January 1990 [SNB.005.8490]

<sup>369</sup> Scottish Office Press Notice, 2 May 1991 [SGH.004.2591]

<sup>370</sup> SNBTS, *Blood Letter*, Spring 2008, pages 21–23 [PEN.017.2468]

## Discussion

### *Should Z8 have been developed earlier?*

**21.190** As discussed above, in England 8Y (dry heat-treated at 80°C for 72 hours) was issued for general release to Regional Transfusion Centres in September 1985. The equivalent PFC product, Z8, was available for general use from April 1987. The question arises whether the PFC ought to have developed a Factor VIII product that did not transmit NANB Hepatitis/HCV earlier. That question involves a consideration of:

- (a) The initial priority given by the PFC to developing a high purity Factor VIII concentrate (NYU) that could be pasteurised.
- (b) Whether PFC ought to have taken the decision at an earlier stage to prioritise the development of an intermediate Factor VIII product that could be severely dry-heated.
- (c) Whether the product that was developed (Z8) ought to have been available for clinical trials before December 1986.
- (d) Whether there was a failure to address timeously Professor Ludlam's concerns in respect of compensation for patients who suffered harm in clinical trials and, if so, whether any such failure resulted in a delay in (i) the commencement of clinical trials and (ii) the availability of Z8 for use by patients.

Each of these issues will be considered in turn.

### **(a) The initial priority given by the PFC to developing a high purity Factor VIII (NYU) and pasteurisation**

**24.191** The development of a high purity Factor VIII product that could be virally inactivated by pasteurisation had priority in the PFC's research and development programme in 1984 and 1985. At that time, the PFC remained alert to the possible introduction of other viral inactivation procedures including, in particular, dry heating. There was ample evidence before the Inquiry that a focus on the development of a high purity product at that time was reasonable given the demands of the Haemophilia Directors for a higher purity product and the initially promising results of the PFC's collaboration with Professor Johnson aimed at producing an appropriate product. Pasteurisation, rather than dry heating, was also supported by evidence available at the time that wet heating of factor concentrates might be effective in preventing transmission of NANB Hepatitis (specifically the Behringwerke work discussed elsewhere in this Report); and that dry heating (at least at 68°C, the temperature in common use at the time) was not effective in preventing the transmission of NANB Hepatitis. There was also evidence that, in the case of some products, dry heating was not effective in preventing the transmission of HIV (paragraphs 24.83 and 24.120).

**24.192** In his evidence Dr Foster explained that during 1985 his judgement was that 'in terms of the data that were available, the better data came from the pasteurisation process in terms of safety to patients',<sup>371</sup> whilst adding that:

[W]e were positioning ourselves to change if we got new information that showed that perhaps dry heat treatment, for very severe conditions, was going to be a good option. And that, if we had to ... heat at 80 or go beyond 80,

---

<sup>371</sup> Dr Foster – Day 56, pages 85–86

the higher purity product should be capable of doing that because it was much more highly purified than 8Y.<sup>372</sup>

**24.193** According to Dr Foster, the understanding, common to English and Scottish scientists, that the PFL/BPL's success in heating 8Y to 80°C was based on its higher purity confirmed that the PFC was following the correct route in focussing on a high purity product. If pasteurisation did not prove effective then severe dry heating might provide an alternative method of viral inactivation.<sup>373</sup>

**24.194** Dr Perry stated:

I think our belief ... was that pasteurisation remained the best option. And colleagues from the BPL to an extent actually agreed with that because there was some experience from the Behringwerke product that pasteurisation was likely to deliver a safe product. So we still felt that was the best option.<sup>374</sup>

**24.195** Other witnesses to the Inquiry shared this view. In particular, Professor Van Aken, who provided expert assistance to the Inquiry, was of the view that at the start of 1985 it was reasonable — given the needs of the market — for the PFC to dry heat-treat their existing intermediate purity NY product (at 68°C for 24 hours) to deal with the immediate threat of HIV while having the long-term aim of applying pasteurisation to a high purity product.<sup>375</sup>

**24.196** Dr Smith of the PFL/BPL gave evidence stating that 'my correspondence etc., shows that, even for someone identified closely with 8Y, pasteurisation seemed likelier than dry heating to defeat NANBH, at least through 1986 ...'.<sup>376</sup> He was of the view, during the whole of 1985, that pasteurisation would have been 'the better horse to back' if the aim was to inactivate NANB Hepatitis.<sup>377</sup>

**24.197** The evidence on the prioritisation of pasteurisation is accepted as reliable, and persuasive of the appropriateness of the course adopted by the SNBTS. There is independent objective support for the pasteurisation option in the evidence, noted in paragraph 21.121, that from about 1986 some commercial pharmaceutical companies were beginning to market pasteurised products. The research and development priorities of the SNBTS were consistent with wider industry practice in those cases, in which the pasteurisation process must have been developed over the material period.

**(b) Whether PFC ought to have decided earlier to develop an intermediate Factor VIII product that could be severely dry-heated**

**24.198** The initial understanding that the PFL/BPL's success in developing 8Y in England in 1984 and 1985 depended on the high purity of the product (which distinguished it from the PFC's existing intermediate purity NY Factor VIII product) changed after Dr McIntosh's discovery in October 1985 that the freeze-drying process appeared to be more important than purity in the product's ability to withstand severe dry heating. Dr Foster wrote at the time that the importance of the freeze-drying step to the product's subsequent ability to withstand heating was 'not entirely unexpected', given the interaction of all of the steps

<sup>372</sup> Dr Foster – Day 56, page 86

<sup>373</sup> Dr Foster – Day 56, page 85

<sup>374</sup> Dr Perry – Day 58, page 54

<sup>375</sup> Professor Van Aken – Day 62, pages 31–32

<sup>376</sup> Dr Smith's statement on Viral Inactivation, 1985–87 [PEN.017.1130] at 1140

<sup>377</sup> Dr Smith – Day 60, page 92

in the production process. However, this had the quality of hindsight (paragraph 24.76), inevitable in a review of what had been discovered. There was no evidence available to the Inquiry to support a view that, prior to Dr McIntosh's discovery, the PFC ought to have considered that severe dry heat treatment of an intermediate purity Factor VIII concentrate was a realistic possibility, or that the priority given to developing a high purity Factor VIII product should be reassessed. The available evidence was to the contrary effect.

**24.199** Dr Perry explained to the Inquiry that the key information which triggered the change of direction at the PFC was, 'the experiments conducted by Dr McIntosh and the realisation that ... you could heat a relatively low purity product at 80 degrees for 72 hours'. He said that information was not available to the PFC before Dr McIntosh's discovery. Their belief prior to that was that 'pasteurisation remained the best option'.<sup>378</sup>

**24.200** In his written evidence Professor Van Aken stated:

In retrospect it may be asked if PFC should have changed its policy at an earlier stage, i.e. before December 1985. In my opinion, which is shared by Dr Smith, PFC had good arguments to pursue the wet heating of factor VIII concentrate as it was doing. Before December 1985 it was uncertain if the BPL product would be safer than the SNBTS/PFC product.<sup>379</sup>

**24.201** Dr Smith's evidence, as noted above, to the effect that even for someone identified closely with 8Y, 'pasteurisation seemed likelier than dry heating to defeat NANBH, at least through 1986'.<sup>380</sup> and that, during the whole of 1985, his view was that pasteurisation would have been 'the better horse to back' if the aim was to inactivate NANB Hepatitis, is material.<sup>381</sup>

**24.202** The novelty of a discovery is not necessarily undermined by analysis after the event that suggests that the discovery could have been anticipated. The evidence that Dr McIntosh's findings, which were at the time unexpected, changed the course of events is accepted. So far as the evidence available to the Inquiry shows, until October 1985 there was no experimental or other scientific data that should have prompted the SNBTS and the PFC to change direction in their dry heating research programme.

**(c) Whether the product that was developed (Z8) ought to have been available for clinical trials before December 1986**

**24.203** In developing the Z8 process, SNBTS scientists were able to draw on elements of the NYU process developed in conjunction with Professor Johnson of New York.<sup>382</sup> Witnesses from the SNBTS and the PFC indicated that certain elements from that programme played a key role in the subsequent development of the Z8 process. Dr McIntosh, for example, was of the opinion that:

[T]he experience and expertise gained during the development of a number of the processing steps in the NYU project (e.g. cryo-precipitate processing, formulation, freeze-drying) were directly transferrable to the Z8 process.<sup>383</sup>

<sup>378</sup> Dr Perry – Day 58, page 54

<sup>379</sup> Professor Van Aken's statement on Viral Inactivation, 1985–1987 [PEN.017.1597] at 1602

<sup>380</sup> Dr Smith's statement on Viral Inactivation, 1985–87 [PEN.017.1130] at 1140

<sup>381</sup> Dr Smith – Day 60, page 92

<sup>382</sup> Dr McIntosh's statement on Viral Inactivation, 1985–87 [PEN.017.1234] at 1238; Dr Cuthbertson's statement on Viral Inactivation, 1985–87 [PEN.017.1200] at 1203; Dr Perry's statement on Viral Inactivation, 1985–87 [PEN.017.1219] at 1225; and Dr Foster's statement on Heat Treatment, 1985–1987 [PEN.017.1556] at 1564

<sup>383</sup> Dr McIntosh's statement on Viral Inactivation, 1985–87 [PEN.017.1234] at 1238



Nevertheless, the evidence suggested that considerable research and development work was required.

**24.204** Although Dr McIntosh discovered in October 1985 that vials of the PFC intermediate purity product withstood dry heat treatment at 80°C, various witnesses commented that this was a very preliminary finding in a laboratory setting and that a significant amount of further research and technological development was needed before a product so heated could be manufactured on a large scale.<sup>384</sup> Dr Foster, for example, explained that the production of Z8 ‘required a new manufacturing process to be established from the recovery of cryoprecipitate onwards’.<sup>385</sup>

**24.205** Dr Cuthbertson set out in detail the steps required to introduce a new product:

The development of a new product is a very detailed process and a large number of steps must be carried out in a meticulous manner in order to ensure that the final product meets the basic pharmaceutical requirements of safety, quality and efficacy. Nowadays it is believed that the development of a new process from development, through clinical trialling to final licensing and routine issue will take of the order of 5 years. In those days, the regulatory requirements were not so rigorous, but even so, implementation of a new process required significant periods of time to include the following steps

- Development of process at R+D scale
- Understanding of safety issues (including virus inactivation studies)
- Clinical evaluation, to include
  - Freedom from adverse reactions, including use in repeat infusions
  - Acceptable recovery of clotting factor in circulating plasma
  - Development of product at pilot scale
  - Acceptable recovery in the circulation and in vivo half life
- Process scale up
- Development of effective quality control (test) and quality assurance procedures
- Demonstration that process can be adopted routinely with acceptable reproducibility (there is no point in producing a product with poor yield or poor reproducibility)
- Production of enough material at manufacturing scale, whilst ensuring that existing product is still available.<sup>386</sup>

**24.206** Professor Van Aken had a similar view of the need for various steps to be taken to progress from laboratory scale to pilot scale and subsequently full production scale, concluding that, ‘in my opinion it is quite an achievement to successfully complete all this within one year (in fact between June and December 1986)’.<sup>387</sup>

<sup>384</sup> Dr McIntosh’s statement on Viral Inactivation, 1985–87 [PEN.017.1234] at 1235–36; Dr Cuthbertson’s statement on Viral Inactivation, 1985–1987 [PEN.017.1200] at 1202; Professor Van Aken’s statement on viral inactivation, 1985–1987 [PEN.017.1597] at 1602; Dr Perry’s written statement [PEN.017.1219] at 1223; and Dr Foster’s statement on Heat Treatment, 1985–1987 [PEN.017.1556] at 1561

<sup>385</sup> Dr Foster’s statement on Heat Treatment, 1985–1987 [PEN.017.1556] at 1563

<sup>386</sup> Dr Cuthbertson’s statement on Viral Inactivation, 1985–1987 [PEN.017.1200] at 1202. For the timing of certain of these phases see Dr Foster’s statement on Heat Treatment, 1985–1987 [PEN.017.1556] at 1561

<sup>387</sup> Professor Van Aken’s statement on viral inactivation, 1985–1987 [PEN.017.1597] at 1602

**24.207** In addition, and perhaps unsurprisingly, when developing and scaling up a new product and manufacturing process, unexpected technical problems arose that required to be overcome. Dr Foster<sup>388</sup> and Dr McIntosh<sup>389</sup> explained that a number of unexpected technical/management issues occurred during the development and production of Z8 which delayed its introduction. In addition to the ‘eleventh hour’ freeze-drying problems in August 1986 discussed above, there were also problems sourcing suitable ultra-filtration pumps which would operate at a larger scale without damaging the Factor VIII<sup>390</sup> and there was a need to revise the Z8 production process so that it could be performed without having to alter existing PFC staffing arrangements, and hence PFC employees’ terms and conditions of employment.

**24.208** The evidence that the time taken between a decision in late 1985/early 1986 to prioritise the development of Z8 and the development, production and availability of that product for clinical trials by the end of 1986 was not unreasonable is accepted. The evidence went further, to the effect that the timescale achieved was remarkably quick, in particular when judged against modern practices and timescales for the development of new pharmaceutical products. That evidence is also accepted.

**(d) Whether there was a failure to address timeously Professor Ludlam’s concerns in respect of compensation for patients who suffered harm in clinical trials and, if so, whether any such failure resulted in a delay in (i) the commencement of clinical trials and (ii) the availability of Z8 for use by patients**

**24.209** The question of compensation for patients who suffered an adverse reaction to clinical trials of PFC products was first raised by Professor Ludlam with the SHHD in late 1983 and, despite his best efforts, remained unresolved by late 1986, when Z8 became available for clinical trial. In particular, Professor Ludlam raised the issue of compensation at a meeting of the Haemophilia and Blood Transfusion Working Group on 14 November 1983 (at which Dr Bell of the SHHD was present);<sup>391</sup> at the meetings of the SNBTS and Haemophilia Directors on 2 February 1984 and 7 March 1985 (at which Drs Bell and McIntyre were present);<sup>392</sup> in his letter dated 19 March 1985 to Dr Boulton;<sup>393</sup> and in his letter dated 4 April 1985 to Professor Cash.<sup>394</sup>

**24.210** When Z8 became available for clinical trials in December 1986, Professor Ludlam, with the support of the other Haemophilia Directors, refused to undertake trials of the product unless satisfactory compensation arrangements were in place for patients suffering damage as a consequence of infusion of the new product. In oral evidence to the Inquiry Professor Ludlam explained:

I had one of two options. One was to roll over and say, ‘There shouldn’t be compensation arrangements,’ and get on and test the product or I should say, ‘I won’t test it’. I’m there as a patient’s advocate in this instance and it seemed to me that if I didn’t draw a line at this point, there might never be

<sup>388</sup> Dr Foster’s statement on Heat Treatment, 1985–1987 [PEN.017.1556] at 1562; and SNBTS Briefing Paper on the development of heat treatment, November 2010 [PEN.013.1309] at 1351–56

<sup>389</sup> Dr McIntosh – Day 61, pages 57–65

<sup>390</sup> Dr McIntosh – Day 61, page 58

<sup>391</sup> Minutes of meeting of Haemophilia and Blood Transfusion Working Group, 14 November 1983 [SNB.001.5188] at 5189–90

<sup>392</sup> Minutes of meeting of SNBTS and Haemophilia Directors, 2 February 1984 [SNB.001.5252] at 5255 and 7 March 1985 [SNF.001.0241] at 0245. At the meeting on 7 March 1985 Professor Cash explained the difficulties the SNBTS had in attempting to resolve the problems through the CSA. Professor Ludlam was noted as requesting that some action be taken ‘urgently’.

<sup>393</sup> Professor Ludlam’s letter to Dr Boulton of 19 March 1985 [SNB.005.7320]

<sup>394</sup> Professor Ludlam’s letter to Professor Cash of 4 April 1985 [SNB.005.7332]

arrangements and there might be some terrible consequence of one of these test infusions and then one would be dependent on the CSA's goodwill. I felt it only fair to the patients that there was something a bit more explicitly available than just the hope that there would be goodwill.<sup>395</sup>

**24.211** SHHD witnesses gave evidence to the Inquiry to the effect that the reason why Professor Ludlam's concerns over compensation for clinical trials had not been resolved by late 1986 was, partly, because the SHHD considered that the issue was one on which the CSA should take the lead and, partly, because Professor Ludlam's concerns over compensation for patients became caught up with the wider, more complex, issue of compensation for trials involving healthy volunteers, specifically trials and immunisation procedures involving SNBTS staff members and blood donors.<sup>396</sup> Reliance on a CSA lead in 1986 could only have related to the consequential financial aspects of a compensation scheme. The policy question whether a scheme was appropriate was a matter for SHHD and ministers.

**24.212** Mr Murray, SHHD, agreed that, in retrospect, the time taken to deal with the question of compensation was unsatisfactory.<sup>397</sup> When asked to explain in more depth why the issue took so long to resolve, Mr Murray explained that:

[I]n reviewing the papers, not from my memory but from my reading of the documentation, there would appear to be a fragmentation of attention. And we have – we have the meetings of the regional directors and those responsible for haemophilia, we have the BTS subcommittee, we have the CSA central administration, we have Scottish Home and Health Department medical officers and then we have the administrative side of the department. The answer to your question, I think, lies in those structures.<sup>398</sup>

**24.213** In his evidence to the Inquiry, Mr Macniven (who was in post from May 1986) indicated that a key issue was lack of focus as regards the scope of the proposed compensation scheme. He stated:

[T]he way to have resolved this much more quickly was to stick to what Dr Ludlam was asking, stick to the narrow question, which, as we demonstrated in early 1987, was relatively simply for Treasury to answer .... The delay was engendered for a number of reasons but because people were uncertain about what breadth of compensation scheme we were talking about: Were we talking about a scheme that involved all clinical trials of all possible future SNBTS products? That's a larger blank cheque for Treasury to write out, or to approve us writing out, than the narrow scheme, which they were used to, as we saw earlier, in other contexts.<sup>399</sup>

**24.214** There is support in the evidence for the view that the SHHD should have taken the lead in resolving Professor Ludlam's concerns in respect of compensation, and that that could have been done relatively easily by disentangling the issue raised by Professor Ludlam from the issue of compensation of healthy volunteers and donors who were trialling different products. The introduction of any compensation scheme of wide application

---

<sup>395</sup> Professor Ludlam – Day 58, page 141–2. See also Day 58, page 107.

<sup>396</sup> Dr McClelland's paper dated 20 August 1984, *Clinical Trials – Compensation for Medicine Induced Injury* [SNF.001.3013]

<sup>397</sup> Mr Murray – Day 61, page 142

<sup>398</sup> Mr Murray – Day 61, page 143

<sup>399</sup> Mr Macniven – Day 61, page 163

raised issues of health policy and had financial implications that would, inevitably, have required the consent of the Treasury. When the SHHD finally did take responsibility for resolving Professor Ludlam's concerns (following Professor Cash's telephone conversation with Dr McIntyre on 30 December 1986), and consulted with the DHSS and the Treasury, they were able to obtain agreement on a compensation scheme by early February 1987 which, in turn, resulted in clinical trials of Z8 being carried out.

**24.215** There was ample evidence that resolving Professor Ludlam's concerns caused delay. Dr Cuthbertson was of the view that 'there is absolutely no doubt that these concerns delayed the initiation of the clinical trial of Z8. Product was released for use in the trial in December of 1986, but the trial did not commence until March 1987'.<sup>400</sup> He was not critical of Professor Ludlam and other clinicians. He considered that the compensation issues 'were legitimate concerns and that nowadays no clinical trial would be allowed to begin if such indemnity arrangements were not in place'.<sup>401</sup>

**24.216** Professor Cash shared Dr Cuthbertson's view on timing, indicating that the issue caused a delay of 'no more than 3 months'.<sup>402</sup> Professor Ludlam agreed that the issue of compensation delayed Z8's assessment in Edinburgh by about two months. He was not in a position to draw valid conclusions about consequential delay in the introduction of Z8 for clinical use.<sup>403</sup>

**24.217** A separate issue that arises on the evidence is whether delay in commencing clinical trials delayed the availability of Z8 for use by patients.

**24.218** The evidence of witnesses from the SNBTS and the PFC was that, with the exception of previously untreated patients, the delay in commencing clinical trials of Z8 probably did not result in a delay in patients receiving Z8. That was because, in accordance with the batch dedication system, patients already in receipt of NY Factor VIII concentrate (heated at 68°C for 24 hours) would in any event have continued to receive that product until existing stocks were exhausted. Stocks of the intermediate purity NY product did not become exhausted until April/May 1987, by which time Z8 was available for use and began to be prescribed to patients. Even if there had been no delay in resolving the compensation issue and clinical trials had been carried out in late 1986/early 1987, prescription of Z8 to existing patients would still not have begun until existing stocks of NY were exhausted in April/May 1987.

**24.219** Dr Perry's evidence relating to the intention to phase in Z8 to existing patients in accordance with the batch dedication is narrated in paragraph 24.114. Underpinning the arrangement was an understanding among manufacturer and users that successive new products would be introduced through the system to established patients when stocks of the previous product had been exhausted.

**24.220** Given that the batch dedication system reflected established policy, the determining factor which affected the timing of the introduction of Z8 was not when clinical trials of the product were carried out but, rather, the point at which stocks of the PFC's existing 68°C/24 hours intermediate purity NY product ran out.<sup>404</sup> Dr Perry indicated

---

<sup>400</sup> Dr Cuthbertson's statement on Viral Inactivation, 1985–87 [PEN.017.1200] at 1203

<sup>401</sup> Ibid [PEN.017.1200] at 1203

<sup>402</sup> Professor Cash's statement on Viral Inactivation, 1985–87 [PEN.017.1085] at 1088

<sup>403</sup> Professor Ludlam's statement on Viral Inactivation, 1985–87 [PEN.017.1620] at 1623–24

<sup>404</sup> Dr Perry's statement on Viral Inactivation, 1985–87 [PEN.017.1219] at 1254 and his supplementary statement on Viral Inactivation, 1985–87 [PEN.017.2201] at 2203

that this point was reached in April 1987.<sup>405</sup> Therefore, according to Dr Perry, although earlier clinical trials would have relieved some of the PFC's concerns about running out of its existing product before Z8 was ready, importantly, they would not have changed the timescale for the Scotland-wide introduction of Z8.<sup>406</sup> Dr Perry's evidence was that the only patients potentially affected by delay would have been previously untreated patients who were not within the existing batch dedication system and would not have been supplied with the 68°C/24 hours product.<sup>407</sup>

**24.221** During the Oral Hearings both Professor Cash and Professor Ludlam agreed with Dr Perry's evidence that, given the batch dedication system, the key to the introduction of Z8 was exhaustion of the remaining stocks of the PFC's 68°C/24 hours product rather than when Z8 first became available for use by patients.<sup>408</sup> In the case of patients with a significant history of factor concentrate treatment (effectively more than five units) previous exposure to NANB Hepatitis/HCV was assumed. The shift to a new product did not affect their risk of acquiring infection.

**24.222** The rationale for distinguishing previously untreated patients was that they would not already have been exposed to the risk of contracting NANB Hepatitis/HCV from treatment with factor concentrate or cryoprecipitate, and therefore clearly required treatment with a safer product when it became available for use. The evidence available indicated that, but for the delay in resolving the issue of compensation, it is likely that Z8 would have been available for use by previously untreated patients some two to three months earlier than April/May 1987, that is in January/February 1987.

**24.223** Professor Ludlam gave evidence that before releasing Z8 for clinical use it would have been 'necessary to have a stock of several batches, at least enough for 1–3 months' supply<sup>409</sup> and that, in his view, any delay during this period would not have disadvantaged previously untreated patients as these could have had access to 8Y:

If there was a delay of approximately 3 months (Z8 introduced for clinical use in May rather than February 1987) untransfused patients (PUPs), who would have been at risk of non-A non-B hepatitis, could have had access to 8Y (a small stock of which had been acquired in August 1986). Thus patients, therefore, should not have been disadvantaged if there was any delay in the introduction of Z8.<sup>410</sup>

**24.224** The Inquiry is aware of one patient (patient 'Alex') who was first treated with Factor VIII concentrate in mid-January 1987.<sup>411</sup> Otherwise, the Inquiry is unaware whether any previously untreated patients contracted Hepatitis C as a result of treatment with insufficiently heat-treated Factor VIII product between January/February and April/May 1987. The total number of patients first treated between 1 September 1985 and 30 June 1987 was 29.<sup>412</sup> If there are any such patients, other than Alex, who were infected between

<sup>405</sup> Dr Perry's supplementary statement on Viral Inactivation, 1985–87 [PEN.017.2201] at 2203. Note that Dr Perry also emphasised the existence of a transition period in his oral evidence beginning in April 1987 up to around July 1987 during which both Z8 and the existing 68°C/24 hours product were in use (see Dr Perry – Day 58, pages 93–94).

<sup>406</sup> Dr Perry – Day 58, page 90

<sup>407</sup> Ibid

<sup>408</sup> Professor Cash – Day 57, page 123 and Professor Ludlam – Day 58, page 129

<sup>409</sup> Professor Ludlam's statement on Viral Inactivation, 1985–87 [PEN.017.1620] at 1623

<sup>410</sup> Ibid [PEN.017.1620] at 1624

<sup>411</sup> See Chapter 6, *An Examination of the Effects of Infection With Hepatitis C on the Patients and Their Families, Including Treatment*, witness Alex.

<sup>412</sup> See Chapter 22, *Haemophilia Therapy – Use of Blood Products 1985–1987*

about January and April 1987, their number is likely to be very small. It is, however, a matter of considerable regret that any patient was or may have been infected in this period.

**24.225** Professor Ludlam's evidence about availability of BPL 8Y for treatment of PUPs is accepted so far as Edinburgh and south east Scotland patients are concerned. As discussed in Chapter 22, *Haemophilia Therapy – Use of Blood Products 1985–1987*, the Inquiry failed to uncover any evidence suggesting that the availability of 8Y was known to other Haemophilia Directors, or that there were in place appropriate protocols for application to the BPL for release of 8Y for what (at the time) would have been part of an extended clinical trial programme.

***Should the PFC have copied the English 8Y process?***

**24.226** The question arises as to why the PFC did not seek simply to copy the BPL's manufacturing processes for 8Y after the decision was taken in Scotland in late 1985/early 1986 to switch from developing a high purity, pasteurised, product to developing a Factor VIII product that could be severely dry heat-treated. The evidence received by the Inquiry, however, indicated that there were practical reasons why that was not a realistic option and that, if it had been adopted, it is unlikely to have led to the more rapid introduction of a Hepatitis C-safe Factor VIII product in Scotland.

**24.227** Dr Foster explained that in 1986:

The option of directly transferring the methods and technologies used by BPL was not chosen because a number of uncertainties remained, in particular:

- use by BPL of a chemical (heparin) at a concentration which interfered with the routine method used by SNBTS for measuring factor VIII activity,
- uncertainty over the practicality and time required to replace the SNBTS method of measuring factor VIII activity with the method used by BPL,
- uncertainty over the omission of aluminium hydroxide adsorption in the BPL process and the possibility that minor process variations might result in instability to factor VIII,
- difficulties previously experienced by the SNBTS in the use of precipitation/centrifugation to recover purified factor VIII from dilute solutions,
- the need to purchase, install and become familiar with large-scale size exclusion chromatography in factor VIII processing.<sup>413</sup>

**24.228** None of these were trivial matters. When examined on these issues during the Inquiry hearings, Dr Foster explained that the problems outlined above were largely technical in nature and that PFC's judgment was that it would be quicker to use the existing PFC processes:

[T]he question we were faced with was, what could we do most quickly, or what did we think we could do most quickly. And that was the judgment that we made, that we could do it most quickly using procedures we were more familiar with and that were more compatible with our operation.<sup>414</sup>

---

<sup>413</sup> SNBTS Briefing Paper on the development of heat treatment, November 2010 [PEN.013.1309] at 1351–52

<sup>414</sup> Dr Foster – Day 56, page 127

**24.229** Dr Foster also pointed out that copying the 8Y process would have involved purchasing expensive new equipment, some of which might have had to have been specially designed and which would have required additional requests for funding.<sup>415</sup> According to Dr Foster these issues could have led to delays.<sup>416</sup>

**24.230** A similar point was made by Dr McIntosh, who explained that there were at least eight technical differences between the 8Y and Z8 processes which the PFC would have had to have overcome in order to replicate 8Y, namely:

- Adjustments to cryoprecipitate processing involving the purchasing of different thawing vessels (the 8Y process used simple batch thawing, whereas the PFC used a continuous thin film thawing technique developed by Dr Foster).
- The purchasing of Sharples centrifuges to match those used in England.
- The reconfiguring of the PFC's coolant supply so as to function with the Sharples centrifuges.
- A change to the PFC's assay method so as to deal with the large concentration of heparin involved in the 8Y process.
- The purchasing and commissioning of chromatography columns to replace the PFC's existing ultrafiltration technology.
- The purchasing of new testing equipment to deal with the fact that 8Y was stoppered when in a vacuum.
- The need to add an additional unit operation step, which would have been difficult to fit into the PFC's existing processing time.
- Potential issues as regards the low yield of 8Y, which could have caused difficulties as regards the Scottish policy of self-sufficiency.<sup>417</sup>

**24.231** Dr McIntosh concluded that it would not have been straightforward to copy all the procedures used to manufacture 8Y. In oral evidence, he indicated that it would not have been feasible to pick and choose certain elements from the 8Y process, explaining that:

[N]either Oxford's understanding of their own process nor our understanding of what the key parameters were was sufficiently developed at that time in order to be able to make what would be a very sophisticated judgment to select key parameters from a process and emerge with a process design which would allow severe heat-treating at 80°C, when this was a brand new, hitherto unachieved development.<sup>418</sup>

**24.232** Dr Smith provided an overview of certain difficulties the PFC would have been confronted with in attempting to copy the English 8Y process.<sup>419</sup> These largely mirror those highlighted by Drs Foster and McIntosh and included:

- The fact that the high residual concentration of heparin used in the 8Y process would invalidate the PFC's Factor VIII assay.

---

<sup>415</sup> Dr Foster – Day 56, page 128

<sup>416</sup> Dr Foster – Day 56, page 128

<sup>417</sup> Dr McIntosh – Day 61, pages 71–78

<sup>418</sup> Dr McIntosh – Day 61, page 81

<sup>419</sup> Dr Smith's statement on Viral Inactivation 1985–87 [PEN.017.1130] at 1139

- The fact that there was likely to be an inherent problem of trying to mimic the 8Y methodology and equipment. There would be a risk in any attempt at duplication of the 8Y methodology that it would fail to identify important variables hidden within the existing process and would therefore be unsuccessful.
- The fact that the full scale 8Y process required at least two shifts of skilled operatives, whereas the PFC did not operate shift-working.
- The use of different centrifugation technology.
- The need for the PFC to change to gel filtration from ultrafiltration.
- The relatively low yield of 8Y, which according to Dr Smith was no more than 200 IU/kg.

**24.233** Dr Smith discussed these technical difficulties during the Inquiry hearings,<sup>420</sup> and also explained in more depth the technical reasons why the heparin used in the 8Y process would have interfered with the PFC's existing Factor VIII assay.<sup>421</sup> Dr Smith's general view was that there were very valid scientific, technical and management grounds for not trying to copy the process and that it is only with hindsight that 8Y can be regarded as providing a Hepatitis-safe Factor VIII — or as Dr Smith put it in his written evidence:

It was never a case of, 'Jim Smith has finally smuggled out the recipe for a hepatitis-free F.VIII. Stop everything you have been doing for three years, we start on Tuesday'.<sup>422</sup>

**24.234** Professor Van Aken was asked whether it was reasonable for the PFC to decide to develop its own process in December 1985 rather than simply copying the 8Y manufacturing process and, in his response, stressed that there were technical obstacles which the PFC would have needed to overcome.<sup>423</sup> In addition, he emphasised, in line with other witnesses, that any decision to follow the 8Y process would have had to have been an 'all or nothing' decision, encompassing all aspects of the process. According to Professor Van Aken:

You cannot say, 'I'll just take this step and the rest I will continue', as you used to do so. You have to do it all or not to do. That is usually the experience, that you cannot, without getting into all sorts of surprises, just say, 'Well, I'll use this element and this element, and the rest I'll leave as it is'.<sup>424</sup>

**24.235** Overall, the evidence before the Inquiry was to the effect that it was reasonable for the PFC to decide not to attempt to copy the English 8Y process but, rather, to seek to develop their own Factor VIII product that could be severely dry-heated, using their own manufacturing processes and plant and building on their existing research work. That evidence is accepted.

---

<sup>420</sup> Dr Smith – Day 60, pages 84–96

<sup>421</sup> BPL/PFL used a so-called 'two-stage' assay whereas PFC used a 'one-stage' assay. The increased sensitivity of the two-stage assay meant, in practice, that heparin was less likely to interfere with the result. For more details see Dr Smith – Day 59, pages 97–109 and also Dr Foster – Day 56, pages 15–18

<sup>422</sup> Dr Smith's statement on Viral Inactivation 1985–87 [PEN.017.1130] at 1140

<sup>423</sup> Professor Van Aken – Day 62, pages 35–37

<sup>424</sup> Professor Van Aken – Day 62, page 38



*Liaison between fractionators in Scotland and England*

**24.236** Communication between the PFC and the PFL/BPL was from time to time inhibited by confidentiality agreements with third parties or by the need to avoid disclosure of patentable inventions. Otherwise, the evidence available to the Inquiry was uniformly to the effect that liaison between the organisations, although mainly conducted informally, was effective in ensuring that researchers in Scotland were aware of significant developments in England and that the sharing of information between fractionators in each facility did not lead to any delay in the development and production of a Hepatitis C-safe Factor VIII product in Scotland.

**24.237** As regards awareness in Scotland of the development of 8Y, for example, Dr Foster explained in his written evidence that he first became aware of the work by the PFL in May 1984 when a letter from Dr Smith alerted him to ‘an intriguing alternative to zinc [precipitation]’<sup>425</sup> (ie the heparin discovery outlined above) and that by late November 1984 he was generally aware of the procedures used in the preparation of 8Y, most probably as a result of informal discussions between Dr McIntosh (PFC) and Mrs Winkelman (PFL) which were communicated to him.<sup>426</sup> Dr Foster’s witness statement also indicated that he was aware at the end of 1984 that, ‘the ability of 8Y to withstand heating at 80°C for 72 hours was believed by Dr Smith and Mrs Winkelman to be due to the higher degree of purification of factor VIII that was obtained by the 8Y process’.<sup>427</sup> He also explained that Mrs Winkelman and colleagues from the PFL/BPL visited the PFC on 27 March 1985 to discuss heat treatment and that she indicated that a final decision had yet to be taken on whether to dry heat the established BPL Factor VIII (ie HL mentioned above in paragraph 24.15) at 70°C for 24 hours or 8Y at 80°C for 72 hours.<sup>428</sup> Dr Foster also explained that he received a copy of the patent application for 8Y from Dr Smith on 16 April 1985.<sup>429</sup> According to Dr Foster, it was not, however, until sometime in late summer 1985 (he did not know precisely when) that he learned that the PFL’s 8Y process had been successfully scaled-up and transferred to the BPL.<sup>430</sup>

**24.238** Dr McIntosh confirmed in his written evidence that the SNBTS/PFC were aware of the major features of the 8Y process prior to receiving a copy of the patent application for 8Y in 1985.<sup>431</sup> During the Inquiry’s hearings Dr McIntosh indicated that he thought that he would have learned of the PFL’s 8Y process in late 1984.<sup>432</sup>

**24.239** When specifically asked about the adequacy of the liaison arrangements, Dr Foster advised that, from his perspective, communications between the SNBTS and the BPL/PFL were ‘excellent’ and involved not only himself and Dr Smith, but included: Dr Pepper (SNBTS Headquarters Laboratory) with Dr Smith; Dr McIntosh (PFC R&D) with Mrs Winkelman and Mr Evans (PFL R&D scientists); Dr Cuthbertson (PFC Head of Quality) with Dr Snape (BPL Head of Quality); and Dr Perry (PFC Director) with Dr Smith and Dr Snape.<sup>433</sup>

<sup>425</sup> Dr Smith’s letter to Dr Foster of 22 May 1984 [SNB.007.4402]

<sup>426</sup> For Dr Foster’s statement and more details of when Dr Foster became aware of PFL’s research into 8Y – including the various documents communicated to the PFC. See Dr Foster’s statement on Heat Treatment, 1985–1987 [PEN.017.1556] at 1556–59 See also Dr Foster – Day 56, pages 20–21

<sup>427</sup> Dr Foster’s statement on Heat Treatment, 1985–1987 [PEN.017.1556] at 1557

<sup>428</sup> Ibid [PEN.017.1556] at 1558

<sup>429</sup> Ibid [PEN.017.1556] at 1557; Dr Smith’s letter to Dr Foster of 11 April 1985 (received at PFC on 16 April 1985) [SNB.007.5065]; Patent application dated 5 March 1985 [SNF.001.1091]

<sup>430</sup> Dr Foster’s statement on Heat Treatment, 1985–1987 [PEN.017.1556] at 1558

<sup>431</sup> Dr McIntosh’s statement on Viral Inactivation 1985–1987 [PEN.017.1234] at 1234

<sup>432</sup> Dr McIntosh – Day 61, page 15

<sup>433</sup> Dr Foster’s statement on Heat Treatment, 1985–1987 [PEN.017.1556] at 1567–68

**24.240** Drs Perry, Cuthbertson and McIntosh also considered that there were good relations, and a satisfactory exchange of information, between fractionators north and south of the border.<sup>434</sup>

**24.241** For his part, Dr Smith of the PFL/BPL indicated that while there was tension at senior (ie Director) level (at least, in the period before Dr Perry became Director at the PFC), that did not hinder fruitful co-operation between scientists or in relation to research.<sup>435</sup>

**24.242** On his reading of the available documentation, Professor Van Aken formed the view that 'there does not appear to have been a lack of shared information which might have impeded the progress of developing heat treated Factor VIII by PFC'.<sup>436</sup>

**24.243** Professor Cash initially provided written evidence to the effect that, in his view, improvements in liaison between the BPL and the PFC were desirable and that it was his belief that had the two organisations been able to pool their limited research and development resources, and perhaps some manufacturing resources, it may have made a significant difference, throughout the 1980s, to the availability of desirable plasma products in the UK.<sup>437</sup> This was explored further during the Inquiry hearings when Professor Cash was asked whether any difficulties between the directors of the BPL and the PFC adversely affected the PFC's work on coagulation factors (in particular Z8). Professor Cash agreed that he would defer to the views of Drs Foster and Cuthbertson that such difficulties did not affect their work, albeit he remained of the general view that there were advantages to more formal arrangements for the exchange of research information.<sup>438</sup>

**24.244** Dr Perry acknowledged that there was an absence of a formal management structure providing a link between the PFC and the BPL, but considered that there were many examples of 'highly productive collaboration'. In the case of Factor VIII, in his view it could perhaps be argued that the lack of formal arrangements was beneficial as it allowed the BPL and the PFC to concentrate on different research and development strategies in the period up to 1985 (ie dry heat treatment and pasteurisation respectively) rather than being forced to back one process which may or may not have been successful.<sup>439</sup>

**24.245** This evidence is accepted. There was ample circumstantial evidence illustrating the extent of cooperation, if seldom actual collaboration, between responsible officers of the two organisations in the exchange of data and of their experimental and development findings. The SNBTS was unable to disclose confidential information obtained from Professor Johnson of New York University under contract. Dr Smith and Mrs Winkelman on the one hand, and Dr Foster and his colleagues on the other were inhibited from time to time by the need to avoid prior disclosure of the inventive steps in processes that were or were intended to be subject of patent applications. The narrow scope of the exceptions is consistent with what otherwise was an open exchange of scientific and technical knowledge. It appears to be clear that this openness was not a characteristic of relationships between senior management of the organisations, but there was no evidence to suggest that there were consequential difficulties among scientists.

---

<sup>434</sup> Dr Perry's statement on Viral Inactivation, 1985–1987 [PEN.017.1219] at 1226; Dr Cuthbertson's statement on Viral Inactivation, 1985–1987 [PEN.017.1200] at 1204–05; and Dr McIntosh's statement on Viral Inactivation, 1985–1987 [PEN.017.1234] at 1239

<sup>435</sup> Dr Smith's statement on Viral Inactivation, 1985–1987 [PEN.017.1130] at 1134 and 1137

<sup>436</sup> Professor Van Aken's statement on Viral Inactivation, 1985–1987 [PEN.017.1597] at 1602

<sup>437</sup> Professor Cash's statement on Viral Inactivation, 1985–87 [PEN.017.1085] at 1089

<sup>438</sup> Professor Cash – Day 57, pages 135–136

<sup>439</sup> Dr Perry's statement on Viral Inactivation, 1985–1987 [PEN.017.1219] at 1229

***Why the PFC was able to produce severely dry heat-treated Factor IX (DEFIX) earlier than severely dry heat-treated Factor VIII (Z8)***

**24.246** The PFC released heat-treated Factor IX (HT DEFIX, dry-heated to 80°C for 72 hours) in October 1985, whereas Z8 Factor VIII (also dry-heated at 80°C for 72 hours) was not available for clinical trials until December 1986, over a year later.

**24.247** The question was not, in the event, controversial and can be dealt with briefly. Factor IX was more stable than Factor VIII and, because of its chemical composition, inherently less likely to be damaged by heating. For these reasons the heat treatment of Factor IX posed far less of a technical challenge than the heat treatment of Factor VIII.<sup>440</sup> In addition, the heating of Factor IX, unlike heating Factor VIII, did not give rise to any yield constraints.<sup>441</sup> Both the PFC and the PFL/BPL had potential problems arising from the risk of thrombogenicity in their heat-treated products. Solving these was a rather singular example of active collaboration between the two services. The SNBTS had access to the facilities necessary for dog studies to determine the risk of thrombogenicity. In the event the collaboration was successful. All technical problems were overcome relatively quickly.

**24.248** On the evidence available, the differences between the products were such that there cannot be meaningful comparison between them in terms of the course of research and development required to resolve the issues raised by heat treatment, or in terms of the time required to reach a solution. That evidence is accepted.

## **Conclusions**

### ***Development of Z8***

#### **Priority of research into pasteurisation**

**24.249** Until it was established that the processing of PFL/BPL's 8Y Factor VIII concentrate was effective to inactivate HIV and NANB Hepatitis/HCV in source plasma, there was no scientific basis for a decision to prefer dry heat treatment over pasteurisation in the manufacture of factor concentrates.

**24.250** Commercial pharmaceutical companies which had developed and marketed dry heat-treated products in the first half of the 1980s<sup>442</sup> changed to pasteurisation or solvent/detergent methods of virus inactivation in products marketed in the second half of the 1980s and early 1990s.<sup>443</sup>

**24.251** The PFC's research aimed at production of a pasteurised product effective to inactivate HIV and NANB Hepatitis/HCV was consistent with accepted industry norms, and, if it had been pursued, would have continued to be consistent with wider industry expectations related to dry heat-treated products, without exception, until early 1988.<sup>444</sup>

<sup>440</sup> Dr Foster's statement on Heat Treatment, 1985–1987 [PEN.017.1556] at 1572; Dr Cuthbertson's statement on Viral Inactivation, 1985–1987 [PEN.017.1200] at 1207; Dr McIntosh's statement on Viral Inactivation, 1985–1987 [PEN.017.1234] at 1242; Dr Perry's statement on Viral Inactivation, 1985–1987 [PEN.017.1219] at 1230

<sup>441</sup> Dr McIntosh's statement on Viral Inactivation, 1985–1987 [PEN.017.1234] at 1242

<sup>442</sup> See Appendix 1 to Chapter 23, *Viral Inactivation of Blood Products for Haemophilia Therapy up to 1985*

<sup>443</sup> Paragraph 24.4 and Tables 24.1 and 24.2 above

<sup>444</sup> The earliest third party support for 8Y found by the Inquiry is a letter dated 29 February 1988, written from the New England Medical Centre Hospitals, Boston, USA to BPL Elstree, asking BPL to apply for US FDA approval of the BPL process for 8Y. The medical centre expressed the view that BPL factor 8Y was the safest concentrate available. [DHF.002.8088]

**24.252** The PFC's decision to change direction, formalised in January 1986, reflected:

- Privileged information about the development of 8Y available to the PFC as a result of informal collaboration between scientists at the PFL/BPL and the PFC respectively.
- Dr McIntosh's discovery that the experimental control sample of PFC's standard Factor VIII concentrate withstood heating at 80°C for 72 hours.
- The insight that purity was not critical to the ability of Factor VIII to withstand heating at high temperature and for prolonged periods.
- Highly innovative research that disclosed the critical role of the crystal structure of the frozen product in making it suitable for heating at high temperature.

**24.253** The random selection of a control sample that had a uniform fine crystal structure may have introduced an element of serendipity into Dr McIntosh's experiment: that is of the nature of invention.

**24.254** It is also of the nature of invention that until the factors contributing to an inventive insight come together speculation about what might have been until that point is idle. One cannot anticipate invention.

**24.255** The PFC's research into pasteurisation was fully justified, and was appropriate, having regard both to comparative industry practice and the progress achieved down to the end of 1985.

**Should the PFC have decided to develop a Factor VIII concentrate that could be severely heat-treated earlier than it did?**

**24.256** The only support for dry heat treatment of Factor VIII in the mid-1980s was the success of the PFL/BPL in developing 8Y.

**24.257** That was (erroneously, as it turned out) understood in Scotland until the end of 1985, and in England until at least the end of 1986,<sup>445</sup> to have depended on having a high purity product.

**24.258** The PFC devoted considerable time and resources in 1984 and 1985 to research and development of a high purity Factor VIII product, initially ZHT and later NYU.

**24.259** According to the perceptions of the period, high purity was a necessary preliminary step towards any form of effective heat treatment.

**24.260** ZHT was not fully developed by the end of 1985 when Dr McIntosh's discovery was made.

**24.261** In short, there is no factual basis for any suggestion that the PFC should have decided to develop a Factor VIII product that could be severely heat-treated earlier than it did.

---

<sup>445</sup> See paragraph 24.72; Dr Smith's letter to Dr Foster dated 8 December 1986 on the effects of plasma conditioning: [SNB.007.6275] and [SNB.007.6276]

**Progress towards clinical trials following the decision to develop a dry heat-treated product (Z8): research and development by SNBTS**

**24.262** The PFC applied appropriate resources in the research and development work necessary to achieve an acceptable Factor VIII product dry heat-treated to inactivate HIV and NANB Hepatitis/HCV.

**24.263** Z8 was developed and made ready for clinical trials within a reasonable time.

**24.264** Professor Van Aken's assessment of the success of the PFC as 'quite an achievement' is accepted.

**24.265** There is no basis for adverse criticism of the work of the PFC in this respect.

**Progress towards clinical trials following the decision to develop a dry heat-treated product (Z8): compensation**

**24.266** The demand by Haemophilia Directors (and Professor Ludlam in particular) for appropriate provision for compensation for individuals who agreed to undergo trials of and treatment with Z8 before licensing of the product was in the interests of patients and was reasonable.

**24.267** The demand was limited in scope and could and should have been dealt with on its own merits with reasonable expedition.

**24.268** The demand raised issues of health policy and funding which were not within the scope of CSA's delegated functions. The CSA was not equipped to deal with issues involving clinical judgement. The CSA was unlikely ever to have been an appropriate body to resolve such issues within its own budgets and competency.<sup>446</sup>

**24.269** The commitment of resources for compensation ought to have been dealt with by the SHHD from the outset in consultation with the Treasury.

**24.270** Failure to address the specific issue with reasonable expedition resulted in the delay of clinical studies and the resultant availability of Z8 for therapy for PUPs by three months.

**24.271** Because of policy decisions related to batch dedication the delay of clinical studies did not affect established patients.

**Should the PFC have copied BPL's 8Y process?**

**24.272** Manufacturing technology and process equipment employed by the PFC and the BPL respectively were not compatible in eight distinct technological areas.

**24.273** In particular, assay procedures for the monitoring of Factor VIII levels during processing, integral to manufacturing, were incompatible, with the BPL using a unique procedure that could not be accommodated by the PFC.

**24.274** Piecemeal adoption of elements from the BPL's integrated manufacturing processes was not a viable option: there was an unavoidable risk of incompatibility.

**24.275** Wholesale adoption of the BPL's 8Y process would have been problematical for the reasons given by Dr Smith: idiosyncratic variables 'hidden' within the BPL's process might not be identified with the result that the PFC could not duplicate the process effectively.

---

<sup>446</sup> See Chapter 17, *Blood and Blood Products Management*, paragraphs 17.24–17.27 and 17.50–17.57

**24.276** The previous point was validated by events. The discovery of the criticality of the crystal structure of the frozen product in vial in the course of processing, and of the importance of plasma conditioning, factors that had not been identified by the PFL/BPL, brought to light idiosyncratic features of the English process that might not have been discovered in time to avoid delay in Scotland.

**24.277** The process of specifying, purchasing and commissioning new equipment would have been time-consuming and expensive and uncertain of success.

**24.278** Modification of the PFC's existing technology was the preferable approach.

**24.279** It was not demonstrated on the evidence that the PFC should, or could, have attempted to mimic the BPL's 8Y process.

### *Summary*

- There is no basis for adverse criticism of the PFC and its scientists over the period ending with the introduction of Z8 for routine clinical use in April 1987. On the contrary, they achieved outstanding results, as evidenced by the fact that Scotland appears to have been the first country in the world that was able to supply all of its haemophilia patients with a Factor VIII product that did not transmit Hepatitis C.
- After the introduction of Z8, research and development work proceeded on new, purer, products to meet changing demands from clinicians. However, safety from transmission of virus had been achieved, and later developments, while demonstrating the SNBTS's commitment to improving quality of products, did not produce safer products.
- Administrative delays by the SHHD in dealing with the Haemophilia Directors' demands for compensation arrangements for patients adversely affected by new products prior to regulatory approval resulted in delay of about three months in trials and availability of Z8.
- However, the only adverse impact on the safety of patients was the unavailability of Z8 during that period of delay for the treatment of virgin and infrequently treated patients.

© Crown copyright 2015

An online version of the report is available at [www.penroseinquiry.org.uk](http://www.penroseinquiry.org.uk)

**ISBN: 978-0-85759-022-0 (Volume 3 of 5)**

**This Inquiry Report comprises an Executive Summary (ISBN: 978-0-85759-023-7), five volumes and a DVD**

Published on behalf of The Penrose Inquiry by APS Group Scotland, 21 Tennant Street, Edinburgh EH6 5NA  
DPPAS43828 (03/15)

THE  
PENROSE  
INQUIRY

# Final Report

**Volume 4:  
Donor Selection and Screening of Donated Blood**



THE  
PENROSE  
INQUIRY

# Final Report

**Volume 4:  
Donor Selection and Screening of Donated Blood**

Laid before the Scottish Parliament by the Scottish Ministers  
under section 26 of the Inquiries Act 2005.

March 2015  
SG/2015/15

© Crown Copyright 2015



This publication is licensed under the terms of the Open Government Licence v3.0 except where otherwise stated. To view this licence, visit [nationalarchives.gov.uk/doc/open-government-licence/version/3](https://nationalarchives.gov.uk/doc/open-government-licence/version/3) or write to the Information Policy Team, The National Archives, Kew, London TW9 4DU, or email: [psi@nationalarchives.gsi.gov.uk](mailto:psi@nationalarchives.gsi.gov.uk).

Where we have identified any third party copyright information you will need to obtain permission from the copyright holders concerned.

This publication is available at [www.penroseinquiry.org.uk](http://www.penroseinquiry.org.uk).

ISBN: 978-0-85759-022-0  
(Volume 4 of 5)

Published on behalf of The Penrose Inquiry by APS Group Scotland, 21 Tennant Street, Edinburgh EH6 5NA  
DPPAS43828 (03/15)

## CONTENTS

<b>Volume 4: Donor Selection and Screening of Donated Blood</b>		Page
25	Screening of Donated Blood for Hepatitis B	1075
26	Donor Selection – Higher Risk Donors	1105
27	Surrogate Testing of Donated Blood for non-A, non-B Hepatitis	1177
28	Donor Selection – AIDS	1281
29	The Discovery of HIV and the Development of Screening Tests	1307
30	Screening of Donated Blood for HIV	1321
31	The Introduction of Screening of Donated Blood for Hepatitis C	1383

## CHAPTER 25

### SCREENING OF DONATED BLOOD FOR HEPATITIS B

#### Introduction

**25.1** Before the discovery of the 'Australia' (or 'hepatitis-associated') antigen, later renamed the Hepatitis B surface antigen (HBsAg), there were few, if any, settled Scottish National Blood Transfusion Service (SNBTS) protocols to guide practice at donation sessions. Individual Regional Transfusion Directors (RTDs) were free to develop and apply their own policies and practices for the protection of recipients of blood, blood components and blood products from transmission of infection. In the early 1970s, the risk of transmission of viral hepatitis, so far as it was understood, was thought to be mitigated by what were regarded as increasingly sophisticated screening tests for the Hepatitis B virus (HBV) antigen and antibody and these became the main means of protecting the blood supply.

**25.2** In this chapter those tests are discussed in an attempt to understand their development and the reliance placed on them at the time. There is no clear end date for the chapter. By the autumn of 1983, attention was moving from non-A, non-B Hepatitis (NANB Hepatitis) to AIDS<sup>1</sup> and the period selected for discussion ends with the emergence of AIDS, growing awareness of the need for protocols on donor selection in that context and implementation of the first structured guidance on donor selection in Scotland. By then a view had emerged that NANB Hepatitis was not a major problem in Scotland and was generally not a serious disease. That view persisted into the late 1980s. Screening for HBV continued, with increasing sophistication, but also with increasing awareness that the results were of little relevance to NANB Hepatitis.

**25.3** Historically, the blood collection procedures followed in Scotland in the course of routine donation sessions provide a context for discussing the impact of screening technology and practice. As discussed in Chapter 18, *Collection of Blood – General*, at the beginning of the reference period those procedures were not well adapted to investigating the health or relevant social factors affecting the prospective donor's suitability to provide blood for transfusion; they relied heavily on volunteered information. In some circumstances, as in collections in prisons, there was particular concern about the reliability of the information provided. Chapter 26, *Donor Selection – Higher Risk Donors*, discusses some groups of individuals who might have been thought to be unsuitable as donors and the methods adopted to identify members of these particular groups. Apart from interview and visual inspection of prospective donors, emphasis was placed on developing scientific tests to identify blood donations that presented risk and the approach to routine collection procedures can best be understood against that background.

#### *Developing knowledge of Hepatitis B and growing awareness of other hepatitis viruses*

**25.4** The effectiveness of an approach that relied heavily on technology depended in the first place on knowledge of the risk against which the tests were directed and, secondly, on the relevance of the test results to total risk, as knowledge of the range of infective agents increased. It became increasingly clear from seminal research during and after

---

<sup>1</sup> See, in particular, Chapter 27, *Surrogate Testing of Donated Blood for non-A, non-B Hepatitis*, and the discussion of the work of the Working Party on Transfusion Transmitted Hepatitis below.

the mid-1970s that tests developed to identify the Hepatitis B antigen or antibody – the primary technology available – did not detect antigen or antibody associated with NANB Hepatitis viruses which were, by definition, different but as yet uncharacterised. The risk of transmission of NANB Hepatitis could not be managed by testing: whether the risk of transmission of those forms of infection was acceptable was thought to depend on the materiality of the risk to the patient (that is, the severity of the disease) as understood from time to time.

**25.5** Knowledge of the natural history of Hepatitis B developed during this period but was not fully understood by the end of it.<sup>2</sup> As was to happen later, following the discovery of the Hepatitis C virus (HCV), it took some years for researchers to match the markers of infection to the liver histology (appearance of liver cells under a microscope) and clinical picture presented by the patient and to the natural history of the disease. By the end of the period, it was known that the Hepatitis B virus damaged the liver cells it invaded and that, at least in the early stages of infection, it was more damaging than the postulated NANB Hepatitis virus(es). A higher proportion of acute Hepatitis B patients had overt clinical illness and jaundice. These signs and symptoms reflected the body's immune response to the virus, proportionate to the virus' attack, and usually would lead to clearance of the virus (in dead liver cells) and, if the virus was completely cleared, regeneration of the liver and restoration of normal liver architecture and function.

**25.6** The vast majority of patients with haemophilia who had overt jaundice in the late 1960s and early 1970s did have acute Hepatitis B. A proportion of these patients went on to have chronic liver disease, marked by persistently elevated transaminases,<sup>3</sup> and it was initially thought that these biometric indications were related to their Hepatitis B infection. By the early 1980s, however, it was increasingly understood that most of these patients probably were infected, or co-infected, with NANB Hepatitis. Many had cleared the Hepatitis B virus and recovered from that disease. Their continuing abnormal liver enzyme levels, indicative of liver disease, were due to NANB Hepatitis infection and, in most of those cases at least, as events were to prove, Hepatitis C infection.

**25.7** Clinically, there are similarities between the types of infection. Most chronic HBV infections, like infections with NANB Hepatitis/HCV, are insidious, with no obvious acute clinical onset. Also like NANB Hepatitis/Hepatitis C, Hepatitis B acquired in infancy is usually chronic but does not present with any symptoms until the patient is aged in the 30s or later. In each case, infection acquired in later life (over about 50 years of age), if chronic, often progresses to cirrhosis in relatively short periods compared with the 20, 30 or more years typical in younger patients. Both diseases are, however, associated with long periods of developing fibrosis (scarring of the liver) before the stage of cirrhosis is reached. Progression to cirrhosis indicates that not only is there significant fibrosis but also that the normal architecture of the liver has changed to include structurally abnormal nodules. Like NANB Hepatitis/Hepatitis C, a small proportion of carriers of Hepatitis B appear to be 'tolerant' of infection. The virus circulates, and the patients are still carriers of the infection and remain infectious to others, but it never does the 'tolerant' patient any harm.

---

<sup>2</sup> See Chapter 15, *Knowledge of Viral Hepatitis 2 – 1975 to 1985* and, in particular, the successive editions of *Diseases of the Liver and Biliary System* by Dame Sheila Sherlock referred to therein.

<sup>3</sup> Typically alanine transaminase (ALT), a protein synthesised in liver cells. Normally present in low levels in the blood, ALT becomes elevated when the liver is disordered.

**25.8** As discussed in Chapter 14, *Knowledge of Viral Hepatitis 1*, the existence of NANB Hepatitis was inferred from observation of hepatitis in patients shown by the best tests available not to have Hepatitis A, Hepatitis B, cytomegalovirus or Epstein-Barr virus infection. Although a test for Hepatitis A was reported in 1973, a screening test for practical application was not available in Scotland until 1978.<sup>4</sup> The Hepatitis B tests available developed and changed over the period are covered in this chapter. From the outset there were tests for Hepatitis B surface antigen (HBsAg) and Hepatitis B surface antibody (anti-HBs). The HBsAg tests indicated whether the patient was currently infectious and might indicate ongoing chronic Hepatitis B liver disease. The anti-HBs test indicated that the patient had been exposed to or infected by Hepatitis B. If HBsAg was absent (and occasionally the two might co-exist) then a positive test for anti-HBs indicated that the patient had previously had Hepatitis B but was now immune and, in the absence of HBsAg, was no longer infectious.

**25.9** These tests improved in sensitivity during this period and additional tests were also developed. In the 1980s, tests for the presence of antibody to Hepatitis B core antigen (anti-HBc) were developed, which added to knowledge of the state of infection in patients.<sup>5</sup> Combining the results of the additional tests with a negative HBsAg test, for example, could provide a reliable indicator of past infection and confirm the absence of current infection. Alternatively, where HBsAg had 'faded' from serum, as it might over time, the additional tests could indicate current infectivity (usually chronic) and show that the Hepatitis B virus was still present in the body, even if only in very small amounts.

**25.10** As these tests relating to Hepatitis B developed in sophistication and in sensitivity, with growing knowledge of the structure of the Hepatitis B virus well into the 1980s, appreciation of the prevalence of NANB Hepatitis/Hepatitis C increased, and increased knowledge of the implications of infection with the Hepatitis B virus (or group of viruses)<sup>6</sup> became better understood. It is important to bear in mind, however, in considering comments made as the period progressed, that understanding of the absolute and relative reliability of tests also increased over the period. Confidence in the effectiveness of Hepatitis B screening assays to identify blood with the potential to transmit 'viral hepatitis', at least until the early to mid-1980s, reflected a lack of understanding both of the efficiency of the technology in identifying Hepatitis B and of the characteristics of NANB Hepatitis that undermined the usefulness of available screening tests more generally. Comments made early in the period may mislead in presenting an apparent state of knowledge of matters that in fact were established only at a later date.

**25.11** The 1973 World Health Organization (WHO) report of the opinions of the expert scientific group on viral hepatitis, discussed in Chapter 14, *Knowledge of Viral Hepatitis 1*, paragraphs 14.31–14.42, commented that it was generally agreed that not all cases of post-transfusion hepatitis were caused by Hepatitis B infection and that 'as more hepatitis B carriers are eliminated from serving as blood donors, the proportion of cases

<sup>4</sup> See paragraph 25.74 below.

<sup>5</sup> Tests for anti-HBc were supplemented by tests for the antigen using specific immunoglobulins, Immunoglobulin M (IgM) and Immunoglobulin G (IgG). The test for anti-HBc became of interest as a possible 'surrogate marker' for NANB Hepatitis and is discussed in that context in Chapter 27, *Surrogate Testing of Donated Blood for non-A, non-B Hepatitis*. The anti-HBc and IgM tests indicated whether the patient had ongoing infection. The IgG test indicated whether the patient had been exposed to or infected with Hepatitis B. It is not necessary, for present purposes, to discuss the nature of these tests in detail.

<sup>6</sup> As with HCV (see Chapter 13, *Knowledge of Viral Hepatitis Now*, paragraph 13.14), HBV is divided into a number of different genotypes (and subgenotypes) with distinct properties.

due to other types of hepatitis will increase'.<sup>7</sup> The comment was speculative, however: the seminal research that led to the conclusion that there were types of viral hepatic disease other than Hepatitis A and B had not yet been published. In a section on 'Changing patterns of infection in certain developed countries', the report noted marked shifts in the age- and sex-specific rates for hepatitis in the USA and some European countries during the previous decade. The patterns of infection noted were not related to blood transfusion or other medical procedures but, rather, suggested a likely association with the illicit use of drugs. It was thought quite possible that, in addition to the increased risk of parenteral transmission,<sup>8</sup> the lifestyles of drug users might increase the level of non-parenteral transmission.<sup>9</sup> The population groups exposed to infection were increasing and the scientific context for the objective testing of blood for agents that might transmit infection was widening. The risks of transmission were accordingly increasing in the absence of effective exclusion policies and practices. In the early and mid-1970s, however, practical steps for eliminating post-transfusion hepatitis were still focused on Hepatitis B and testing for that infection in particular.

### The demand for a serological test for Hepatitis B

**25.12** The need for screening for hepatitis had been identified at an early date, sometimes generally but more often related to Hepatitis B. In November 1969, a letter to the *British Medical Journal (BMJ)* reflected a general view:

[U]ntil a reliable serological test for viral hepatitis is available the donor with anicteric hepatitis [hepatitis, that is, that does not present with clinical jaundice] will go undetected. Cryoprecipitate will remain a potential source for the transmission of hepatitis virus until previous attacks of this form of hepatitis can be reliably diagnosed or an effective means of sterilization ... is produced.<sup>10</sup>

**25.13** At a meeting of the UK RTDs on 15 October 1969, a contributor from the London School of Hygiene and Tropical Medicine (name redacted but almost certainly Professor Arie Zuckerman) presented a talk on the discovery of the Australia antigen, on methods of detecting it and on its possible relationship with serum hepatitis.<sup>11</sup> In discussion it was agreed that there were few reported cases of Hepatitis B transmission and none of other viral hepatitis transmission in major surgery. Six cases of viral hepatitis transmission related

<sup>7</sup> The group met in Geneva on 25–30 September 1972. Their report, dated 1973, was published in 1975 as 'Viral Hepatitis: Report of a WHO Scientific Group', *World Health Organization technical Report Series*, No. 512 [SGH.002.9746] at 9754. See, also, at 9762 where it was noted that '[t]he present widely employed techniques for detecting Hepatitis B antigen in blood are thought to be capable of preventing approximately 30% of cases of post-transfusion hepatitis. The effect the introduction of more sensitive techniques will have on the rate of post-transfusion hepatitis is not yet clear, but preliminary evidence suggests that it will not be great... Cases not due to virus B are thought to be due to a variety of causes, including Hepatitis A virus, cytomegalovirus, and other, as yet unidentified agents'. See, also, Dr McClelland – Day 9, pages 106–108

<sup>8</sup> Parenteral transmission typically refers to a blood-borne route of transmission. See Chapter 13, *Knowledge of Viral Hepatitis Now*, footnote 5 for a fuller discussion of the term.

<sup>9</sup> 'Viral Hepatitis: Report of a WHO Scientific Group', *World Health Organization Technical Report Series*, 1975; No. 512 [SGH.002.9746] at 9755. Strictly speaking, an enteral infection is one spread through the introduction of a pathogen to the gastrointestinal tract. A parenteral infection is one spread by a means other than by the introduction of a pathogen to the gastrointestinal tract and, in this general way, does not refer only to blood-borne infections. Medical literature of the time, however, used the term parenteral, at least as regards hepatitis, to mean 'blood-borne' and this usage is retained here.

<sup>10</sup> Fitzpatrick and Kennedy, 'Serum hepatitis in a haemophilic', *British Medical Journal*, 1 November 1969; 299 [LIT.001.0249]

<sup>11</sup> Minutes of meeting [DHF.002.7801]. At this period the expressions 'Australia/Australian antigen' (Au), 'Hepatitis Associated Antigen' (HAA), and 'Australian (Hepatitis Associated) Antigen' are used interchangeably, all superseded by the term 'Hepatitis B surface antigen' (HBsAg). See the second report of the Maycock Advisory Group, [SGH.003.0079] at 0083, for a wider range of terminology. In this chapter, 'Australia antigen' and 'Hepatitis B surface antigen /HBsAg' are used, except where it facilitates cross-reference to a source of evidence to use an alternative. See Chapter 14, *Knowledge of Viral Hepatitis Now*, for a discussion of the term 'serum hepatitis' (and the associated term 'infectious hepatitis' referred to below).

to transfusions of cryoprecipitate, not apparently due to Hepatitis B, had been reported to the Oxford Haemophilia Centre.<sup>12</sup> Testing for the presence of Australia antigen required serum samples containing antibody reacting with the antigen ('anti-sera' or 'reagents'). At that stage, only a handful of such samples had been detected in the UK and testing was therefore largely dependent on gifts of reagents from colleagues in the USA.

**25.14** The introduction of tests for the Australia antigen was discussed at the UK RTD meeting on 11 March 1970:

There were several aspects of the problem which would affect any decisions made regarding the general introduction of tests for this antigen: (i) Although the antigen appears to be associated with serum hepatitis and not with infectious hepatitis, it has not yet been shown to be the cause of the former disease although a causal association seems very probable. (ii) If all donors were screened and those with positive tests for Australia antigen were removed from the panel, it was estimated that the incidence of hepatitis might be diminished by about 40 per cent (iii) the antibody containing anti-sera (at present all of human origin) necessary for testing were scarce, of varying potency and possibly of differing specificity (iv) the most reliable method of detecting the Australia antigen was not yet established, (v) the overriding need was to obtain supplies of anti-sera, preferably of animal origin and to establish a reference preparation of anti-serum.<sup>13</sup>

**25.15** The meeting agreed that, in the circumstances, a more precise definition of the status of the Australia antigen and of the methods of detecting it should be awaited before planning to screen donors and also that, if routine testing were to be introduced, it should be on a national (UK-wide) basis because of the possible medico-legal significance of the procedure. Extracts from the minutes of the meetings on 15 October 1969 and 11 March 1970 were later appended to the minutes of the first meeting of the Medical Research Council (MRC) Working Party on Post-Transfusion Hepatitis on 14 February 1980.<sup>14</sup>

**25.16** There had been significant international public health interest in the screening of blood for hepatitis infection before the reference period, but also a great deal of uncertainty. The uncertainty in the UK, and in Europe as a whole, was reflected in a paper presented to the sub-committee of specialists on blood problems of the Public Health Committee of the Council of Europe in April 1970.<sup>15</sup> The paper noted a close association between hepatitis and the Australia antigen but commented that a similar close association between hepatitis and the relative antibody was less well established. The paper stated:

Because of the obvious implications ... it should be considered whether introduction of routine screening should not be deferred until more is known about the nature of the antigen or antigens and the corresponding antibody or antibodies and their relationship to hepatitis.<sup>16</sup>

<sup>12</sup> Minutes of MRC Working Party on Post-Transfusion Hepatitis, 14 February 1980 [DHF.002.4845] at 4846

<sup>13</sup> Minutes of UK RTD meeting [DHF.002.7782] at 7786

<sup>14</sup> Minutes of MRC Working Party on Post-Transfusion Hepatitis, 14 February 1980 [DHF.002.4845] at 4849–50

<sup>15</sup> Paper [DHF.001.1745]

<sup>16</sup> Ibid [DHF.001.1745] at 1746



**25.17** There were technological and practical difficulties in the way of universal screening, according to that advice. In April 1970, however, the burden of the advice submitted to the sub-committee was uncompromising: donations should be tested by effective methods of screening when supplies of antisera were assured and infected blood should not be used. A 1970 WHO bulletin similarly recommended the detection and exclusion of blood donors carrying Australia antigen.<sup>17</sup>

**25.18** The major Scottish Blood Transfusion Centres in Edinburgh and Glasgow were engaged in research into screening tests in 1970. Systematic study of virus transmission by therapeutic blood products had begun in Edinburgh in the 1960s while in Glasgow research was a direct response to the WHO bulletin.<sup>18</sup> In each case the available tests were found to be lacking in sensitivity<sup>19</sup> for detection of the Australia antigen.

**25.19** The published sources, and indeed the Scottish research, appear to have left open a number of questions. The Council of Europe report recognised, in common with other contemporaneous opinion, that the available testing methods would not detect all Hepatitis B antigen-positive donations. Anticipating a point that was to be developed later, as tests became more sensitive, among the patients found negative on the Australia antigen test there would be an increasing proportion of hepatitis caused by 'other' transmissible agents in infected blood samples. It appears to have been clearly understood that there was no assay to detect these groups: other means would have to be relied upon.

**25.20** The problem of reducing the risk of transmission of the Australia antigen by blood and blood derivatives was discussed at a meeting convened by the Department of Health and Social Security (DHSS) on 20 July 1970, where competing views were noted.<sup>20</sup> One view was that screening should be introduced as and when possible, notwithstanding that the methods and reagents used would not be uniform. The other was that attempts to institute screening should not be pressed until much more was known about the Australia antigen and methods of testing for it; and that routine screening should not be introduced except on a national scale with uniform methods of testing and reagents. After extensive discussion, in which it was suggested by one participant that donors whose blood contained antigen or antibody should be permanently excluded from donation, it was recommended that the DHSS should facilitate in every way it could the testing of blood donations for the presence of the Australia antigen and its antibody. The discussion concluded:

As long as antisera for testing were scarce it would not be possible to organize testing on a national scale. The Department might therefore consider starting testing in a few centres ... to test the feasibility of routine screening .... It was agreed that each donation from a given donor should be tested and that the donor should be excluded if antigen or antibody were found. At present it seemed that such a donor should be permanently excluded.<sup>21</sup>

<sup>17</sup> See Wallace et al, 'Total screening of blood donations for Australia (hepatitis associated) antigen and its antibody', *British Medical Journal*, 11 March 1972 [SGH.002.9831]

<sup>18</sup> Chapter 14, *Knowledge of Viral Hepatitis* 1, paragraph 14.59

<sup>19</sup> 'Sensitivity' is a function of the test's ability to capture all cases of infection with the target pathogen. 'Specificity' is a function of the test's ability to identify only the target pathogen.

<sup>20</sup> Note of DHSS meeting [DHF.001.1751]

<sup>21</sup> *Ibid* [DHF.001.1751] at 1755

**25.21** In the light of this recommendation, a further group was set up by the DHSS, the Scottish Home and Health Department (SHHD) and the Welsh Office in September 1970 under the chairmanship of Dr William Maycock: the Advisory Group on Testing for the Presence of Australia (hepatitis-associated) antigen and its antibody (the Maycock Group). Its terms of reference were:

To advise the Health Departments on:

- i the organisation of and responsibility for testing blood donations and other specimens of blood for Australia (hepatitis-associated) antigen and its antibody in the hospital service;
- ii the provision of reagents, choice of methods and whether, and if so, what kind of, training facilities are required;
- iii the scale of accommodation, staffing, equipment and other services necessary to implement the group's proposals.<sup>22</sup>

**25.22** The Maycock Group held its first meeting on 5 October 1970.<sup>23</sup> By then, partial screening of donations had already started in some regions. In the Glasgow and the West of Scotland RTC, partial testing was introduced for a six month period in 1970<sup>24</sup> and was implemented in full in the region on 13 October 1970.<sup>25</sup> In a note of discussions with a commercial supplier dated 10 November 1970, it was recorded that commercial supplies of anti-serum for testing were available.<sup>26</sup>

**25.23** The first report of the Maycock Group was available (probably in draft) in September 1971.<sup>27</sup> It recommended that Regional Transfusion Centres (RTCs) should begin testing at the earliest possible date using immunodiffusion, complement fixation or immunoelectro-osmophoresis technology at the Director's discretion.<sup>28</sup> It was agreed that donors should be excluded if antigen or antibody were found in their blood.<sup>29</sup> It was estimated that testing for the presence of the Australia antigen and its antibody would reduce the incidence of serum hepatitis by about 25%, given the relatively insensitive nature of the tests.<sup>30</sup> The proposal for screening was implemented throughout Scotland by the end of 1971 or early 1972.<sup>31</sup>

<sup>22</sup> Report of the Advisory Group on Testing for the Presence of Australia (hepatitis-associated) Antigen and its Antibody, 1971 [SNB.002.1339] at 1341

<sup>23</sup> Ibid [SNB.002.1339] at 1341

<sup>24</sup> Wallace et al, 'Total screening of blood donations for Australia (hepatitis associated) antigen and its antibody', *British Medical Journal*, 11 March 1972 [SGH.002.9831]

<sup>25</sup> Memorandum from Dr Wallace, dated 6 September 1971 [SGH.002.9885]

<sup>26</sup> Memorandum dated 10 November 1970 [DHF.001.1791]

<sup>27</sup> Memorandum from Dr Wallace's Memo dated 6 September 1971 [SGH.002.9885]

<sup>28</sup> Report of the Advisory Group on Testing for the Presence of Australia (hepatitis-associated) Antigen and its Antibody, 1971 [SNB.002.1339] at 1346

<sup>29</sup> Ibid [SNB.002.1339] at 1362

<sup>30</sup> Ibid [SNB.002.1339] at 1343; the Bulletin of the World Health Organization, 1970, as reported in Wallace et al, 'Total screening of blood donations for Australia (hepatitis associated) antigen and its antibody', *British Medical Journal*, 11 March 1972 [SGH.002.9831]. On the relatively low sensitivity of the early Hepatitis B IEOP tests see also: Report of the Advisory Group on Testing for the Presence of Australia (hepatitis-associated) Antigen and its Antibody, 1971 [SNB.002.1339] at 1345-46; Note by Dr Macdonald, SHHD, of a meeting at the DHSS on 20 July 1970 on Hepatitis and the Australia Antigen [SGH.002.3155]; Cash, 'Principles of Effective and Safe Transfusion' *Proceedings of the Royal Society of Edinburgh*. (B) 71 (Supplement), 5, 1971/72 [PEN.002.0559] at 0566, 'While it is accepted that the CIEOP technique is basically simple it is full of pitfalls ... and liable to give false-positive and negative results. Both of these events could have serious consequences on the donor and recipient respectively'.

<sup>31</sup> Cash, 'Principles of Effective and Safe Transfusion', *Proceedings of the Royal Society of Edinburgh* (B) 71 (Supplement) 5, 1971/72 [PEN.002.0559] at 0565: Dr Cash refers to the 'recent' introduction of screening in his talk in February 1972.

**25.24** Testing to screen for the Australia antigen was introduced for all blood donations in the rest of the UK from December 1972.<sup>32</sup>

**25.25** There was, however, a degree of scepticism on the part of some Scottish scientists at this time. John Watt, Director of the Protein Fractionation Centre (PFC), and colleagues presented a paper on plasma fractionation at a Joint Symposium held by the Royal College of Physicians of Edinburgh and the Royal Society of Edinburgh in February 1972.<sup>33</sup> They discussed hepatitis transmission and the identification by Dr Baruch Blumberg and others of the 'hepatitis associated antigen' (HAA – another term for the 'Australia antigen', HBsAg). They commented:

A screening programme which results in identification of HAA carriers among blood donors, even if such identification be less than totally accurate, is bound to reduce the incidence of infection in recipients of whole blood, cellular components and whole plasma. However, it is equally certain that such screen procedures, unless they be absolutely infallible, will not greatly influence the infectivity of plasma products. This must remain the province of the fractionator and the characteristics of his technology until such time as screening systems are capable of identifying HAA presence in dilutions at least six orders of magnitude greater than can presently be detected .... Many commercial fractionators and some state organisations process pools containing as many as 30 000 donations of plasma; one unidentified infected donation would be enough to make the whole of such a pool suspect.<sup>34</sup>

**25.26** Chemical processing to inactivate pathogens, in the absence of infallible screening methodology, was identified by fractionators as the solution to virus transmission. Professor John Cash, who would become the Medical and Scientific Director of the SNBTS, referred to a range of screening techniques and commented:

This work clearly implies that the routine screening of donor blood for Australia antigen will decrease the total incidence of post-transfusion hepatitis. Although the urgency and importance of this approach cannot be overemphasised, the degree of protection offered remains uncertain, as the final analysis will be dependent upon the prevalence of antigen-positive donors in a community, which can vary widely (Prince 1970), the quality of the methods used to detect the antigen and the frequency of other potential hepatotoxic agents in the donor population.<sup>35</sup>

**25.27** Professor Cash discussed a range of clinical practices that might reduce the risk of virus transmission and commented on the tests available for the Australia antigen. He said that the recent introduction of total donor screening in Scotland was a major step forward but left much still to be done. More sensitive tests were required and there was a need for improved facilities and for a national reference laboratory for the supply of standardised reagents. He concluded:

---

<sup>32</sup> *A v The National Blood Authority*, (2001) 3 All ER 289, paragraph 8, [PEN.017.0302] at 0308

<sup>33</sup> Watt et al, 'New Developments in Large-scale Plasma Fractionation', *Proceedings of the Royal Society of Edinburgh (B)* 71 (Supplement), 3, 1971/72 [PEN.002.0538]. See Chapter 14, *Knowledge of Viral Hepatitis 1*, paragraphs 14.49–14.59

<sup>34</sup> Watt et al, 'New Developments in Large-scale Plasma Fractionation', *Proceedings of the Royal Society of Edinburgh (B)* 71 (Supplement) 3, 1971/72 [PEN.002.0538] at 0551

<sup>35</sup> Cash, 'Principles of Effective and Safe Transfusion', *Proceedings of the Royal Society of Edinburgh (B)* 71 (Supplement) 5, 1971/72 [PEN.002.0559] at 0564

[W]e must not assume that the elimination of all antigen-positive units will solve the post-transfusion hepatitis dilemma. Current evidence strongly suggests that the present limitations, which have been calculated to represent a detection rate as low as 25 per cent, cannot be entirely explained on insufficient sensitivity of existing methods, and that other agents are responsible for a significant proportion of the problem.<sup>36</sup>

**25.28** In May 1972, the Maycock Group published a revised report in which it repeated its recommendation that RTCs should begin, at the earliest possible date, to test all blood donations for the presence of the Australia antigen and its antibody using, initially, an immunoelectroosmophoretic method of testing.<sup>37</sup> The report noted that knowledge of all aspects of the Australia antigen was accumulating very rapidly and that its recommendations should be regarded as interim and subject to modification at a later date.<sup>38</sup>

**25.29** Leaving aside the reservations of Scottish scientists noted at paragraph 25.25 about the effectiveness of screening in relation to large-pool plasma products, there was concern expressed in Scotland in October 1972 about the delay in introducing more sensitive screening tests for Australia antigen and its antibody.<sup>39</sup>

**25.30** The 1973 WHO report identified the tests available and commented on them.<sup>40</sup> With regard to effectiveness, it stated:

The present widely employed techniques for detecting hepatitis B antigen in blood are thought to be capable of preventing approximately 30% of cases of post-transfusion hepatitis. The effect the introduction of more sensitive techniques will have on the rate of post-transfusion hepatitis is not yet clear, but preliminary evidence suggests that it will not be great. A further significant reduction in the rate of post-transfusion hepatitis may require the development of biological tests for the hepatitis B virus, as well as a better understanding of the complex etiology of this form of the disease. Cases not due to virus B are thought to be due to a variety of causes, including hepatitis A virus, cytomegalovirus, and other, as yet unidentified agents.<sup>41</sup>

**25.31** On that assessment of the situation, the techniques then available were not very sensitive in detecting Hepatitis B and failed to detect an important proportion of cases of that type of infection, though 30% effective screening was an improvement on the Maycock Group's estimate of 25%. Further, the detection rate left unexplained other cases of post-transfusion hepatitis. As events were to prove, those included the non-A, non-B form or forms of hepatitis postulated after 1974.<sup>42</sup> Following Stephen Feinstone's identification of the Hepatitis A virus (HAV) and subsequent confirmation by 1978 that its mode of infectivity was enteral and not parenteral, HAV could be excluded as a cause of post-transfusion hepatitis. There were two remaining variables: the sensitivity of existing screening tests for Hepatitis B and the range of non-B agents capable of transmitting infection. The interaction of these variables was little understood.

<sup>36</sup> Ibid [PEN.002.0559] at 0564

<sup>37</sup> Revised Report of the Advisory Group on Testing for the Presence of Australia (Hepatitis-Associated) Antigen and its Antibody [DHF.001.1980] at 2000

<sup>38</sup> Ibid [DHF.001.1980] at 1983

<sup>39</sup> Minutes of SHHD Central Consultative Committee on Blood Transfusion meeting on 10 October 1972 [SGH.001.0690]

<sup>40</sup> 'Viral Hepatitis: Report of a WHO Scientific Group', *World Health Organization Technical Report Series*, 1979; No. 512 [SGH.002.9746] at 9758–60

<sup>41</sup> Ibid [SGH.002.9746] at 9762

<sup>42</sup> Dr McClelland – Day 9, pages 106–108

**25.32** What was increasingly understood, however, was that the problem of transfusion-associated transmission of hepatitis was more widespread than had been appreciated previously. In addition to the increasing prevalence of infection among new population groups (see paragraph 25.11 above) the report also commented:

Hepatitis B antigen has now been found in all components of plasma that are derived by the Cohn method of fractionation from plasma known to contain the antigen.... It is important to exclude antigen-positive plasma from the pool to be used for preparing blood derivatives for clinical use.<sup>43</sup>

**25.33** The risk to patients with coagulation deficiencies who required replacement therapy was recognised. There was also a need to protect transfusion patients from infected blood and blood components.

**25.34** The Maycock Group was reconvened on 6 December 1973. Its second report, dated September 1975, noted that by that date the antigen had become known as the 'Hepatitis B surface antigen' (HBsAg) and that information about the subject continued to accumulate very rapidly. During this phase of its operations, improved serological assays for HBsAg were being developed and applied routinely in the UK, including Scotland. The second report stated:

Published reports show that the incidence of hepatitis B in recipients of antibody positive [blood] is no greater than that of recipients of blood in which neither HBsAg nor anti-HBs is demonstrable. Therefore, while confirming ... that those donors whose blood is HBsAg positive should be permanently excluded from the panel and their donations rejected for clinical use, we now recommend that donors whose blood contains anti-HBs may be retained on the panel and their donations used clinically.<sup>44</sup>

**25.35** The second report of the Maycock Group was approved by the Minister of State in October 1975 and endorsed by the Standing Medical Advisory Committee (SMAC) at their meeting on 11 November 1975.<sup>45</sup> The recommendation was reflected in the advice of the National Blood Transfusion Service in 1977;<sup>46</sup> 1983;<sup>47</sup> and 1985.<sup>48</sup> The clinical use of blood containing antibodies to Hepatitis B, without detectable antigen, was now recommended.

**25.36** In the introduction to its third report, published in 1981, the Maycock Group again emphasised the rapidity with which information on the subject had been accumulating and the need to avoid regarding its recommendation as final.<sup>49</sup> It is appropriate to emphasise that there was rapid change throughout the 1970s. The deliberations and subsequent advice of the Maycock Group were based on the premise that Hepatitis B antigen-positivity remained the principal transfusion-related risk of transmission of hepatitis, although a challenge of that position was already emerging. On 3 August 1974 *The Lancet* published the important paper by Dr Alfred Prince and his colleagues which suggested that, in the USA, 'a large proportion of long-incubation post-transfusion hepatitis is unrelated to

<sup>43</sup> 'Viral Hepatitis: Report of a WHO Scientific Group', *World Health Organization technical Report Series*, 1979, No. 512 [SGH.002.9746] at 9761

<sup>44</sup> Second Report of the Advisory Group on Testing for the Presence of Hepatitis B Surface Antigen and its Antibody [SGH.003.0079] at 0084

<sup>45</sup> Memorandum from TE Dutton to Dr Waiter dated 16 March 1976 [SGF.001.2841] at 2842

<sup>46</sup> *Memorandum on the Selection etc of Blood Donors 1977* [SNB.002.5348] at 5350

<sup>47</sup> *Guidance for the Selection etc of Blood Donors 1983* [SGF.001.0377] at 0388

<sup>48</sup> *Guidance for the Selection etc of Blood Donors 1985* [DHF.001.8931] at 8943

<sup>49</sup> Third Report of the Advisory Group on Testing for the Presence of Hepatitis B Surface Antigen and its Antibody [DHF.003.0037] at 0042

hepatitis B and that control of post-transfusion hepatitis will require identification of a hepatitis virus(es) type C'.<sup>50</sup>

**25.37** The advice of the Maycock Group was not universally applauded. In a reply to the Group's second report, a representative of the Royal College of Physicians (RCP) commented as follows:

I do however have some misgivings about discontinuing the current practice of permanently excluding from the panel, donors with a past history of jaundice or hepatitis. Even with the most sensitive techniques false negatives may occur, and furthermore transfusion hepatitis may be caused by viruses other than Hepatitis B for which at present no tests are available (the existence of Hepatitis C was postulated recently). Although the chance that such individuals might transmit hepatitis is admittedly remote, the risk is there and not worth taking unless it can be shown that many donors are being lost to the panel in this way — what are the figures for such rejections at present[?]<sup>51</sup>

**25.38** A draft reply dated July 1976 from the DHSS to the RCP noted that the Maycock Group's recommendation agreed with a recommendation contained in the 1975 WHO Report. The draft considered the historic background of the exclusion of donors with a history of jaundice and noted the developments in the knowledge of and testing for HBsAg. It stated that no evidence had been collected yet in the UK to substantiate the presence of the postulated 'Hepatitis C' and concluded that, for these reasons, it was proposed to retain the recommendation of the Maycock Group that donors with a history of jaundice should no longer be permanently excluded from donating.<sup>52</sup>

**25.39** The DHSS distributed the second report of the Maycock Group with an accompanying circular to all regional health authorities and other bodies in England and Wales in November 1976, intimating Ministers' acceptance of the report subject to reservations and recommending implementation.<sup>53</sup> The circular drew attention to the Group's recommendation that the practice of permanently excluding donors with a history of jaundice could be discontinued, provided that HBsAg was not detected by a reversed passive haemagglutination assay (RPHA), or a test of equal sensitivity, and that the donor had not suffered from hepatitis or jaundice during the previous 12 months.

**25.40** Meantime, by about 1974 all blood donated in Scotland was screened for the presence of Hepatitis B surface antigen and anti-Hepatitis B by counter-immunoelectrophoresis (CIEP) or immunoelectro-osmophoresis (IEOP) (the 'second generation' tests).<sup>54</sup> The technology was still, in routine application, dependent on human observation. Dr Brian Dow, Glasgow and the West of Scotland BTS, explained the process as it was applied in 1974.<sup>55</sup> A sugar derived from seaweed (agarose gel) was spread on glass plates where it

<sup>50</sup> Prince et al, 'Long-incubation post-transfusion hepatitis without serological evidence of exposure to hepatitis-B virus', *The Lancet*, 3 August 1974; 241 [LIT.001.0363]. Professor Cash said: 'I saw Alfred Prince in my 1969 visit to the States, he gave me a small vial of Australia antigen in New York and I brought it back, and that was the first beginnings of testing for Australia antigen, certainly in Scotland. This was an outstanding group'. Day 10, page 101

<sup>51</sup> Second Report of the Advisory Group on Testing for the Presence of Hepatitis B Surface Antigen, comment by Royal College of Physicians [DHF.001.2819] at 2823 (emph. orig.)

<sup>52</sup> Final draft reply to the Second Report of the Advisory Group on Testing for the Presence of Hepatitis B Surface Antigen [DHF.001.2819]

<sup>53</sup> Health Services Development — Hepatitis B Surface Antigen — letter to Regional Health Authorities [DHF.001.2898]. Ministerial approval in October 1975 had been followed by extensive external consultation. See memo dated 24 March 1976 [SGF.001.2841]

<sup>54</sup> Dr Dow — Day 8, page 83. Glasgow and Edinburgh used different test methods. By the end of 1984, Edinburgh used a haemagglutination inhibition technique, see [SGF.001.2786]

<sup>55</sup> Dr Dow — Day 8, pages 84–87

formed a milky coloured surface. Test samples were added, typically in three 'wells'. Each plate comprised a reagent in one well, for example a specimen from a donor known to have Hepatitis B surface antigen-positive blood; the test sample in the middle well; and a second reagent in the third, ie a sample from a donor known to have anti-HBs. If the test sample had HBs antibody, the application of an electric current would develop a visible white line (a 'precipitin line') in the gel between the test sample and the sample with Hepatitis B surface antigen by osmosis. The same process would disclose anti-HBs, if the test sample had it, by a precipitin line in the other direction.

**25.41** The test was not very sensitive and required a far greater concentration of antigen or antibody for detection than the next generation of tests.<sup>56</sup> Dr Dow thought, however, that Glasgow had achieved a higher rate of reduction in post-transfusion hepatitis than indicated in the first Maycock Group report, achieving 30–50% success as against the 25% estimated by the report.<sup>57</sup> Success depended on observation by the technician, the quality of the reagents<sup>58</sup> and the reference laboratory back-up available.<sup>59</sup> Good technicians were required as identifying the precipitin line was a subjective exercise and technicians differed in their interpretations.<sup>60</sup> To achieve the level of success it had, Glasgow made sure that a supply of good reagents was available and had used the same reagents consistently from about 1970.<sup>61</sup>

**25.42** In England, Dr Rosemary Biggs published a report of the Haemophilia Directors' study in 1974, indicating that testing had reduced the incidence of infection in donations but also pointing to the insensitivity of the available tests.<sup>62</sup> Referring for comparison to an earlier report<sup>63</sup> from 1972 by Dr John Wallace and others, Glasgow, she wrote:

The incidence of the Hepatitis B virus in the donor population was of the order of 1 per 800 donations at the time that these observations were made. Since then the screening of all donors for Hepatitis B antigen has been instituted and the incidence of samples grossly contaminated with Hepatitis B virus is now certainly less. Screening, however, is unlikely to remove all infected samples because more than one virus is involved and because the screening method is not sufficiently sensitive to detect all samples infected with Hepatitis B virus.<sup>64</sup>

**25.43** At this time, the Glasgow and Edinburgh Blood Transfusion Services were actively engaged in research into the development and application of screening techniques and continued to develop test technology. Information on research in Edinburgh was passed to the Maycock Group following a meeting of the Central Consultative Committee on 14 October 1974.<sup>65</sup>

<sup>56</sup> Dr Dow explained that the IOEP test detected down to 1 microgram per ml of HBV surface antigen whereas current tests would get down to picogram levels: a thousand times the number of individuals with HBV surface antigen would be detected. But that did not necessarily increase the numbers detected, because most were detected by IOEP in the first place, and only a few additional individuals were picked up by RIA, the more sensitive test, when it was introduced, and later developments. Day 8, pages 100–102.

<sup>57</sup> Dr Dow – Day 8, pages 95–96

<sup>58</sup> Ibid page 90

<sup>59</sup> Ibid page 69

<sup>60</sup> Ibid pages 85–86. See Dr Helske's paper [LIT.001.3562] at 3576: 7 out of 124 positive samples were detected by one technician only of two reading the plates independently.

<sup>61</sup> Dr Dow – Day 8, pages 90–91

<sup>62</sup> Biggs, 'Jaundice and antibodies directed against Factors VIII and IX in patients treated for haemophilia or Christmas Disease in the United Kingdom', *British Journal of Haematology*, 1974; 26:313 [LIT.001.0099]

<sup>63</sup> Wallace et al, 'Total screening of blood donations for Australia (hepatitis associated) antigen and its antibody', *British Medical Journal*, 11 March 1972; 663 [SGH.002.9831]

<sup>64</sup> Biggs, 'Jaundice and antibodies directed against Factors VIII and IX in patients treated for haemophilia or Christmas Disease in the United Kingdom', *British Journal of Haematology*, 1974; 26:313 [LIT.001.0099] at 0100

<sup>65</sup> Extract from CCC minutes [SGF.001.2786]

**25.44** The second report of the Maycock Group, published in September 1975, described the principles of testing and commented that the association between the presence of HBsAg in donor blood and the occurrence of HBsAg positive hepatitis in the recipients after an incubation period of 40–180 days was established. It noted that blood and blood products could also transmit other forms of hepatitis which did not appear to be associated with the presence of HBsAg.<sup>66</sup> The results of testing by various techniques were set out and the incidence of icteric hepatitis (hepatitis, that is, accompanied by clinical jaundice) was discussed. The likely outcome of testing was noted:

Several studies in [the] USA have shown that exclusion of HBsAg positive donors diminishes the incidence of hepatitis B in transfused patients. Although comparable surveys in UK have not yet been reported, it seems likely that exclusion of HBsAg positive donors here will also be associated with a diminution in the number of cases of hepatitis B transmitted by blood and blood products.<sup>67</sup>

**25.45** The report commented that infection with Hepatitis B was associated with the appearance in the serum of a specific surface antigen, HBsAg, and its homologous antibody, anti-HBs. A second antigen-antibody system, the Hepatitis B core, appeared to be intimately related to the infection.<sup>68</sup>

**25.46** The report also noted that published information showed that the incidence of Hepatitis B in recipients of antibody-positive blood was no greater than that of recipients of blood in which neither HBsAg nor anti-HBs was demonstrable.<sup>69</sup> This led to the recommendations on donor management discussed above.<sup>70</sup>

**25.47** Notwithstanding this advice, the report stressed that a negative result for antigen and antibody, even by the most sensitive of the available methods of testing, did not necessarily imply the absence of an infective agent or agents.<sup>71</sup> Having reviewed the methods available, the Group recommended that RPHA should be adopted by RTCs in place of CIEP to screen every blood donation for the presence of HBsAg.<sup>72</sup>

**25.48** The emphasis at this stage was firmly on HBsAg identification. The confidence shown in recommending the selection of a specific method implied a step change in knowledge of Hepatitis B at about the beginning of the reference period. The history of developing scientific knowledge over the period would suggest that there was a perception that there had been significant progress, although the prevailing understanding of the virus was still incomplete. It appears that there was growing confidence in the effectiveness of the screening process to reduce, if not totally eliminate, the risk of transmission of Hepatitis B. The Maycock Group's second report noted:

In the light of the developments which have occurred since the publication of our last Report we no longer consider that CIE should be the recommended

<sup>66</sup> Second Report of the Advisory Group on Testing for the Presence of Hepatitis B Surface Antigen and its Antibody [SGH.003.0079] at 0083

<sup>67</sup> Ibid [SGH.003.0079] at 0084

<sup>68</sup> Ibid [SGH.003.0079] at 0083

<sup>69</sup> Ibid [SGH.003.0079] at 0084

<sup>70</sup> Ibid [SGH.003.0079] at 0090. The report also made particular recommendations relating to the use of blood and plasma donated by donors who were born or had lived in endemic malarial areas. These were related to the risk of transmission of malaria and are not relevant for present purposes.

<sup>71</sup> Second Report of the Advisory Group on Testing for the Presence of Hepatitis B Surface Antigen and its Antibody [SGH.003.0079] at 0086

<sup>72</sup> Ibid [SGH.003.0079] at 0089



technique for the routine screening by RTCs for the presence of HBsAg. The choice for a replacement method lies, in our view, between RPH and RIA .... RIA is, admittedly, more sensitive than RPH, but even so cannot be relied upon to detect HBsAg in every donation in which it is present. In our opinion the extra degree of sensitivity which RIA affords is outweighed by the considerable advantages which RPH offers in other, no less important, respects .... We therefore recommend that RPH should be adopted as soon as possible by all RTCs in place of CIE to screen every blood donation for the presence of HBsAg....<sup>73</sup>

**25.49** 'Third generation' HBsAg screening tests were introduced from 1975.<sup>74</sup> The Maycock Group noted that RPHA showed a 50% improvement in sensitivity over CIEP and approached the sensitivity of the best available test, radioimmunoassay (RIA). Dr Harvey Alter and colleagues reported on retrospective re-testing of samples previously tested by CIEP by RIA. They found that three of four patients who developed Hepatitis B infection, but were negative by CIEP, tested positive by RIA.<sup>75</sup> With the third-generation tests, from 1975, the process was increasingly automated: there was progressively less 'art' and more 'science' in testing. Tests, thought at the time to be sensitive and accurate, were beginning to be widely available for infections with Hepatitis B. Research and development continued and further improvements in the sensitivity of screening methods for HBsAg and anti-HBs continued to be made thereafter.

**25.50** Progress on consultation of the second report of the Maycock Group was reported in a memorandum by TE Dutton, DHSS, dated 16 March.<sup>76</sup> It recorded that the report was approved by the Minister of State in October 1975 and endorsed by the SMAC at their meeting on 11 November 1975, as already noted, and provided a summary of responses. Although consulted, the RTDs' responses (if any) were not summarised.<sup>77</sup> A copy of the memo was appended to a memo sent by Dr Archibald McIntyre, SHHD, on 24 March 1976, to Dr McCreadie, Dr Graham Scott and others.<sup>78</sup> It recorded that in Scotland sensitive tests for the detection of HBsAg were being used in all five RTCs.

**25.51** Until the adoption of the third-generation tests, testing for Hepatitis B was not efficient. In addition, there were no tests for hepatitis agents other than Hepatitis B. A practical assay for Hepatitis A was not available in Scotland until 1978. The inability to identify what came to be called the NANB Hepatitis viruses had, as a necessary corollary, the inability to develop any screening test or assay that would enable the exclusion of infected donations from the source materials used as whole blood, blood components or in the manufacture of blood products. (It is important to emphasise, however, that the developing knowledge that there was a form or were forms of hepatitis that did not have the characteristics of Hepatitis A or Hepatitis B logically had to mean that the most effective tests for Hepatitis A or Hepatitis B, which had to reflect the identifying characteristics of those diseases, could not detect NANB Hepatitis). Increased confidence in the sensitivity of the tests for HAV and HBV hence led to increased confidence in the existence of other 'non-A, non-B' Hepatitis virus(es). In time, a major debate would take

<sup>73</sup> Ibid [SGH.003.0079] at 0089

<sup>74</sup> Dr Dow – Day 8, pages 117–118

<sup>75</sup> Alter et al, 'Clinical and serological analysis of transfusion-associated hepatitis', *The Lancet*, 1 November 1975; 838–841 [LIT.001.3926]

<sup>76</sup> Mr Dutton's memo of 16 March 1976 [SGF.001.2841] at 2842

<sup>77</sup> Scottish National Blood Transfusion Services, 'Donor Selection Policies and Procedures', September 2010 [PEN.010.0365] at 0370

<sup>78</sup> Dr McIntyre's minute of 24 March 1976 to Dr McCreadie and others [SGF.001.2841]

place over the use of 'surrogate' tests for NANB Hepatitis.<sup>79</sup> For the time being, however, there was no means of identifying any NANB Hepatitis transmissible agent in blood.

**25.52** Similar views were expressed in other countries. A study in Finland of carriers of Hepatitis B antigen and transfusion hepatitis was published in 1974.<sup>80</sup> The report stated that in most series in the literature only 40–60% of cases of post-transfusion hepatitis could be traced to a donor with HBsAg. The report listed a number of possible reasons for that, including, with reference to the paper by Prince and others in 1974 already mentioned at paragraph 25.36, that some cases of post-transfusion hepatitis might be caused by a virus not yet known.<sup>81</sup> It concluded:

The present series suggests that screening by the counter-immunoelectrophoresis [CIE] method will reduce the number of cases of transfusion hepatitis by about a third, to which the radioimmunological method [RIA] will add 10–20 per cent. It seems that the solution of the transfusion hepatitis problem demands more sensitive and more specific HBsAg testing methods that are expressly suited for routine screening, as well as methods for the demonstration of other infectious viruses in the blood.<sup>82</sup>

**25.53** In his evidence to the Inquiry, Professor Leikola of the Finnish Red Cross Blood Transfusion Service said:

[It] was realised that not all Hepatitis B cases were recognised by [the HBsAg] test, that a good part of the people that were screened were negative with the new test but were still carrying the Hepatitis B virus and [it] was known that it was a serious disease.

In addition to that, [there] was the possibility [of] other viruses existing and probable existence of other viruses.<sup>83</sup>

**25.54** In 1975, the Glasgow Blood Transfusion Centre introduced RIA testing for HBsAg and continued to use that technique until about 1977–78.<sup>84</sup> The relative effectiveness of the test was to become an issue in Scotland in and after 1976. The Maycock Group's recommendation in favour of RPHA was challenged by Glasgow transfusion experts and scientists who thought that, while the RPHA test approached the effectiveness of RIA, it ultimately fell short of it.<sup>85</sup> Dr Dow agreed that certain RIA tests developed 'in-house' (apparently a reference, for example, to the RIA favoured by the Blood Transfusion Service in England and Wales) tended to be relatively slow and tedious, taking two or three days to complete, but noted that Glasgow used a commercial test that was quick to carry out, being completed within four hours.<sup>86</sup>

**25.55** By letter to Dr McIntyre dated 22 June 1976, Dr Wallace, Glasgow & West of Scotland BTS and a member of the Maycock Group, advised that his region had continued to research the use of RIA with the cooperation and financial support of Abbott Laboratories and the agreement of General Jeffrey (National Medical Director of the SNBTS). They had

<sup>79</sup> See Chapter 27, *Surrogate Testing of Donated Blood for non-A, non-B Hepatitis*.

<sup>80</sup> Helske, 'Carriers of Hepatitis B antigen and transfusion hepatitis in Finland', *Scandinavian Journal of Haematology*, 1974; Supplement No 22 [LIT.001.3562] at 3563

<sup>81</sup> Ibid [LIT.001.3562] at 3606-07

<sup>82</sup> Ibid [LIT.001.3562] at 3563

<sup>83</sup> Professor Leikola – Day 13, pages 93–94

<sup>84</sup> Dr Dow – Day 8, pages 111–112

<sup>85</sup> Ibid pages 115–116

<sup>86</sup> Ibid page 116

found that the RIA test was more sensitive in detecting HBsAg positive donors than the RPHA method.<sup>87</sup>

**25.56** Dr Wallace provided evidence that the RIA test was more effective. On the basis of a study conducted to assess the sensitivity of RIA and RPHA tests it had been established that, in a nine month period using RPHA, seven HBsAg-positive donations identified by RIA had not been detected. He referred to a Fatal Accident Inquiry involving the transmission of Hepatitis B to a patient who had died and a second case where the patient had survived: each had involved false negative reactions on RPHA testing. Dr Wallace was concerned about the lack of sensitivity of the RPHA test which, he implied, might lead to further deaths if it were to continue to be used. He referred to the possibility of informing the Scottish Legal Office or his own Defence Union if a way could not be found to maintain a sensitive method of testing donations. He sought additional funding to continue screening with the Abbott RIA test after withdrawal of commercial support.<sup>88</sup>

**25.57** In a memorandum dated 28 June 1976, Dr McIntyre referred Dr Scott to Dr Wallace's letter.<sup>89</sup> He stated that Dr Wallace had been involved in the 'problems of hepatitis' right from the beginning and knew that Hepatitis B was 'only the tip of the iceberg'. In his evidence to the Inquiry, Dr Scott explained the SHHD's view: 'Well, we knew that there were other hepatitis agents involved that hadn't emerged then. Non-A non-B. Nobody had developed a test for the other forms of hepatitis'.<sup>90</sup> It is implicit in the letter that SHHD medical officials had also been aware that Hepatitis B was 'only the tip of the iceberg'.

**25.58** In other respects, Dr McIntyre expressed concern about what he perceived to be 'professional blackmail' in the letter from Dr Wallace. It seems that Dr McIntyre interpreted Dr Wallace's letter as containing a thinly-veiled threat that, if he was not given funding to continue with his study, he would report his misgivings to the professional medical and other authorities. Dr Scott replied to Dr McIntyre to the effect that the Maycock Group, of which Dr Wallace was a member, took account of the sensitivities and cost of the different tests and had recommended that testing by RPHA be introduced.<sup>91</sup> The SHHD had control of the budget and the issue was effectively disposed of on the basis of comparative cost.

**25.59** The Inquiry has been unable to recover a copy of the SHHD's response to Dr Wallace but the nature of the response is indicated in a subsequent letter dated 26 July 1976 by Dr Wallace to Chief Administrative Medical Officers in his region in which he noted:

The reply from SHHD states that RPHA is the recommended method of testing and is the method which should be employed in this region after the middle of August 1976. Accordingly, RIA testing of donations for the presence of HBsAg will cease on 14 August, 1976, and thereafter RPHA will be the method used for total screening. In the light of the evaluation it is estimated that in the course of one year from 9 to 16 donors who are chronic carriers of HBsAg detectable by RIA will not be detected by RPHA.<sup>92</sup>

<sup>87</sup> Dr Wallace's letter of 22 June 1976 [SGF.001.2836]

<sup>88</sup> Ibid [SGF.001.2836] at 2837-38

<sup>89</sup> Dr McIntyre's minute to Dr Scott dated 28 June 1976 [SGF.001.2834]

<sup>90</sup> Day 11, page 153

<sup>91</sup> Dr McIntyre's minute to Dr Scott dated 28 June 1976 [SGF.001.2834] containing handwritten note by Dr Scott dated 29 June 1976

<sup>92</sup> Dr Wallace's letter of 26 July 1976 [SGF.001.2827]. See also Barr et al, 'HBsAg detection – results of comparative large scale testing of blood donations', *Medical Laboratory Sciences*, 1979; 36:109 [PEN.013.0393] at 0397 in which the authors compared the RPH and RIA methods of detecting HBsAg and observed that the '[f]inding of RPHA negative RIA positive HBsAg carriers therefore appears not to be a rare event. It is likely that a considerable number of such donors exist and can transmit type B hepatitis.'

**25.60** Dr Dow took up this issue in his written statement and in oral evidence.<sup>93</sup> Glasgow was, at this time, at the forefront of Hepatitis B testing.<sup>94</sup> He said that RPHA testing was a less sensitive test than Glasgow's (Abbott) RIA test. The RIA would identify a lower level of virus infectivity and, as a corollary, exclude a higher percentage of infected donations.<sup>95</sup> Dr Wallace had written to the west of Scotland haematologists because of his concerns about sensitivity, having been forced to use the less sensitive RPHA test because he was not funded for the RIA test. While RIA was in use, no confirmed cases of HBsAg post-transfusion infection were reported; after the change, four cases were reported in a year.<sup>96</sup>

**25.61** Mr Barr, Dr Dow and others wrote up the Glasgow work and published in 1979.<sup>97</sup> The paper reflected the strong views held at the time. It noted that since 1970 all blood donations in the west of Scotland had been screened for the presence of HBsAg. The method of testing in the first five years was CIEP. In that period, several cases of proven viral Hepatitis B transmission were notified, consistent with the known sensitivity of the test. In the final year of the study period, 1975–76, 8589 plasma pools were tested by a long incubation RIA method and four positive results were obtained. These four examples of HBsAg were RPHA-negative and RIA-positive and it was considered possible that was an underestimate, as factors such as neutralisation and dilution of HBsAg in the plasma pools could have influenced the number of positive results obtained. They reported that, among the three RPHA systems they had tested, there was remarkable variation in both sensitivity and specificity. The Abbott Diagnostics (Auscell) test appeared to be the most sensitive and specific, although it did fail to detect some antigen-positive donations. The British Wellcome Diagnostics (Hepatest) test was cheaper. From one year of testing using RIA, 12 of the antigen-positive donations detected by RIA failed to give a positive reaction when tested by RPHA. The conclusion was that finding RPHA-negative/RIA-positive carriers was not a rare event, an indication of the relative insensitivity of RPH assays.

**25.62** Notwithstanding the Glasgow experts' reservations, the Maycock Group's recommendations were consistent with international thinking at the time, which recognised RPHA and RIA as equally acceptable. In 1976, the International Society of Blood Transfusion published a guide to the *Hazards of Blood Transfusion*.<sup>98</sup> It stated:

Tests for HBsAg ... are now available. Although these will detect no more than about 50% of hepatitis B virus carriers, no blood or blood product should be transfused unless the donor is known to have been negative for HBsAg. It is recommended that each blood donation should be tested by such a method as counter-immunoelectrophoresis [CIE] or, preferably, radioimmunoassay (RIA) or reverse passive haemagglutination (RPHA).<sup>99</sup>

**25.63** The guide noted that the incidence of Hepatitis B was not known and was likely to vary from area to area. The report did not express a preference between RIA and RPHA: a sensitivity rate of 50% was expressed as a general feature of the available tests. Dr Wallace's preference for the Abbott RIA did not receive support from the guide. By the date of publication, with government support, the Maycock recommendations had taken effect as noted above.

<sup>93</sup> Dr Dow's statement on the acceptance of blood from 'higher risk' donors [WIT.003.0094] at 0097

<sup>94</sup> Dr Dow – Day 8, pages 114–115

<sup>95</sup> Ibid page 112

<sup>96</sup> Ibid pages 113–114

<sup>97</sup> Barr et al, 'HBsAg detection – results of comparative large scale testing of blood donations', *Medical Laboratory Sciences*, 1979; 36:109 [PEN.013.0393]

<sup>98</sup> *ISBT Guide 2. Hazards of Blood Transfusion*, International Society of Blood Transfusion, Paris 1976 [DHF.001.2692]

<sup>99</sup> Ibid [DHF.001.2692] at 2703

**25.64** There were, however, continuing issues. There was interest in collecting data relating to all forms of adverse reaction to factor products as production increased at the PFC and concentrates became available. The clinical value of the products required reporting and study. There was a report of adverse reactions to the PFC intermediate Factor VIII, at a meeting of the SNBTS Directors on 1 July 1976.<sup>100</sup> A specific batch, batch 127, had caused reactions in Aberdeen and in Edinburgh.<sup>101</sup> Dr David Dane<sup>102</sup> had shown that the product was free of HBsAg 'at conventional test limits (and a bit beyond)'. Edinburgh and south east Scotland had found that (uniquely, according to the minute) the batch had contained no antibody to HBsAg. At a meeting of the SNBTS Directors on 4 October 1976,<sup>103</sup> the investigation of two suspect batches, including batch 127, by Dr Cash and Dr Dane, using a more sensitive test, was reported.<sup>104</sup> Batch 127 was thought to have contained one positive HBsAg donation. From the context it appears that the 'adverse reaction' reported was jaundice. It was agreed to receive information about Dr Dane's more sensitive test for examination.

**25.65** It is of interest, in assessing contemporaneous attitudes, that a question was raised at the SNBTS Directors meeting in October, apparently by Mr Watt, whether it was of real value to investigate patients who developed jaundice following the administration of Factor VIII. Mr Watt thought that it was not justified on grounds of cost effectiveness. Dr Cash and Dr Charles Cameron, East of Scotland BTS, prevailed: investigation would continue. It was thought that Edinburgh in particular had benefited by changing their technology to meet the situation that had arisen from the investigation of batch 127. More generally, the episode is an indication that the differences of opinion between fractionators and clinicians that had been expressed in the early 1970s had not been resolved.

**25.66** In his book *Blood Transfusion for Clinicians* (1977), Dr Wallace observed:

The recognition of HBsAg as a marker for the infective agent of type B hepatitis introduced the possibility of testing every blood donation for the presence of HBsAg. Considerable discussion ensued as to the benefits resulting from the costly, and time-consuming procedure of total screening. Some authorities stated that the exclusion of HBsAg positive donors would at best reduce the incidence of post-transfusion hepatitis by only 25 per cent. The inability to prevent 75 per cent of cases of transfusion-transmitted hepatitis was considered to be multifactorial:

- i. the methods of detecting HBsAg by large scale screening were the relatively insensitive immunodiffusion (ID) and counterimmunoelectrophoresis (CIEP) techniques.
- ii. it was suspected that HBsAg was not homogeneous, and that different subtypes would make detection difficult.
- iii. other infective agents might transmit hepatitis: these included virus A, CMV, EBV and viruses not yet identified, such as the predicted virus C.
- iv. the use of absolutely fresh untested donations: some clinicians considered that fresh blood had clinical merit and insisted on its use.

<sup>100</sup> Minutes of SNBTS Directors Meeting, 1 July 1976 [SGF.001.0282]

<sup>101</sup> Ibid [SGF.001.0282] at 0285

<sup>102</sup> A member of the Maycock Group, Dr Dane led the team of scientists who, in 1970, discovered the complete Hepatitis B virus.

<sup>103</sup> Minutes of SNBTS Directors Meeting, 4 October 1976 [SGH.001.1320]

<sup>104</sup> Ibid [SGH.001.1320] at 1321. (The reference to 'batch 124' in the header to this paragraph appears to be a typographical error).

- v. a route of transmission other than transfusion: it was recognized that various hepatitis viruses could be transmitted by parenteral routes other than transfusion and by close contact.

The prevention of even 25 per cent of cases of post-transfusion hepatitis was however regarded as statistically impressive.<sup>105</sup>

**25.67** Dr Wallace referred to the work of Dr Prince and others in the USA that concluded that an infective agent other than Hepatitis B was involved in causing post-transfusion hepatitis.<sup>106</sup> He wrote:

Evidence from the USA indicates that a long incubation form of hepatitis other than type B exists, and this has been named type C or 'non-A non-B'. Present evidence on this infection in Britain is scanty, but most cases of post-transfusion hepatitis seem to be type B, although some cases with relatively short incubation periods are associated with type A or CMV or EBV infections. It may be that at present type C infection is rare in Britain. More evidence on this subject will emerge as RPHA and RIA are introduced as the method of testing donations for HBsAg.

....

While type B hepatitis seems to be the form of post-transfusion hepatitis most commonly encountered in Britain, it would be advantageous to recognize markers for the infective agents of 'non-B' hepatitis, such as type A and type C, if the latter really exists.<sup>107</sup>

**25.68** The book was written in 1976 and published in 1977. It reflected Dr Wallace's views at a time when he would clearly have thought that the choice between RIA and RPHA was open for discussion by the Maycock Group and when the prospects for both test formats seemed promising. In addition, the text must have been written shortly before it became clear that Hepatitis A was not a material cause of post-transfusion hepatitis.

**25.69** Commenting on the position at 1977, the date of publication, Dr McClelland, who became a consultant in the Edinburgh and South East of Scotland Blood Transfusion Service in 1977 and Director in 1979, was less sanguine.<sup>108</sup> In his written evidence,<sup>109</sup> he pointed to two apparent underlying assumptions: (i) that testing donations with a very sensitive test for HBsAg and removing all donations with positive test results would virtually exclude the risk of transfusion-transmitted Hepatitis B and (ii) that, provided Hepatitis B transmission was avoided, the blood would be safe. He commented that this seemed somewhat at odds with the statements that referred to 'other infective agents that might transmit hepatitis, such as the predicted virus C' and with the fact that Hepatitis B screening was thought to detect only 25% of cases of post-transfusion hepatitis. In his written statement, Dr McClelland said:

I think this apparent inconsistency must be a reflection of the prevailing sense at the time that hepatitis, if not due to Hepatitis B virus, was not a serious condition.<sup>110</sup>

<sup>105</sup> Wallace, J. *Blood Transfusion for Clinicians*, Churchill Livingstone, 1977 [LIT.001.3058] at 3100–01

<sup>106</sup> Ibid [LIT.001.3058] at 3110

<sup>107</sup> Ibid [LIT.001.3058] at 3111–12

<sup>108</sup> Dr McClelland – Day 9, page 50

<sup>109</sup> Dr McClelland's statement on the acceptance of blood from 'higher risk' donors [WIT.003.0072]

<sup>110</sup> Ibid [WIT.003.0072] at 0079

**25.70** He expanded on these matters in oral evidence. He was asked whether, at the time of publication of Dr Wallace's book, he would have shared that 'prevailing sense'. He replied:

I have found this very confusing when I read it again because it seemed to be saying several conflicting things. I would not have shared that view. I do think that, lying in back of this is something which I think came through to me in reading a lot of this material again, that there was a very strong sense within the UK that non-A non-B hepatitis wasn't a big problem in the UK.

There was clearly awareness that it was a big problem in the United States, that is in spite of the fact that the only prospective study of transfusion-transmitted hepatitis that was done for many years was organised by the Medical Research Council in the UK and published in 1974. The data, [were] actually interpreted as saying that it wasn't a problem apart from Hepatitis B. Non-A non-B hepatitis wasn't a problem but actually, if you look at the data for five minutes, it actually clearly is a problem and that, you know, coming from a group of eminent academics seems – again, I had real difficulty understanding that when I looked at it again.

It does seem to me that there must have been a very strong received belief that somehow non-A non-B hepatitis just wasn't a problem in the UK sufficient to cause highly intelligent people doing research study to actually really ignore their own findings and interpret them quite inappropriately, in my view. So I think that sort of attitude, the power of that sort of attitude must underlie this statement of Dr Wallace. It's speculation.<sup>111</sup>

**25.71** It would seem reasonable to assume that Dr Wallace's book reflected accepted knowledge among senior practitioners in Scotland, and among experts throughout the UK, at the beginning of Dr McClelland's career in transfusion medicine. As already noted, Dr Wallace was a member of the Maycock Group. On the other hand, Dr McClelland's interest in transfusion-transmitted viruses was engaged by US research, including the report of the Transfusion-Transmitted Viruses Study and the work of Dr Jay Hoofnagle and others.<sup>112</sup> For him, the view that somehow NANB Hepatitis was not a big problem in the UK was inconsistent with the knowledge that only 25% of cases of post-transfusion hepatitis could be explained by Hepatitis B and that other (known) causes including Epstein-Barr virus were not significant. In his view, the data could be interpreted as indicating NANB Hepatitis was quite a large problem: there was quite strong evidence that something was going on.

**25.72** A similar view to Dr McClelland's was taken in Finland. In his evidence to the Inquiry, Professor Leikola was asked about his understanding of NANB Hepatitis in the mid-to-late 1970s and replied:

Well, I would say that after summer 1978, when I came back from my sabbatical year in America, when I was not involved in these cases at all – but after that I think that it became clear in our minds that there is definitely a virus, or maybe maximum two viruses, causing hepatitis that is like Hepatitis B and unlike Hepatitis A.

---

<sup>111</sup> Day 9, pages 44–45

<sup>112</sup> Ibid page 55

However, in those circumstances we also were feeling that, yes, it may cause a disease. It is mentioned in this article<sup>113</sup> that in most cases the disease is mild and non-symptomatic and there were very little means to avoid [it] because we did not know any particular risk groups, even though it's clearly referred in this article that in most cases it is related to some parenteral contact with blood, either by tattooing, needle sharing or transfusion. But, yes, I would say that at that time, 1978, 1979, 1980 it became clear to us that such a disease exists.<sup>114</sup>

**25.73** The views of Dr McClelland and Professor Leikola reflected the influence of developing thought in the USA, where it was recognised that there was a significant prevalence of NANB Hepatitis. At this stage there were few reported NANB Hepatitis cases in Scotland.

**25.74** In relation to reported cases, Dr Dow said that, although he was aware of reports elsewhere in the world, he was not aware of NANB Hepatitis in Scotland until 1979 when Dr Follett, the Head of the Hepatitis Reference Laboratory, raised the issue with Dr Ruthven Mitchell, Director of the Glasgow and West of Scotland BTS.<sup>115</sup> In 1979, Dr Follett had a reliable test for Hepatitis A which had become available during 1978 (five years after Feinstein and others reported the isolation of the Hepatitis A virus) and could differentiate acute cases of Hepatitis A and B, allowing for effective screening for both viruses. The balance – outstanding cases of post-transfusion hepatitis – became potential non-A non-B cases. He had identified a few cases of post-transfusion hepatitis which, following testing, were found to be definitely neither Hepatitis B nor Hepatitis A. Again this evidence pointed to a material change of position shortly after the date of Dr Wallace's book, coinciding in time with Dr McClelland's appointment as consultant. It appears that the risk of transmission of NANB Hepatitis, previously recognised in theory, was becoming acknowledged as an existing risk in Scotland by the end of the 1970s.

**25.75** On 5 May 1979 *The Lancet* published a paper by Robert Galbraith and colleagues on an outbreak of HBsAg-negative hepatitis in a renal unit at Fulham Hospital, London, in 1968–70.<sup>116</sup> The paper explained that to clarify the aetiology of the outbreak serological tests for antibody to HAV were carried out retrospectively on serum samples obtained at the time of the outbreak.<sup>117</sup> The authors concluded:

Overall these results must indicate that the development of chronic liver disease was not related to hepatitis A infection and that this outbreak falls into the category of [NANB] hepatitis. More and more data point to this as the cause of a substantial proportion of cases of post-transfusion hepatitis negative for HBsAg and to its role in the subsequent development of chronic liver disease.<sup>118</sup>

<sup>113</sup> Berman et al, 'The chronic sequelae of non-A, non-B Hepatitis', *Annals of Internal Medicine*, July 1979; 91:1 [LIT.001.0189]

<sup>114</sup> Day 13, pages 71–72

<sup>115</sup> Dr Dow – Day 8, page 129

<sup>116</sup> Galbraith et al, 'Non-A non-B hepatitis associated with chronic liver disease in a haemodialysis unit', *The Lancet*, 5 May 1979; 951 [LIT.001.0395]. C.f. an earlier report of the same outbreak, which made no mention of the possibility that the outbreak may have been caused by NANB hepatitis: Galbraith et al, 'Chronic liver disease developing after outbreak of HBsAg-negative hepatitis in haemodialysis unit', *The Lancet*, 8 November 1975; 886 [PEN.013.1426]. In his evidence to the Inquiry, Professor Cash spoke of a fatal outbreak of hepatitis at the renal dialysis unit in Edinburgh in 1969–70 having, once Hepatitis C tests became available, been shown to have been caused by both Hepatitis B and Hepatitis C: Day 10, pages 102–103

<sup>117</sup> In his evidence to the Inquiry, Dr Dow explained that although the Hepatitis A virus had been identified in 1973, it was not until about 1978 that reliable tests for Hepatitis A became available: Day 8, pages 130–131

<sup>118</sup> Galbraith et al, 'Non-A non-B hepatitis associated with chronic liver disease in a haemodialysis unit', *The Lancet*, 5 May 1979; 951 [LIT.001.0395] at 0397



**25.76** In August 1979 Dr Ajay Chaudhuri and others reported on patients thought to have viral hepatitis admitted to the Infectious Diseases Units at Ruchill and Belvedere Hospitals, Glasgow, in 1976 and 1977.<sup>119</sup> During that two-year period, 164 patients with viral hepatitis were admitted to these hospitals. Of these patients, 52 were positive for Hepatitis B antigen, with males still greatly outnumbering females and with most cases in the 16–29 year age group. The authors noted: 'As in previous years, drug abuse was associated with the largest number of cases, with 22 patients admitting use of intravenous narcotic drugs with shared syringes and needles. They were mostly men (19 male: 3 female) in their twenties'. In the 112 patients who were HBsAg-negative, a diagnosis of non-B hepatitis was made with, in the majority of these patients, epidemiological findings and clinical course suggesting a diagnosis of Hepatitis A.

**25.77** In a discussion of non-A, non-B Hepatitis the authors noted:

In four patients with non-B hepatitis, hepatitis developed within 2-6 months of transfusion of blood products. Three male haemophiliacs and a female patient with Christmas disease had received numerous transfusions of factor VIII and cryoprecipitate. These four patients and also two drug addicts with hepatitis had no evidence of hepatitis B infection, nor of hepatitis A infection nor of infection with cytomegalovirus, nor EB virus. At present they are classified as cases of [NANB] hepatitis. Evidence from other countries suggests that a virus (or viruses) may be associated with this type of hepatitis and that a carrier state is possible. With laboratory tests now permitting definitive diagnosis of hepatitis A virus infection, as well as hepatitis B, in 1979 it should be possible to determine the prevalence of [NANB] hepatitis in the general population in West Scotland.<sup>120</sup>

**25.78** It appears, therefore, that there was an attitude in the UK among some experts that persisted into 1979, that NANB Hepatitis, particularly following blood transfusion, was common in the USA but that it had not become a major problem in the UK generally and in Scotland in particular. This attitude was to find an echo five or six years later in early responses to the arrival of HIV/AIDS in the USA. Attitudes were, however, changing by the end of the decade, under the influence of US research. Dr McClelland and the west of Scotland experts were taking a fresh look at the issue and research in this country picked up pace.

**25.79** In 1978 Dr Rosemary Biggs, the Director of the Oxford Haemophilia Centre, published the second edition of her textbook, *The Treatment of Haemophilia A and B and von Willebrand's Disease*. One of the four complications that was said to arise from treatment with plasma fractions was the transmission of an infective organism, in particular hepatitis, to the patient.<sup>121</sup> Dr Biggs identified infective hepatitis, virus A and virus B, as transmissible agents, distinguishing them in the first place by their respective incubation periods and secondly discussing modes of transmission. The text proceeded:

Donor testing is important but at present no testing procedure will eliminate all samples infected with hepatitis B virus. The very high incidence of HBsAg in the blood of commercial donors means that even when the known positive

<sup>119</sup> Chaudhuri et al, 'Viral hepatitis in Glasgow 1976-1977', *CDS 79/8*, viii [PEN.002.0511]

<sup>120</sup> Ibid [PEN.002.0511] at 0513

<sup>121</sup> Biggs, R. *The Treatment of Haemophilia A and B and von Willebrand's Disease*, 1978, Blackwell Scientific Publications, Oxford, page 181

samples are excluded, the blood products made from commercial donor blood are liable to be more infective than similar products made from volunteer donor blood.

A rather high proportion of haemophilic patients who develop hepatitis have no serological evidence of hepatitis B virus infection. These patients may have hepatitis A for which no serological tests are at present available. They may also have long incubation type hepatitis the causative agents for which have as yet not been identified. They may even develop jaundice for other reasons, for example haemolytic response to the infusion of blood group antibodies.<sup>122</sup>

**25.80** The book was probably written in 1977, when Dr Biggs may not have been aware of research in the west of Scotland. It would be 1978 before Dr Follett, for example, had a reliable test for Hepatitis A. Dr Biggs' book recognised, however, that the 'long incubation type' hepatitis might have infected the haemophilia community.

**25.81** Work on identifying the extent of NANB Hepatitis in the west of Scotland, begun in the late 1970s, was continued by Dr Dow, Dr Follet, Dr Mitchell and Professor Norman Grist (University of Glasgow) with grant support from the Scottish Hospital Endowments Research Trust.<sup>123</sup> However, a full prospective study would have been wide-ranging and expensive and was not undertaken.<sup>124</sup> Throughout 1980–1985, Dr Dow carried out ALT<sup>125</sup> testing on a sporadic basis, using prison sessions. Prison sessions were an obvious target as prisoners had already been shown to have a high incidence of Hepatitis B and NANB Hepatitis was also thought to be blood-borne. People with haemophilia, intravenous drug users and renal dialysis patients were also obvious populations.<sup>126</sup>

**25.82** Thus, while established UK transfusion experts (including those practising in Scotland) were sceptical, at this stage, of the frequency of one or more non-B blood borne-viruses, some transfusion doctors and haemophilia doctors were implicitly acknowledging that such viruses were probably by no means rare, even if their apparent pathological importance had yet to be appreciated.

**25.83** It was suggested in Dr Biggs' book that mildly affected haemophilia patients who had never or rarely been transfused should not receive large-pool commercial concentrates. Rather, Dr Biggs suggested, they should be given cryoprecipitate or small-pool concentrates. Dr Biggs concluded, however, that treatment with concentrates should not be withheld from severely affected patients because of the danger of hepatitis since 'the danger of death from haemorrhage and crippling' was of 'more immediate importance'.<sup>127</sup> (There was no mention of NANB Hepatitis in the book, apart from what might be inferred from the passage quoted.)

**25.84** It seems likely that Dr Biggs' book, which was presented as 'an authoritative and up-to-date guide for haematologists, physicians and surgeons who care for haemophilia patients', would have had a wide circulation among clinicians, as would Dr Wallace's book of the year before. Dr McClelland's retrospective review of Dr Wallace's book left him

<sup>122</sup> Ibid page 181

<sup>123</sup> Dr Dow's statement on the acceptance of blood from 'higher risk' donors [WIT.003.0094] at 0098

<sup>124</sup> Ibid [WIT.003.0094] at 0099

<sup>125</sup> Dr Dow's research refers to SGPT, serum glutamic-pyruvic transaminase, another term for alanine transaminase, ALT.

<sup>126</sup> Dr Dow – Day 8, pages 149–150

<sup>127</sup> Biggs, R. *The Treatment of Haemophilia A and B and von Willebrand's Disease*, 1978, Blackwell Scientific Publications, Oxford, pages 186–187

confused. In the case of Dr Biggs' book, the lack of comment on the work of Feinstone and others on testing for Hepatitis A from 1973 onwards,<sup>128</sup> or on the application of the test reported by Alter and others in *The Lancet* in 1975,<sup>129</sup> might similarly be questioned. On the other hand, it is likely that, typically, textbooks for practitioners report generally accepted science, and it is right to bear in mind that there can be a significant gap between the level of understanding and what can be gleaned in retrospect from a wide reading of specialised professional literature.

**25.85** On 20 August 1978 the Haemophilia Centre Directors' Hepatitis Working Party, chaired by Dr Craske, produced a report which discussed the pilot project initiated by Dr Craske to investigate the incidence of chronic liver disease in patients treated with Hemofil (a brand of commercially produced Factor VIII) in 1974–75.<sup>130</sup> Under the heading 'Prevention of Virus Infections', the report expressed doubts about screening tests for HBsAg:

#### Screening tests for HBsAg

Further studies have been carried out over the past year with batches of factor VIII suspected of having been contaminated with hepatitis B virus .... Since 1975, all batches of concentrate known to be associated with cases of acute hepatitis B have been negative for HBsAg by radioimmunoassay. However, despite improved donor screening in the USA, cases of overt hepatitis B still occur associated with every brand of large pool factor VIII, including NHS factor VIII.

It is evident, therefore, that screening tests for HBsAg are not sensitive enough to detect all donor plasma infected with hepatitis B virus, even when the concentrate is prepared from donations of plasma from volunteer donors.

....

Efforts are being made to increase the sensitivity of screening tests, but it seems unlikely that this will significantly reduce the incidence of hepatitis B from the present level.<sup>131</sup>

**25.86** By 1979, therefore, the position in Scotland can be summarised as follows:

- It was known that the best available screening tests for Hepatitis B still failed to detect a significant minority of Hepatitis B-infected donations.
- It was known that NANB Hepatitis had been found in the Scottish population by the exclusion of Hepatitis A and B by Dr Follett and his group using tests covering both infections which were available from 1978.
- There was still no screening test for NANB Hepatitis infection.
- The prevalence of NANB Hepatitis infection was not known.
- There was a clear need for further relevant research.

<sup>128</sup> Ibid. Book jacket.

<sup>129</sup> Alter et al, 'Clinical and serological analysis of transfusion-associated hepatitis', *The Lancet*, 1 November 1975; 838–841 [LIT.001.3926]

<sup>130</sup> Report of the Haemophilia Centre Directors' Hepatitis Working Party – 1978 [SNB.001.7192]

<sup>131</sup> Ibid [SNB.001.7192] at 7197–98

**25.87** The detection rate on screening for Hepatitis B was probably over 80%, and the risk of transfusion-transmitted Hepatitis B was reduced accordingly. However, for large-pool concentrates screening was virtually ineffective having regard to the likelihood of the pool containing infected donations that had escaped detection on screening.

### The early 1980s

**25.88** There was official recognition of the need for further research early in 1980. An undated internal DHSS note, probably circulated in early 1980, commented on the reasons for a proposal to set up an Advisory Group on Viral Hepatitis. The purpose of this group was to advise on the public health aspects of hepatitis.<sup>132</sup> The context, reflecting knowledge of hepatitis infection among officials, is, however, relevant. The introduction to the note narrated that three and possibly more agents were known to cause viral hepatitis, with differences in their mode of spread and other epidemiological features. Increased knowledge had led to an even greater awareness of the problems which were arising. The note stated: 'At present hepatitis B presents the majority of problems and is responsible for the majority of enquiries but [NANB] hepatitis is already becoming a major source of concern'.<sup>133</sup>

**25.89** The terms of reference proposed for the new Advisory Group were to advise the Chief Medical Officers (CMOs) of the Health Departments of the UK on all aspects of communicable hepatitis. The most important problems anticipated were related to: health and safety for NHS staff in direct contact with individuals who were carriers of Hepatitis B antigens; risks to patients from NHS staff; prevention and control of hepatitis; hazards associated with equipment; and hazards associated with blood and blood products in particular. It marked the beginning of a new phase in official recognition that there were public health issues relating to transmission of hepatitis. It is significant, however, that Hepatitis B was still identified among the most important problems. NANB Hepatitis was noted as becoming a cause for concern but was not included in the list of the most important problems in the field.

**25.90** As appears from the discussion in Chapter 27, *Surrogate Testing of Donated Blood for non-A, non-B Hepatitis*, other groups among the several that became active in the early 1980s were more relevant for present purposes, although provision was made for cross-representation of membership and the sharing of minutes of meetings.<sup>134</sup> The evidence indicates that a more structured approach was taken by the Health Departments to obtaining advice from this stage on.

**25.91** In 1981 the Maycock Group published its third report.<sup>135</sup> While the report mainly dealt with testing for Hepatitis B, it also noted:

[NANB] hepatitis viruses are a common cause of [post-transfusion hepatitis] in the United States and are thought to have been responsible for cases of [post-transfusion hepatitis] in the UK. Hepatitis due to these viruses is common among haemophiliacs and follows the administration of imported, and occasionally of British Factor VIII and Factor IX. There is evidence for the occurrence of sporadic

<sup>132</sup> See Minutes of the MRC Working Party on Post-Transfusion Hepatitis of 14 February 1980 which anticipated the early formation of the DHSS Advisory Group [PEN.017.1710]

<sup>133</sup> DHSS note 'Advisory Group on Hepatitis' [DHF.002.9099]

<sup>134</sup> For example with the UK Working Party on Transfusion-Associated Hepatitis [PEN.017.1716]

<sup>135</sup> Third Report of the Advisory Group on Testing for the Presence of Hepatitis B Surface Antigen and its Antibody: 1981 [DHF.003.0037]

cases of [NANB] hepatitis in the general adult population and in association with cryoprecipitate therapy in the UK.

There are at the present time no screening tests for detecting [NANB] hepatitis viruses in blood donations.<sup>136</sup>

**25.92** In oral evidence relating to donations collected in European penal institutions in the period 1975–83, Professor Leikola commented that he believed that many Europeans thought at the time that the problem of intravenous drug use in prisons was much smaller as compared to the problem in US institutions.<sup>137</sup> He went on to comment more generally:

Most of the research on Hepatitis B was done in the United States. Therefore I think that the investigators were readily willing to accept that the denial of using intravenous drugs was true. Secondly, in the 1970s it was well established that the occurrence of hepatitis virus was more common in prisoners as compared to the population at large. Wallace et al, 1972, assumed that the high incidence may be related to social habits and hygiene. This assumption was more or less copied to the later report by Barr and others in 1981. At the time when Wallace et al wrote their report, probably 1971, knowledge on the routes of infection was not as clear as it was later. Hepatitis A virus in contrast to Hepatitis B virus is water-borne and an infection could be related to poor hygiene. Other more realistic thoughts about the aetiology of Hepatitis B were expressed by Dr Helske in 1973.<sup>138</sup>

## Discussion and Comment

**25.93** Testing blood donations for infection at the beginning of the reference period was still relatively rudimentary and was necessarily related to contemporaneous knowledge of the risks of transmitting disease by use of human blood, blood components and blood products. Developing knowledge of these risks is a major topic for this Inquiry and is dealt with, in relation to hepatitis, in Chapters 14–16, *Knowledge of Viral Hepatitis 1 to 3*.<sup>139</sup>

**25.94** There is a degree of artificiality in separating out topics such as the developing knowledge of the risk of transmitting disease, particularly hepatitis, donor selection, technological change and even manufacturing capacity. Similarly, a strict chronological account of events would fail to capture the atmosphere of medical and scientific research and development at the beginning of the reference period. Reference to the events of the preceding decade in particular, and some earlier events, has been required. In particular, setting out the evidence on a simple chronological basis would not present a satisfactory historical perspective, therefore a more analytical approach has been adopted. Chapter 18, *Collection of Blood – General* will deal with collection procedures generally and in particular the exclusion of individuals with a history of hepatitis or of transfusion. In this chapter, the emphasis is on the relevance of the early assays for infection with hepatitis viruses to donor exclusion policies.

---

<sup>136</sup> Ibid [DHF.003.0037] at 0045–46

<sup>137</sup> Day 13, page 74

<sup>138</sup> Ibid pages 74–75

<sup>139</sup> See also Chapters 23 and 24 on viral inactivation of blood products; Chapter 25 on screening donated blood for HBV; Chapter 27 on surrogate testing for NANB Hepatitis; and Chapter 31 on screening for HCV.

**25.95** The difference of opinion illustrated by the controversy over the adoption of RPHA technology in preference to RIA set out in paragraphs 25.54–25.56 demonstrates that there was active research into the best available methods and that two groups of scientists took different views at the time. In Dr Wallace's view, the less sensitive test was selected but the Maycock Group's recommendation for that test was supported by relevant expert opinion, in the UK and internationally, and cannot be criticised as inappropriate. Of course, the emphasis was on Hepatitis B at a time when there was evidence suggesting that NANB Hepatitis was a threat that was not addressed by either test.

**25.96** It is clear that until the early to mid-1970s there was a strand of belief that, once screening for Hepatitis B had been dealt with, the problem of post-transfusion hepatitis would have been solved.<sup>140</sup> It was thought, correctly as events were to show, that there is no chronic carrier state for Hepatitis A infection which, in any case, is almost never transmitted by transfusion. Until 1973 or 1974 (depending on whether one has regard to the most advanced research) only Hepatitis B was relevant to transmission. The methods of detection of Hepatitis B until then were, however, inefficient. Two factors emerged in the mid-1970s. First, it was realised that the assays available were not able to detect all cases of Hepatitis B infection due to a significant problem of false negatives. Secondly, it was generally agreed that not all cases of post-transfusion hepatitis were caused by Hepatitis B type infection and that, as more Hepatitis B carriers were eliminated from serving as blood donors, the proportion of cases due to other types of hepatitis would increase.<sup>141</sup>

**25.97** The original rationale for the exclusion from donation of individuals with a clinical history of hepatitis was based on evidence that some of them remained infectious long after the apparent resolution of their illness. It was thought that most were Hepatitis B patients. That was correct up to a point: most haemophilia patients in the 1960s and 1970s had been infected with Hepatitis B. It may have been an acceptable view more generally so long as only the Hepatitis A and Hepatitis B viruses were believed to exist. Once it was realised that more efficient tests were throwing up an increasing proportion of cases that were not Hepatitis B or Hepatitis A, however, there was a problem, obvious with the benefit of hindsight at least. When two potential causes of disease were increased to three, there could be no logical basis for a view that all cases of continuing illness were associated with the first two identified, and with them alone, to the exclusion of the newly postulated virus. It was never suggested that NANB Hepatitis was a 'new' virus in the sense of a virus affecting humans for the first time (as was to be suggested in the case of HIV); rather, it was an undiscovered virus of undetermined epidemiology. The early HBsAg assays identified 25–30% of 'hepatitis' cases as associated with Hepatitis B. That left a very large balance of cases that might have been associated with Hepatitis A, Hepatitis B or NANB Hepatitis: they were all cases of 'hepatitis', generally defined. In the light of later scientific developments, and perhaps even in the light of contemporaneous US literature, Dr McClelland's concerns about Dr Wallace's views were well founded. After 1979, with more sensitive tests for Hepatitis B and routine testing for Hepatitis A becoming available, the identification and definition of NANB Hepatitis cases among all cases of hepatitis would become much more clear cut.

<sup>140</sup> Dr McClelland – Day 9, pages 106–107

<sup>141</sup> 'Viral Hepatitis: Report of a WHO Scientific Group', *World Health Organization Technical Report, Series 1979*, No. 512 [SGH.002.9746] at 9754 and 9762

**25.98** The natural history of NANB Hepatitis was assumed to be mild, or benign, until biopsy evidence began to change perceptions of its seriousness. It can now be seen that the assumption was wrong. The facts, however, are clear: for a significant period after the discovery that there had to be one or more viruses causing hepatitis that was neither type A nor type B, many experts thought that NANB Hepatitis was a mild or benign condition. The confusion and complexity arising from co-infection by both Hepatitis B and NANB Hepatitis, mentioned at the outset of this chapter, in many cases 'cloaked' any NANB Hepatitis infection for a period. Hepatitis B causing more overt clinical illness allied with the relatively un-symptomatic nature of NANB Hepatitis infection in most cases provides at least part of the answer to the problem.

**25.99** So far as positive identification of NANB Hepatitis viruses is concerned, the technology had not been developed: it was not developed until the very end of the 1980s. There was nothing that could have been done to identify the virus or viruses. In time, the dangers presented by NANB Hepatitis infection were recognised. As indicated in Chapter 15, *Knowledge of Viral Hepatitis 2 – 1975 to 1985*, Patrick Mollison's textbook on blood transfusion medicine indicated a view in 1983 (the end of the current period of discussion) that NANB Hepatitis was as a rule symptomatically mild, though a majority of patients had abnormal liver enzyme results and 10% of liver biopsies showed evidence of cirrhosis. Knowledge of the risk was beginning to emerge. Whether anything could have been done to reduce risk, while making available therapeutic materials for treatment of coagulation defects, blood and blood components for transfusion, short of the development of an effective assay, is discussed in Chapter 27, *Surrogate Testing of Donated Blood for non-A, non-B Hepatitis*.

**25.100** The proposal to set up an Advisory Group on Viral Hepatitis, together with the Maycock Group and the MRC and BTS initiatives (discussed in Chapter 15, *Knowledge of Viral Hepatitis 2 – 1975 to 1985*) indicate a more structured approach by the Health Departments and National Health Service agencies to obtaining advice on hepatitis generally from the early 1980s onwards. The developments are best understood in the context of specific topics. In general, however, it is clear that the early years of the 1980s marked a change in the appreciation of the nature of the risks of transmission of viral hepatitis. Hepatitis B remained a significant problem. The importance of NANB Hepatitis was beginning to be appreciated.

## Conclusions

**25.101** In about 1983, on the eve of the AIDS epidemic as it was to develop in the UK, Hepatitis B was known to be a disease with potentially serious outcomes for patients. It was known that HAV was almost never transmitted by blood, while HBV was not the only hepatitis virus that presented risk of transfusion-transmitted hepatic disease. However:

- Screening tests for Hepatitis B remained imperfect and were still believed to fail to identify a significant minority of Hepatitis B infected donations.
- Samples testing negative for Hepatitis B (and, where tested for Hepatitis A, also negative for that infection) necessarily still included an unknown proportion that were infected with Hepatitis B and an unknown proportion that were infected with NANB Hepatitis or both.
- The exact proportion of donations infected with NANB Hepatitis could not be determined by exclusion using existing screening tests for Hepatitis A and Hepatitis B.

- There was no serological or other screening test for the NANB Hepatitis agent of transmission.
- Knowledge of the prevalence of NANB Hepatitis in the UK, including Scotland, was at a very early stage of development.
- Because of the emphasis on clinical symptoms and overt jaundice as indications of viral hepatitis, NANB Hepatitis was thought to be rare in Scotland.
- NANB Hepatitis was generally thought to have a benign prognosis.
- The risks for the patient that might be associated with the transmission of NANB Hepatitis were thought to be low relative to the risks associated with the conditions for which they required blood transfusion in surgery or in medical treatment of their primary conditions.





## CHAPTER 26

### DONOR SELECTION – HIGHER RISK DONORS

#### Introduction

**26.1** This chapter sets out donor selection policies and practice in the 1970s and early 1980s relating to the acceptance of blood from particular groups of donors who, either at the time or with the benefit of hindsight, might be considered to present a higher risk of transmitting hepatitis viruses than the general population. The main groups under discussion in the chapter are intravenous drug users and prisoners. Military personnel from the USA are also discussed.

#### Intravenous drug use

**26.2** Intravenous drug users (IVDUs) presenting at ordinary SNBTS public sessions as prospective donors would be received, interviewed and observed as would any other member of the general public. The prospects of their identification as IVDUs would be related to general practice at interview and observation of the prospective donor, as discussed in Chapter 18, *Collection of Blood – General*. In relation to prospective donors who used or were suspected of using intravenous drugs, particular questions arise in the case of those detained in penal institutions. That topic is discussed later in this chapter.

**26.3** It was a feature of the evidence about donor selection from the earliest years of the reference period that a recent or current history of injecting drugs, or physical evidence of having injected drugs, was seen as a ground for exclusion. Whether the prospective donor would have been asked about drug use was a different matter, however. As noted in Chapter 18, *Collection of Blood – General*, there was relatively little face-to-face questioning of donors presenting at sessions. Intravenous drug use was not necessarily one of the features drawn to the prospective donor's attention as affecting their suitability as a donor. Dr Brian McClelland, who joined the Edinburgh and South East of Scotland Blood Transfusion Service (BTS) as a Consultant in 1977 and became Regional Director in 1979, thought that the majority of staff would have asked about drugs, but he could not be sure that it happened in the period before routine questioning of the donor was instituted in his area in 1982 or 1983.<sup>1</sup>

**26.4** A new comprehensive guide was prepared at that time, in response to the observations of the Medicines Inspectorate, for use in the Edinburgh and South East of Scotland BTS. The copy of the guide recovered by the Inquiry is only partly legible. In relation to drug use, however, the guide advised SNBTS staff to consult the doctor or sister on duty. As general guidance, it stated:

At least 6 months should elapse after the use of parenteral drugs because of the risk of serum-hepatitis.

Donors under the influence of oral drugs should not be accepted.

In both cases, bear in mind the possibility that the history given by these donors regarding the abuse of drugs may be unreliable.<sup>2</sup>

---

<sup>1</sup> Chapter 18, *Collection of Blood – General*

<sup>2</sup> SEBTS Response to Medicines Inspectorate [SGH.003.5059] at 5101

**26.5** Temporary deferment of IVDUs appears to reflect a view that a six-month deferment period was sufficient for Hepatitis B to have become detectable on screening. On the copy available to the Inquiry is a manuscript note: ‘International policy’.<sup>3</sup> Such a policy, however, would not have excluded donors who had become infected with non-A, non-B Hepatitis (NANB Hepatitis) as a result of injecting drug use.

**26.6** So far as Glasgow and the west of Scotland was concerned, the evidence of Mrs Rosalind Prior, who was employed by the SNBTS as a Mobile Team Assistant in the region between 1969 and March 1974, was that in the early 1970s staff were never told to ask any donors if they had ever used intravenous drugs.<sup>4</sup> Dr Ruthven Mitchell, Director of the Glasgow and the West of Scotland BTS from 1978 to 1995, stated that:

Throughout the life of the UK transfusion services, it was always thought that donors were selected on the basis of ‘tinker, tailor, soldier, sailor, rich man, poor man, beggar man, thief’, great efforts are made to avoid any discrimination.<sup>5</sup>

**26.7** He was, however, quite clear that known drug addicts were not to be bled as donors.<sup>6</sup>

**26.8** In international guidance, an association between intravenous drug use and transmission of Hepatitis B was noted before the beginning of the reference period. The 1971 World Health Organization (WHO) *Guide to the Formation and Operation of a Transfusion Service*<sup>7</sup> stated that, during the physical examination of the blood donor, ‘the medical officer should be able to pick out those prospective donors who may be, for example ... drug addicts’.<sup>8</sup> Dr McClelland’s evidence was that the interview routine was supplemented by observation.<sup>9</sup> A matter of interest for SNBTS staff would be whether, when the donor’s arm was exposed to take a sample, evidence of needle injection tracks might be disclosed. It is not clear to what extent a ‘physical examination’ was carried out in the first half of the 1970s, however. Mrs Prior’s account of the procedure in her area does not mention what the doctor in attendance at donor sessions did routinely.

**26.9** Relying on such observation as was possible in those circumstances, was never likely to expose all prospective donors who might transmit viral infection. Needle track marks on the lower arm of a person currently using drugs by injection might or might not have been identified during the process of taking a blood sample while evidence of injection elsewhere on the body would not. As was to be recognised at least by 1987,<sup>10</sup> the problem was related to the risk of parenteral transmission at any time during the individual’s life: injection of controlled drugs might have ceased long before the donor session or might have been a single act of an individual otherwise free from the use of illicit drugs.

**26.10** In the United Kingdom, the problem of drug use was dealt with under the Misuse of Drugs Act 1972, in which the range of offences recognised both the use and supply of controlled drugs as social problems that required to be addressed. On the evidence before

<sup>3</sup> The ISBTS Guide *Criteria for the selection of blood donors* [DHF.001.2672] applied a six-month cut off for measures aimed at reducing the risk of transmission of viral agents. See Chapter 18, *Collection of Blood – General*, paragraph 18.91, and paragraph 26.250 et seq below.

<sup>4</sup> Mrs Prior’s Written Statement [PEN.019.0107] at 0110. See also Chapter 18, *Collection of Blood – General*, paragraph 18.38

<sup>5</sup> Dr Mitchell’s Witness Statement [WIT.003.0106]

<sup>6</sup> Day 9, page 152

<sup>7</sup> WHO Guide [PEN.002.0462]. The guide was edited by CC Bowley, KLG Goldsmith and W d’A Maycock on behalf of the International Society of Blood Transfusion and the League of Red Cross Societies, with contributions from experts from England, Canada, France, the Netherlands and Switzerland.

<sup>8</sup> WHO Guide [PEN.002.0462] at 0488

<sup>9</sup> Day 9, page 20; Chapter 18, *Collection of Blood – General*, paragraphs 18.40–18.41

<sup>10</sup> Paragraph 26.20 below.

the Inquiry, it appears that drug use was not recognised as a problem in prisons until later in the reference period. In transfusion practice in the USA, intravenous drug was probably initially a problem, reducing somewhat as paid donation reduced and then ceased. There was a tendency, however, for paid donors, drug addicts and other disadvantaged members of society to be grouped together by commentators.

**26.11** Since the establishment of the Scottish National Blood Transfusion Association (SNBTA) in 1940, paid donation had not been a practical issue in Scotland, so far as transfusion and the manufacture of NHS blood products were concerned.<sup>11</sup> In other respects, however, Scotland experienced a similar range of problems.

**26.12** In 1973 the WHO published a report of a meeting of an expert scientific group on viral hepatitis.<sup>12</sup> In a section on 'Changing patterns of infection in certain developed countries', the report commented on an increasingly large proportion of cases of Hepatitis B infection, particularly among males in the 15–29 year age group, suggesting a likely association with the illicit use of drugs.<sup>13</sup>

**26.13** In December 1975 a *World in Action* television programme, 'Blood Money', was broadcast in the UK. The programme was about the risk of transmission of hepatitis from blood products manufactured by US commercial companies using blood taken from high-risk paid donors.<sup>14</sup> Professor Arie Zuckerman, who was to play a central role in developing policy advice on blood transfusion in the UK, was quoted in the programme:

Well it's been recognised for a number of years now that bought blood does carry a higher risk. And it's difficult to actually pinpoint the reason, but it seems that individuals who are willing to sell their blood are normally from a background which appears to be rather poor socio-economically.

In the past, many of them were alcoholics and indeed the well known dictum which originated in the United States was Ooze for Booze. This has recently been replaced by perhaps a more serious element, namely drug addicts.<sup>15</sup>

**26.14** Two US researchers, Dr Harvey Alter and Dr Leonard Seeff, commenting on commercial blood collection, noted that:

Prior to the advent of hepatitis serological assays, by far the most important hepatitis risk factor identified was the origin of the donor blood.<sup>16</sup>

**26.15** By 1975, when Professor Zuckerman made his observation that 'bought blood does carry a higher risk', the broad group of individuals thought to present risk had not changed. Risk was associated with poor, socio-economically disadvantaged people but the characteristic behaviour that was the subject of comment had moved from alcohol to drug use.

<sup>11</sup> As noted in Chapter 17, *Blood and Blood Products Management*, paragraph 17.20, the Scottish National Blood Transfusion Association (SNBTA) was formally constituted on 5 March 1940. The organisation was renamed the Scottish National Blood Transfusion Service (SNBTS) in 1974. Paragraph 17.13 notes that small payments or other forms of reward had been made to donors in some areas in Scotland prior to the establishment of the SNBTA but that, with the formation of a national service, paid donation was phased out and voluntary donations became the norm.

<sup>12</sup> Viral Hepatitis – Report of a WHO Scientific Group [SGH.002.9746]

<sup>13</sup> Ibid [SGH.002.9746] at 9755

<sup>14</sup> A transcript of the programme is available at [PEN.013.1400]

<sup>15</sup> Transcript [PEN.013.1400] at 1404

<sup>16</sup> Alter and Seeff, 'Transfusion-associated hepatitis' in Zuckerman, AJ and Thomas, HC (eds) *Viral Hepatitis: Scientific Basis and Clinical Management*, 1993, Churchill Livingstone, Oxford, page 473

**26.16** The move away from collecting blood from paid donors began in the USA in the early 1970s as a result of the higher incidence of post-transfusion hepatitis associated with such donations. In 1974, Alfred Prince and others reported that, in their series of investigations, the risk of non-B Hepatitis was 10 times higher among recipients of blood obtained from commercial sources than among those given blood from volunteer donors.<sup>17</sup>

**26.17** It appears that, as paid donation in the USA was phased out, there was greater emphasis on identifying donor groups that presented increased risk of transmission of infection by reason of their behaviour. In a paper published in February 1976 on 'Blood Transfusion and Transmissible Disease', Dr John Wallace, at that time Director of the Glasgow and the West of Scotland BTS, noted that, '[g]roups known to have a high prevalence of antigenaemia [a high prevalence of Hepatitis B antigen] include immigrants or returned travellers from tropical areas, drug addicts, male homosexuals, prisoners, the tattooed and the sexually promiscuous'.<sup>18</sup> Although Scotland did not have an issue with paid donation, parts of the country, and in particular Edinburgh, came to be associated with serious drug use and there was increasing emphasis on excluding those using intravenous drugs from donation.

**26.18** The International Society of Blood Transfusion (ISBT) Guide *Criteria for the selection of blood donors* published in 1976,<sup>19</sup> in a section on viral hepatitis, listed groups of prospective donors who should be excluded from donating blood. The list included those 'suspected to be parenteral drug addicts'.<sup>20</sup> The use of the present tense 'to be' may suggest a focus on current, or at least recent, drug use. In addition, in a section on medication and drugs, the document stated:

Those who admit to occasional use of marijuana, LSD, and similar hallucinatory drugs may be accepted if they have not taken any in the previous 72 hours and their arms show no signs of needle-puncture marks or scars indicating that they might have been taking drugs parenterally. Regular users of hallucinatory drugs may, however, be unable to give an accurate history with regard to injectable narcotics or exposure to hepatitis; for this reason they should be disqualified.<sup>21</sup>

**26.19** Dr McClelland received the ISBT documents but did not know whether this guidance influenced thought and practice in Scotland at the time.<sup>22</sup> His general evidence, however, was that evidence of drug use disqualified potential donors.

**26.20** From 1974, the CSA had the duty of providing blood supplies for transfusion and for the production of blood fractions. However, the Regional Transfusion Centres remained largely autonomous entities as far as many professional matters were concerned. The SNBTS stated that, in respect of blood donor selection, the Regional Transfusion Director (RTD) and his/her consultant colleagues determined their own local policies and issued guidance to medical and nursing staff.<sup>23</sup> From 1977 to about 1982, when the SESBTS produced their own guidance, all RTDs used the *Memorandum on the Selection, Medical*

<sup>17</sup> Prince et al, 'Long incubation post transfusion hepatitis without serological evidence of exposure to Hepatitis-B virus', *The Lancet*, 1974; 2:241–6 [LIT.001.0363] at 0367

<sup>18</sup> Wallace, 'Blood transfusion and transmissible disease', *Clinics in Haematology*, 1976; 183 [PEN.015.0492] at 0495

<sup>19</sup> ISBT Guide *Criteria for the selection of blood donors* [DHF.001.2672]

<sup>20</sup> Ibid [DHF.001.2672] at 2684

<sup>21</sup> Ibid [DHF.001.2672] at 2683

<sup>22</sup> Day 9, page 124

<sup>23</sup> SNBTS, 'Collection of Blood in Prisons', 2011 [PEN.018.1521] at 1525. See similar comments by Dr McClelland in his statement [WIT.003.0072]

*Examination and Care of Blood Donors* prepared on behalf of the NBTS in 1977 and amended in 1983, 1985 and 1987 for guidance. In 1985, it was agreed that the SNBTS should prepare guidance for Scotland based on the SESBTS documents. The 1977 version of the NBTS *Memorandum* stated that ‘illicit drug taking if suspected or admitted should debar’.<sup>24</sup> That wording persisted in the 1983 version of the same memorandum but, in addition, under the section on ‘Medical History’ the document indicated in relation to ‘Drug Abuse’ that disqualification should occur.<sup>25</sup> The 1987 edition advised staff who might be concerned that a potential drug user had presented as a donor to consult the sister or doctor and stated: ‘Anyone who has ever injected drugs to be deferred permanently’.<sup>26</sup>

**26.21** The express recognition in 1987 that risk may have been created in the past as much as by current IVDU was a significant change of emphasis. The 1979 edition of the Department for Health and Social Security (DHSS) *Standards for the Collection and Processing of Blood and Blood Components and the Manufacture of Associated Sterile Fluids*, applicable throughout the United Kingdom, had stated that ‘[i]llicit drug taking’ would ‘disqualify a person from acting as a donor’.<sup>27</sup> As in the 1977 edition of the NBTS *Memorandum on the Selection, Medical Examination and Care of Blood Donors*, the question whether the prospective donor had ever taken drugs was not expressly addressed at that time.

**26.22** The ISBT guidance of 1976, that suspected drug addicts should be excluded from donating blood, was not universally followed. The response by the Edinburgh and South East of Scotland BTS to a report of the Medicines Inspectorate, published in January 1983, noted that, as a routine for all donors, a detailed health check questionnaire had been introduced.<sup>28</sup> The questionnaire did not, however, ask if the donor had a current or recent history of intravenous drug use, far less if they had ever injected drugs.<sup>29</sup> In addition, as noted in paragraphs 26.4 above, guidance on donor selection made available to staff in the Edinburgh and South East of Scotland BTS at that time, was to the effect that a history of intravenous drug use did not result in indefinite deferral but instead resulted in deferral for a period of at least six months, ‘because of the risk of serum-hepatitis’. However, in response to AIDS in 1983 a leaflet, ‘AIDS and Blood Transfusion’ issued by the Edinburgh and South East of Scotland BTS, included IVDUs among those at risk of contracting AIDS and asked them to avoid giving blood until a screening test was available.<sup>30</sup>

**26.23** A donor leaflet apparently in use by the Glasgow and West of Scotland BTS in 1983 listed a number of matters to be reported by prospective donors to the doctor in charge of the session.<sup>31</sup> It asked whether the donor had experienced a serious illness such as jaundice. Again, the leaflet did not ask whether the donor had a current or recent history of intravenous drug use or if they had ever injected drugs, nor were those questions contained in a donor leaflet seemingly in use in England and Wales in 1983.<sup>32</sup>

<sup>24</sup> Memorandum on the Selection, Medical Examination and Care of Blood Donors [SNB.002.5348] at 5352

<sup>25</sup> 1983 Guidance [SGF.001.0377] at 0378

<sup>26</sup> 1987 Guidance [SNB.006.6410] at 6415 (emphasis in original)

<sup>27</sup> Standards for the Collection and Processing of Blood and Blood Components and the Manufacture of Associated Sterile Fluids [PEN.002.0249] at 0253, para 1.5.1

<sup>28</sup> SEBTS Response to Medicines Inspectorate [SGH.003.5059] at 5063. See 26.105–26.110 below.

<sup>29</sup> SEBTS Questionnaire (appended to SEBTS Response to Medicines Inspectorate) [SGH.003.5059] at 5123

<sup>30</sup> Leaflet [SNF.001.3397] at 3398

<sup>31</sup> Glasgow and West of Scotland BTS Leaflet [PEN.013.1395]. Dr Mitchell has explained that though the date 6/6/83 is marked on the leaflet it was issued in about late April 1983.

<sup>32</sup> NBTS Leaflet [SGF.001.0397]. Professor Leikola of the Finnish Red Cross Blood Transfusion Service was examined on how donor sessions were conducted in Finland and did not think that the donor questionnaire in use in Finland in the late 1970s/early 1980s included a question as to whether the donor had ever injected or used drugs. That, however, changed in 1983 with the arrival of AIDS: Day 13, pages 20 and 73.

In this respect the Glasgow and West of Scotland leaflet was consistent with Mrs Prior's evidence about practice in the west of Scotland during the 1970s.

**26.24** In his evidence to the Inquiry, Dr McClelland stated that he could only be confident that the majority of staff would have asked donors about current or past drug use only from the early 1980s, when there was an awareness of AIDS.<sup>33</sup> Dr Mitchell was asked whether, in the late 1970s and early 1980s, it was the practice at donor sessions to ask donors if they had ever injected drugs. He replied, 'I think – no, I don't think so in the 1970s. I can't remember it being there. It might have been later in the consideration of AIDS'.<sup>34</sup> Professor John Cash, Medical Director of the SNBTS during much of the reference period, did not know whether donors were asked whether they had ever injected drugs but said, 'my gut feeling is certainly when we got into the area of AIDS, there was great difficulty for some of our staff asking very straight questions about people's lifestyles'.<sup>35</sup>

**26.25** Prior to the advent of AIDS, therefore, evidence of current or recent intravenous drug use, whether in the prospective donor's response to enquiry or by observation, had been recognised in published statements as a ground for exclusion for a considerable period. However, before the advent of AIDS there appears to have been no direct questioning of donors in relation to any recent or current history of intravenous drug use. Evidence of use of intravenous injection of drugs at any time in the past was beginning to be recognised as a ground for exclusion only in the later 1980s, as it came to be understood that NANB Hepatitis viraemia might persist indefinitely. Prior to the advent of AIDS reliance was placed on observation and donor responses to questionnaires.

## Prison collections

### *International guidance*

**26.26** There was limited guidance in international literature on the practice of collecting blood in penal institutions. The 1971 *Guide to the Formation and Operation of a Transfusion Service*, already mentioned in paragraph 26.8 above, recommended that countries setting up a donor recruitment scheme should take initial steps to form panels of donors within groups such as the armed forces, the police, large industrial or commercial undertakings, universities, prisons and social or religious foundations.<sup>36</sup> Since it was aimed at those with the responsibility of establishing and developing transfusion services in their own countries, it focused on the effectiveness of management of the new services rather than on specific risks.

**26.27** In defining preferential sources of blood, the aim of the 1971 Guide was to facilitate the early stages of development of a service where none had previously existed and the reference to the collection of blood from prisons has to be seen in that context. In addition, the *Guide* was written before, or at least around the same time as, evidence began to become available in the UK that prison donors had a higher prevalence of 'Australia antigen' (the early name for the Hepatitis B surface antigen, HBsAg) than non-prisoner donors. This is discussed more fully in Chapter 15, *Knowledge of Viral Hepatitis 2 – 1975 to 1985*. Having regard to these factors, it is not possible to rely on the recommendation in

<sup>33</sup> Day 9, pages 22–23

<sup>34</sup> Ibid pages 153–154

<sup>35</sup> Day 10, page 77

<sup>36</sup> WHO Guide [PEN.002.0462] at 0475. The guide was edited by CC Bowley, KLG Goldsmith and W d'A Maycock on behalf of the World Health Organization, the International Society of Blood Transfusion and the League of Red Cross Societies, with contributions from experts from England, Canada, France, the Netherlands and Switzerland.

the *Guide* to form donor panels in prisons in drawing particular inferences about practice in Scotland.

**26.28** The ISBT *Criteria for the Selection of Blood Donors* proposed in 1976 that prospective donors should be excluded if they were ‘inmates of a correctional institution’.<sup>37</sup> As noted in paragraph 26.19, Dr McClelland did not know whether the ISBT guidance influenced thought in Scotland in the late 1970s and early 1980s.

**26.29** In 1978 the WHO Expert Committee on Biological Standardization published a report.<sup>38</sup> The report noted that it had been agreed that it would be useful to have a single set of requirements applicable to all organisations and laboratories involved in the collection of blood for fractionation and for blood products. It also set out a range of proposals in an Annex on *Requirements for the Collection, Processing and Quality Control of Human Blood and Blood Products*.<sup>39</sup> In respect of individuals who might fall within proscribed groups, the report stated:

Donors shall have a negative history of viral hepatitis, of close contact with an individual with hepatitis within six months, of receipt within six months of human blood or any blood component or fraction that might be a source of transmission of viral hepatitis, or of tattooing within six months.

....

Donor populations showing a prevalence of acute or chronic hepatitis higher than that found in the general population should be avoided for collection both of single donor products (whole blood and its components) and of plasma for pooling for the manufacture of plasma fractions known to be capable of transmitting hepatitis, such as clotting factor concentrates.<sup>40</sup>

**26.30** As regards the last recommendation quoted, Professor Juhani Leikola of the Finnish Red Cross Blood Transfusion Service stated in his evidence to the Inquiry that he would not place much weight on a recommendation relating to the avoidance of a donor population showing ‘a higher prevalence of acute or chronic hepatitis than in the general population’. He explained that this is because (i) direct markers of disease (eg the presence of antigen) should be used when identifying a group with a higher prevalence of disease, rather than indirect markers such as ‘acute or chronic hepatitis’ and (ii) the recommendation does not say how much higher the prevalence of disease should be in a donor group for that group to be excluded. He also commented that the committee that produced the recommendation comprised biologists, virologists and fractionators rather than those with practical experience of blood collection or transfusion.<sup>41</sup> Subject to those reservations, which are accepted to be valid, the last paragraph would have applied to prison donor populations in Scotland in the later 1970s when data on the prevalence of HBsAg in prison populations became available.<sup>42</sup> Prison populations as such were not, however, targeted.

<sup>37</sup> ISBTS Guide *Criteria for the selection of blood donors* [DHF.001.2672] at 2684

<sup>38</sup> WHO Expert Committee on Biological Standardization – Twenty-ninth Report [LIT.001.3627]

<sup>39</sup> *Ibid* [LIT.001.3627] at 3640

<sup>40</sup> *Ibid* [LIT.001.3627] at 3651–52; Professor Leikola Day 13, pages 57–58

<sup>41</sup> Day 13, pages 57–58

<sup>42</sup> Dr McClelland – Day 9, page 129



**26.31** None of the Scottish or UK guidance documents on the selection of donors contained any reference to the collection of blood from prisons or young offenders' institutions at this period. Reservations about collections from prisoners were expressed in the Annual Report of the Edinburgh and South East of Scotland BTS for 1973–74, which included an address given by Professor Anthony Ritchie, Chairman of the Central Consultative Committee of the SNBTS.<sup>43</sup> He contrasted donations of blood drawn from prisoners, where 'there is little enough "voluntary" aspect to donation', with the general British system in which virtually all blood donors were true volunteers.<sup>44</sup> There is no evidence that his views influenced practice at that time, however.

**26.32** The SNBTS Regional Directors were aware of the NBTB *Memorandum on the Selection, Medical Examination and Care of Blood Donors* and there was evidence that the RTDs based their donor selection policies on that document.<sup>45</sup> However, in this, as in other matters, the individual Transfusion Directors will have exercised their own discretion in the manner in which they did so. They had a high degree of autonomy in donor selection and it is not possible to state that there was uniform practice.

### *International practice*

**26.33** Reaction against collection in prisons started early in the 1970s in the United States of America. Professor Richard Titmuss' book *The Gift Relationship* had a powerful impact.<sup>46</sup> When he published, in 1970, it was well-established in the USA that there was a relatively high prevalence of serum hepatitis among certain donor populations and, in particular, among the 'cloistered residents of Skid Row' and prisoners.<sup>47</sup> The risk of transmission of infection associated with these groups was said to be at least ten times as great as that arising from voluntary donors.

**26.34** It was not until 8 June 1995 that the US Food and Drug Administration (FDA) issued a formal recommendation that current and recent inmates of correctional institutions should be deferred, for a period of 12 months from the last date of incarceration, as donors of whole blood, blood components, source leukocytes and source plasma.<sup>48</sup> While this timing may appear surprising, the FDA recommendation has to be seen in the context that blood transfusion practice in the USA was regarded as a matter for local rather than Federal regulation. In a paper submitted to the Inquiry, 'Collection of blood in prisons', for example, the SNBTS stated:

However as [Douglas] Starr recorded in his book, 'Blood' 'the Americans had stopped harvesting prison plasma for clotting factor by 1983 ...'. Although this was never formally documented, this is believed to be the case.

There was an informal (unpublished) agreement in late 1982 between the FDA and commercial companies to cease prison sessions ... (although it does appear that the American Red Cross may have still been collecting in prisons in 1983).<sup>49</sup>

<sup>43</sup> Annual Report [SGH.003.1305] at 1313

<sup>44</sup> Ibid [SGH.003.1305] at 1316

<sup>45</sup> Dr McClelland – Day 9, page 92 and Dr Gillon – Day 11, page 46. In addition, as noted below, the SNBTS had an input into at least the 1983 version of the Memorandum, through Dr Brookes' membership of the relevant Working Party.

<sup>46</sup> Titmuss, R. *The Gift Relationship*, 1970, George Allen and Unwin, London. Titmuss compared the blood donor system in England and Wales with that in the USA. See discussion in the Preliminary Report, paragraphs 5.39 to 5.42.

<sup>47</sup> Titmuss, R. *The Gift Relationship*, 1970, George Allen and Unwin, London page 204

<sup>48</sup> Memorandum dated 8 June 1995 by the Director, Center for Biologics Evaluation and Research, FDA, to all registered blood establishments, on 'Recommendations for the deferral of current and recent inmates of correctional institutions as donors of whole blood, blood components, source leukocytes and source plasma'. [PEN.012.0173]

<sup>49</sup> Collection of blood in prisons [PEN.018.1521] at 1530. See also the reference at the meeting of the English Transfusion Directors on 6 October 1971, noted below at paragraph 26.61, that the American Red Cross had from July 1971 stopped collecting blood from donors in correctional institutions.

**26.35** In addition, the Inquiry does not have sufficient evidence about the practice in the USA to place the FDA recommendation in its proper context or to draw any meaningful conclusions from it. In particular, the Inquiry has not heard evidence on how much blood was collected in US prisons, by which organisations and when, or the purpose to which any such blood or plasma so collected was put. A detailed investigation of these matters was outwith the Terms of Reference of the Inquiry. For these reasons, it would be difficult to draw any meaningful conclusions from a consideration of the FDA recommendation in isolation. Douglas Starr's comments appear to be a more reliable indication of when the practice stopped.

**26.36** Internationally, practice varied. The Canadian Red Cross ceased collecting donations from prison inmates in 1971 after results from the Hepatitis B surface antigen test demonstrated conclusively that prison inmates in Canada had a significantly higher prevalence of hepatitis than the rest of the population. The decision was made as a matter of Red Cross policy and not in response to regulation.<sup>50</sup>

**26.37** A study in Finland of carriers of Hepatitis B antigen and transfusion hepatitis was published in 1974.<sup>51</sup> The study found a higher incidence of Hepatitis B antigen among prisoner donors when compared with the non-prison donor population.<sup>52</sup> The author of the report, Dr Timo Helske, commented:

The high frequency of carriers among prisoners (0.9 per cent) was consistent with the findings by other investigators.

There is at present no satisfactory explanation for these differences between various population groups. Drug addiction has been suggested as one possibility, since drug addicts are found most frequently among young adults. Illicit use of drugs no doubt accounts for a part of the acute cases of hepatitis type B and consequently for a few of chronic antigenaemia with chronic hepatitis. Together with tattooings this might at least to some extent explain the high prevalence of carriers among prisoners.

The HBAG carrier state has been related to socioeconomic and hygiene factors. A low socioeconomic standard might favour the circulation and dissemination of hepatitis B virus.<sup>53</sup>

**26.38** Dr Helske went on to note that in Finland, 'prisoners are indisputably a risk group in which a high HBAG carrier rate appears to be associated with a high risk of acute and chronic hepatitis'.<sup>54</sup> By the time Professor Leikola joined the Finnish Red Cross Blood Transfusion Service in February 1975, a decision had already been taken to stop collecting blood in prisons.<sup>55</sup> Professor Leikola considered it likely that the decision was taken on the basis of Dr Helske's study. He commented on two factors. Firstly, it was realised that not all Hepatitis B cases were recognised by the HBsAg test and that a good part of the people who screened negative were still carrying the Hepatitis B virus, then known to be the cause of potentially serious disease. Secondly:

<sup>50</sup> Krever Commission of Inquiry on the Blood System in Canada, Final Report, Part III, page 618, <http://publications.gc.ca/collections/Collection/CP32-62-3-1997-2E.pdf> (last accessed 7 January 2015)

<sup>51</sup> Helske, 'Carriers of Hepatitis B Antigen and Transfusion Hepatitis in Finland', *Scandinavian Journal of Haematology*, 1974, Supplementum No.22 [LIT.001.3562]

<sup>52</sup> Ibid [LIT.001.3562] at 3571–72. The mean HBAG carrier rate among donors was found to be 0.16% whereas the frequency among prison donors was found to be 0.9% (at 3614).

<sup>53</sup> Ibid [LIT.001.3562] at 3577–78

<sup>54</sup> Ibid [LIT.001.3562] at 3611

<sup>55</sup> Written Statement by Professor Leikola, 'Donations in prisons and donors with jaundice' [WIT.003.0027]. See also Day 13, page 25.

In addition to that, [there] was the possibility of other viruses existing and [the] probable existence of other viruses. So if we would avoid transfusing Hepatitis B, that was not detectable by those tests that were used at that time, then an additional factor was that we would also avoid those viruses that presumably were also within prisoners.<sup>56</sup>

**26.39** When preparing his written statement to the Inquiry, Professor Leikola had discussed the collection of blood in prisons with Dr Helske. In oral evidence, Professor Leikola stated:

I discussed this matter with him and he said that he didn't remember when it was formally decided but he told me that when he showed his findings to Professor Nevanlinna,<sup>57</sup> Professor Nevanlinna was, let's say, almost shocked, when he saw the difference between the prisoners and the donors in the general population. They had also thought that maybe within [the] army, where the conscripts would come voluntarily and in groups and so on, that was not a closed institution but not very far from that. They were a little bit afraid whether there would be a higher incidence of Hepatitis B also and they were quite relieved when they saw that it was 0.2 per cent, which was the same as from mobile units from the Helsinki larger area.

Dr Helske told me that after he had shown these results to Professor Nevanlinna, these were discussed by the senior staff and everybody agreed that, because of this high prevalence, it was probably much safer to stop the donations at prisons, especially because only a small proportion of the blood supply was coming from prisons.

If I may add here, I have the feeling that these results were discussed at the meeting of the Council of Europe expert committee in May 1974. I was not personally involved so I have been thinking of these connections, because in the same group there was Dr Maycock from the UK. He was representing the UK to that group. There were Dr Moore, Dr Freiesleben from Copenhagen, Dr Hogman from Stockholm who wrote this ISBT recommendation,<sup>58</sup> including also avoidance of prisons as a source of blood.

So I think that this has been discussed at that time within a larger European group, especially because Dr Helske refers here to the finding being of similar magnitude as in other Scandinavian countries. And I'm quite sure that he refers to Sweden and Denmark and therefore these people were aware of the higher incidence of Hepatitis B antigen within prison inmates.<sup>59</sup>

**26.40** The practice of other European countries in respect of the collection of blood in prisons is helpfully shown in a 2004 survey conducted by the European Blood Alliance (EBA).<sup>60</sup> The Table 26.1 in the Appendix to this chapter contains a summary of replies of the EBA member states.<sup>61</sup>

<sup>56</sup> Day 13, page 94. See also pages 36-37.

<sup>57</sup> Director of the Finnish Red Cross Blood Transfusion service between 1948 and 1988.

<sup>58</sup> That is, the 1976 ISBT guidance referred to above [DHF.001.2672]

<sup>59</sup> Day 13, pages 38-39

<sup>60</sup> The European Blood Alliance is an association of not-for-profit blood establishments, with 22 members throughout the European Union and EFTA States.

<sup>61</sup> The table is appended to the SNBTS paper, 'Collection of blood in prisons' [PEN.018.1521] at 1541. (In fact, as can be seen from the next table, collections in prisons in the west of Scotland region continued into early 1984, albeit on a greatly reduced scale, ceasing in March of that year.)

**26.41** There was a clear difference of practice among European blood transfusion services in respect of collecting blood from prisoners. In particular, as reflected in the table:

- Some countries never collected blood from prisoners (Denmark, the Netherlands<sup>62</sup> and Eire).
- Some countries introduced a permanent or temporary deferral of blood collected from prisoners in the 1970s (Switzerland, 1970;<sup>63</sup> Belgium, mid-1970s; Finland, 1975).
- Some countries ceased the collection of blood from prisons in the 1980s (England and Northern Ireland, both 1983; Scotland, 1984; Luxembourg, 1985; France, 1985–89).<sup>64</sup>
- Other countries did not introduce permanent or temporary deferral of blood donation by prisoners until the 1990s (Portugal, 1990; Austria, 1995; Germany, 1996; Norway, 1997).<sup>65</sup>

### Collection of blood in Scottish penal institutions

**26.42** The evidence obtained by the Inquiry indicates that blood was collected from penal institutions in Scotland from at least 1957 until the last prison session took place in each individual region.<sup>66</sup> The last prison donor sessions took place respectively in the south east (Edinburgh) on 22 December 1981; north (Inverness) on 24 February 1983; north east (Aberdeen) on 28 July 1983; east (Dundee) on 2 August 1983; and west (Glasgow) on 25 March 1984.<sup>67</sup>

**26.43** The donations collected in each Scottish RTC between 1971 and 1984, as shown in extant records, are shown in Table 26.2 in the Appendix to this chapter.

**26.44** The percentage of total blood donations in Scotland collected from penal institutions fell from 2.38% in 1975 (5915 of 248,558 donations) to 0.11% in 1984 (342 of 308,617 donations), with an annual average over that period of 1.097%.<sup>68</sup>

<sup>62</sup> It was also Professor Leikola's understanding, based on discussion with Professor van Aken of the Netherlands Red Cross Blood Transfusion Service, that the Netherlands never collected blood in prisons: Day 13, pages 58–59

<sup>63</sup> See also the evidence of Professor Leikola – Day 13, pages 59–62

<sup>64</sup> See also the evidence of Professor Leikola – Day 13, pages 62–64

<sup>65</sup> See also the discussion in the SNBTS paper 'Collection of blood in prisons' [PEN.018.1521] at 1529

<sup>66</sup> The commencement of the practice of prison collection in 1957 is taken from the SNBTS paper 'Collection of Blood in Prisons' [PEN.018.1521] at 1525.

<sup>67</sup> 'SNBTS Blood Collection 1975–1991' [PEN.010.0003] at 0012. The prisons visited by each RTC are listed in 'SNBTS Blood Collection 1975–1991 – further response' [PEN.010.0026] at 0028.

<sup>68</sup> In fact, these figures are likely to be slightly higher as the number of prison donations collected from the North RTC (Inverness) are not available as a result of records being destroyed in a flood – see para 1 of 'SNBTS Blood Collection 1975-1991' [PEN.010.0003]

**26.45** The donations collected by each Scottish RTC from penal institutions between 1971 and 1984, as shown in extant records, were:

**Table 26.3: Donations collected at Penal Institutes in each Scottish RTC 1971–84**

Year	Region				
	West RTC	South east RTC	East RTC	North east RTC	North RTC*
1971	n/a	1126	n/a	n/a	
1972	n/a	902	n/a	n/a	
1973	n/a	875	n/a	n/a	
1974	2716	973	905	531	
1975	3532	807	952	624	
1976	501	792	780	560	
1977	1462	264	886	98	
1978	1929	151	840	516	
1979	2516	689	716	450	
1980	1920	283	770	91	
1981	2274	203	609	274	
1982	1526	0	543	287	
1983	2622	0	322	176	
1984	342	0	0	0	

\* From 1971 to 1983 NRTC visited 1 prison, Inverness (Porterfield) Prison. Donation numbers are not available as the records were lost in a flood.

**26.46** With the exception of 1976, in each year between 1974 and 1984, Glasgow and the West of Scotland collected the greatest number of donations from prisons (averaging about 59% of the total for the period). The West, having the largest centre of population in Scotland, accounted for around 47–50% of all donations collected in Scotland over the period for which total donation values are available. Prison collections made a proportionately higher contribution to total donations in that region than elsewhere in Scotland.

**26.47** Caution is needed when interpreting these figures on an annual basis.<sup>69</sup> In all regions, at some periods while the practice continued, prison donations were collected at certain times in the year rather than throughout the year, in some instances to plug a gap in the supply from the non-prison population. For a local holiday week, the prison collection might have been more than half the transfusion centre's total supply and critically important.<sup>70</sup> As Professor Cash understood it from Dr Mitchell, it was believed that the Glasgow Fair holiday would have created a significant problem but for collections in prisons at certain periods.<sup>71</sup> The annual average underestimated the impact that would follow from ceasing prison sessions during such vulnerable periods.

<sup>69</sup> Professor Cash's Witness Statement [WIT.003.0120] at 0120–21

<sup>70</sup> Professor Cash – Day 10, page 18

<sup>71</sup> Ibid page 19

**26.48** The pattern of collections in prisons has to be considered in the light of historical facts, so far as they can be ascertained. Much of the written material dealt with drug addicts, paid donors and inmates of penal institutions together and is taken as a whole where necessary, since context and the sense of the evidence may be lost by selective citation.

### *Conduct of prison sessions*

**26.49** A question arises whether, during the periods when blood was collected in prisons, borstals and other similar institutions, any modification of the procedures at routine donor sessions was adopted to reflect the particular circumstances of the closed environment and the particular population involved.

**26.50** So far as SNBTS policy was concerned, the conduct of donor sessions in penal institutions was, as far as possible, identical to that of donor sessions anywhere else. The sessions were arranged through a member of staff in the institution, usually the director, who would delegate organisation to a medical officer. The dates were set well in advance. The same mix of personnel attended. SNBTS staff would work on the premise that the donors were volunteers when they attended. Dr McClelland acknowledged that there would be discussion around the nature of volunteering in a penal institution. For the purpose of the sessions, however, it had to be accepted that the donors were volunteers. Dr McClelland was unaware of there being any ‘unique’ or ‘explicit’ measures for sessions in prisons.<sup>72</sup>

**26.51** Superficially, the structure of donor sessions was in accord with that description. The evidence of Mrs Rosalind Prior on the practice in Glasgow and the west of Scotland in the early 1970s up to the beginning of the reference period has been set out in Chapter 18, *Collection of Blood – General*, paragraph 18.38.

**26.52** Mrs Prior’s account emphasised the degree of dependence on donor recollection and reliability that was inherent in the system. In relation to prison sessions, she said:

When we attended the prisons to collect blood from prisoners it was the same process. However, as it was generally a bigger set-up we would generally have more staff present. During the year the mobile unit attended Shotts, Polmont, Corntonvale, Lowmoss and Barlinnie prisons. The unit always attended Barlinnie Prison for the two weeks of the Glasgow Fair holiday in July. My impression was that the incentive for prisoners to donate blood was that it was just a way of getting away from what they would normally be doing. However, the prisoners at Barlinnie Prison, Glasgow told me that they had been informed by the “screws” (prison officers) that if they donated blood they would be given a cigarette and sugar. They were not pleased when they found out that this wasn’t the position ... I am asked whether there was any pre-selection/exclusion by the prison authorities of prisoners who were allowed to donate blood. I am unaware of whether there was or was not such a policy.

....

There was no difference in the procedure, including questions asked, between prison and other donor sessions. I do not recall any suggestion being made that blood collected from prisons was different from blood collected elsewhere.<sup>73</sup>

---

<sup>72</sup> Day 9, pages 18–19 and 26

<sup>73</sup> Mrs Prior’s Written Statement [PEN.019.0107] at 0109–10

**26.53** Mrs Prior had identified two differences between donation by prisoners and donation by members of the general public. There was an opportunity to escape prison routine, even for a short period, and there was the potential for incentives to be offered, genuine or otherwise. So far as Mrs Prior's evidence is concerned, neither of these differences appears to be material for present purposes. A different perspective was presented by Dr Ewa Brookes. Prior to her appointment as Regional Director at the Dundee RTC in May 1981, Dr Brookes had worked as a Consultant in the South London RTC. She scheduled herself as session medical officer on three successive sessions in a London prison, possibly in 1978–79. She summarised her experience:

- While volunteers might mention a past history of jaundice, or a self-limiting illness long ago, any admission of recent injury, or an illness which might be a sign of weakness, eg heart disease or diabetes, was never made.
- If admission was made (one man told her of a myocardial infarct [heart attack] three weeks before), it was whispered, for fear of making him appear vulnerable to the other prisoners.
- Apart from the obvious attraction of a group of professionally courteous women as donor assistants, prisoners had a change of activity and an easier day after donating, so were keen to do so.<sup>74</sup>

**26.54** The third point gives a slightly different colour to the points made by Mrs Prior. The other two draw attention to an aspect of institutional life that made it much more likely that relevant information would be withheld by institutional donors than donors from the general public. Dr Brookes' response indicates that she was concerned about the practice. Following these sessions, she met the Prison Medical Officer of the London prison she had attended (a senior and very busy man), indicating the reasons for the BTS prison sessions and the expectation that volunteers were pre-screened. She was forcefully advised that he had duties in more than one prison and many much greater problems than those of donor selection. The information was reported to her Director and discussed at the Senior Staff Meeting in her Transfusion Centre. It reinforced previously held concerns and the decision was made to phase out sessions in prisons and young offenders institutions.<sup>75</sup>

**26.55** The Inquiry sought the views of the Scottish Government about the role of prison medical officers. It was explained:

The Secretary of State had a statutory power to appoint prison officers, including medical officers (being medical practitioners duly registered under the Medical Acts), but in practice medical services were the responsibility of each respective prison; there was no national prison medical service. Each prison, other than Barlinnie which directly employed two or three full-time medical officers, had a contract with a local surgery or health centre. There could therefore be a number of different GPs providing medical services to each prison on a part-time basis. Medical officers received very little, if any, guidance from prison management, and the expectation was that they would

---

<sup>74</sup> Dr Brookes' Witness Statement [WIT.003.0057] at 0059

<sup>75</sup> Ibid [WIT.003.0057] at 0060. Dr Brookes went on in her statement to say: 'The desirability of stopping donor sessions in prisons and other corrective establishments was taken to an NBTS Directors meeting where it was felt that, in view of the Government recommendation outlined above [i.e. that prisoner donation was consistent with rehabilitation], this decision should not be made nationally without further consideration'. The consideration given by the NBTS to prison collection and government policy in that regard is discussed further below, in the chronological narrative section.

bring knowledge and independence from their respective general practices. This meant that the practice between, and even within, prisons was varied.<sup>76</sup>

**26.56** As regards the involvement, if any, of prison medical officers in the collection of blood at prisons the Scottish Government advised:

Up until 1983 SNBTS might visit each prison twice a year. Usually the chief nurse officer in each prison was the SNBTS contact and authorised the routine visits. Medical officers were not involved and, not attending the prison every day, often might not even have known the visit was taking place. Also, given that medical officers dealt with their prison patients on the same basis as community patients, in terms of confidentiality, the identities of those known to have been misusing drugs were not disclosed to SNBTS on a routine basis.

It is likely that the SNBTS doctors who attended the donor sessions would have been able themselves to identify those prisoners who were misusing drugs intravenously, through sight of needle marks.<sup>77</sup>

**26.57** In answer to a query as to whether any steps were taken by those in the prison medical service and/or by the Scottish Prison Service to prevent prisoners who were dependent on drugs or had a history of drug use from attending donor sessions in penal establishments, the Scottish Government replied:

We have been unable to ascertain whether any such steps were taken. Neither medical officers within prisons nor the government staff in the Scottish Prison Service were involved with SNBTS visits to prisons.<sup>78</sup>

**26.58** In summary, there was no evidence before the Inquiry that any additional steps were taken at prison donor sessions in Scotland to seek to screen out higher risk donors such as those who had ever injected drugs. The response from the Scottish Government noted above suggests that no such additional steps were taken, as does the evidence of Dr McClelland and Mrs Prior that there was no difference in the procedure, including questions asked, between prison and other donor sessions.

**26.59** Whether that was appropriate depends to a considerable extent on whether there were grounds for distinguishing donors in penal institutions from donors in the general public. The question is whether there were features of the prison population that gave rise to risks that were relatively greater than among donors from the general public. This question is discussed below.

### **Chronological narrative of United Kingdom views on prison collection**

**26.60** In the absence of any comprehensive statement of developing policy in the United Kingdom, and Scotland in particular, it is appropriate to set out a chronological statement of the evidence obtained.

---

<sup>76</sup> Letter dated 18 July 2011 from Ms Robson of the Scottish Government Legal Directorate to the Inquiry [PEN.012.1904], para 2, in response to a list of questions by the Inquiry [PEN.012.1782]

<sup>77</sup> Letter dated 18 July 2011 from Ms Robson of the Scottish Government Legal Directorate to the Inquiry [PEN.012.1904] at 1905–06, para 4

<sup>78</sup> Ibid [PEN.012.1904] at 1906, para 6



**1970-1974**

**26.61** At a meeting of the English and Welsh RTDs on 6 October 1971,<sup>79</sup> it was noted that the American Red Cross had stopped collecting blood from donors in correctional institutions from July 1971, because it was generally accepted in the USA that the incidence of infective, but Australia antigen-negative, donations was higher among prisoners than from voluntary unpaid donors and because the incidence of Australia antigen among prisoners was ten times greater than among voluntary unpaid donors.<sup>80</sup> At the time, all RTCs collected blood in prisons, borstals or other similar institutions. The RTDs reported differing experiences and impressions.

**26.62** Several RTDs did not consider that the association of donations from such sources with cases of hepatitis was any greater than that of donations from other donors. Two reported a greater incidence of Australia antigen-positive (Au-positive: that is, positive for the Hepatitis B surface antigen HBsAg) results among prisoners than among other donors. Recorded discussion included comments on the great difficulty in following up prisoners found to be Au-positive and arranging for confirmatory tests, particularly after prisoners had been discharged. In one prison the names of donors were not given to the RTC. One attendee at the meeting, Dr Grant, said it was sometimes difficult to keep any record at all of prisoner donors. Another Director suggested that prison and borstal governors should be asked to prevent any individuals known to be or to have been a drug user from volunteering as a donor. The outcome was indecisive:

After further discussion the meeting ... decided that before considering whether to stop collecting blood in prisons etc. more information should be obtained about the association of such donations with cases of serum hepatitis.<sup>81</sup>

**26.63** The suggestion that prison authorities should be asked to prevent any individual known to be, or to have been, a drug user from volunteering as a donor came to naught. At a meeting of the English and Welsh RTDs on 12 January 1972,<sup>82</sup> several Directors reported that they had been informed by prison governors or medical officers that there were no drug addicts in the prisons concerned. It was suggested that any prisoner should cease to be a donor if their blood, whether HBsAg-positive or not, had been associated with a case of serum hepatitis. The minutes record that it was agreed to leave the matter until there was more information about the incidence of HBsAg-positive test results among inmates of prisons and borstals.<sup>83</sup>

**26.64** In March 1972 the *British Medical Journal* published a paper by Dr Wallace and colleagues at the Glasgow and West of Scotland RTC on the prevalence of Australia antigen in donors in that region.<sup>84</sup> During a period of one year all of 105,724 blood donations were tested for Australia antigen and its antibody using a modified immunoelectroosmophoresis (IEOP) test. It was found that, in donors tested for the first time, male prisoner donors had a significantly higher incidence of Australia antigen (0.65%) than non-institutionalised male donors (0.12%). In addition, non-institutionalised male donors had a higher incidence of Australia antigen than female donors (who had an incidence of 0.05%). Overall, the

<sup>79</sup> Minutes of Meeting [DHF.002.7687]. In accordance with normal practice, there was at least one representative from the Scottish National Blood Transfusion Association present at the meeting. Participants' names have been redacted from the minutes.

<sup>80</sup> Ibid [DHF.002.7687] at 7690–91

<sup>81</sup> Ibid [DHF.002.7687] at 7691

<sup>82</sup> Ibid [DHF.002.7687]

<sup>83</sup> Ibid [DHF.002.7687]

<sup>84</sup> Wallace et al, 'Total screening of blood donations for Australia (Hepatitis Associated) Antigen and its Antibody', *British Medical Journal*, 11 March 1972 [SGH.002.9831]

incidence of Australia antigen-positive donations among prison donors (0.65%) was just under seven times higher than that in males and females in the general public (0.10%). The authors stated:

The high incidence of Au antigen of ... 0.653% ... in men prisoners has no obvious explanation. Viral hepatitis is not a serious clinical problem in the two institutions concerned, and the positive donors are not drug addicts. What is not known is whether or not these men were Au positive at the time of their first imprisonment. The high incidence may be related to social habits and to hygiene.<sup>85</sup>

**26.65** Professor Leikola was of the view that, had he read Dr Wallace's article in 1972, he would probably have felt that the explanation for the higher prevalence of Hepatitis B in prison donors being due to 'social habits and hygiene' was a plausible one.<sup>86</sup> As noted below, his views were to change after reading Dr Helske's paper in 1975.

**26.66** The English and Welsh Regional Transfusion Directors met on 7 June 1972.<sup>87</sup> The Directors had made attempts to collect data reflecting the incidence of infection in the donor population from before the reference period. There was particular interest in the risk associated with prisoners, especially drug addicts. The results in England and Wales were reported.<sup>88</sup> An overall incidence of 1:1500 antigen-positive and 1:1300 antibody-positive donors was reported. No antigen- or antibody-positives were observed among 1449 armed forces donors (including US Air Force personnel). On the other hand, in two borstal institutions and two prisons, antigen and antibody were detected in one in 488 donors (total donations tested, 976). In a discussion on the incidence of Australia antigen in the general and other populations, it was noted that of 107 donations involved in 19 cases of serum hepatitis, the incidence among donors from prisons and borstals was the same as that among all donations collected, 'which might suggest that the risk attaching to blood from such donors (normally bled only once) was not, in fact, higher than that from new general public donors'.<sup>89</sup> The minutes note that, 'It was reported that RTC Edgware ... had discontinued collecting blood in prisons and borstal institutions'.<sup>90</sup> Various figures, based on small population sizes, were given for the incidence of Australia antigen in donations from prisoners and members of the public in different regions in England. The minutes note that, '[i]n view of these discrepancies the meeting agreed that further information should be collected before it was decided to discontinue collecting blood in prison and borstal institutions'.<sup>91</sup>

**26.67** The English and Welsh RTDs next met on 20 September 1972.<sup>92</sup> Detailed returns from the English regions indicated a significantly higher incidence of Australia antigen among prisoners than among the general and university populations.<sup>93</sup> By then, almost all donations were being tested and quarterly returns of positive tests were required.<sup>94</sup> The minutes record discussion of a donor who was found to be Australia antigen-positive

<sup>85</sup> Ibid [SGH.002.9831] at 9832

<sup>86</sup> Day 13, page 77

<sup>87</sup> Minutes of Meeting [DHF.002.7651]. Again, there were representatives from the SNBTA and SHHD present.

<sup>88</sup> Ibid [DHF.002.7651] at 7658

<sup>89</sup> Ibid [DHF.002.7651] at 7658–59

<sup>90</sup> At the next meeting of the English and Welsh RTDs on 20 September 1972 the minutes were corrected by deleting 'RTC Edgware and all Scottish RTCs' and by substituting 'RTCs Edgware and Brentwood'. See Minutes of Meeting [DHF.002.8014] at 8015

<sup>91</sup> Minutes of Meeting [DHF.002.7651] at 7659

<sup>92</sup> Minutes of Meeting [DHF.002.8014]

<sup>93</sup> Revised minutes of meeting of 20 September [DHF.002.8022] at 8026 (Appendix 1)

<sup>94</sup> Minutes of Meeting [DHF.002.8014] at 8019

in prison and, before the result could be confirmed or the donor informed, he had been released and all trace of him lost. The RTC of the region where he was thought to live and neighbouring RTCs had been informed. It was agreed that the names and addresses of untraced Australia antigen-positive donors should be sent under confidential cover to all RTCs. The minutes noted that Edinburgh and Glasgow RTCs were collecting blood from prisons and that, 'In Edinburgh the incidence of Australia antigen positive tests in prisoners is no higher than among the general population; in Glasgow the incidence in prisoners is significantly higher'.<sup>95</sup>

**26.68** The minutes include an appendix showing the incidence of Australia antigen among different groups of donors at the Sheffield, Tooting, Bristol, Cambridge and Wessex RTCs in 1971–72.<sup>96</sup> In each RTC the incidence of Australia antigen among prison donors was significantly higher than that among the general public. Overall, the incidence of Australia antigen in these centres among prison donors was 0.373% (22 Au-positive donors out of a total of 5903 prison donors), compared with an overall incidence of Australia antigen among the general public at these centres of 0.051% (175 Au-positive donors out of 342,948 donors). Investigations over the middle of 1972 had shown that the incidence among prison donors in these English regions, of just over seven times that in donations from the general public, was similar to the increased incidence of Australia antigen reported in prison donors in Glasgow and the west of Scotland.<sup>97</sup>

**26.69** The English and Welsh RTDs met on 26 September 1973.<sup>98</sup> Representatives from the Scottish Home and Health Department (SHHD) and the SNBTA were present. An SNBTA Director had also been present at the meetings held in October 1971 and June 1972. It was noted that the incidence of Australia antigen in prison donors was higher than in the general public.<sup>99</sup> It was recorded that the adjusted data appeared to show that the frequency of antigenaemia among members of the armed forces was similar to that among new donors from the general public. The minutes state:

The meeting considered whether NBTS should stop collecting blood in prisons. Seven directors<sup>100</sup>... thought prisoners should no longer be bled because the incidence of antigenaemia not detectable by IEOP was probably higher in this population than among the general public. Seven<sup>101</sup>... thought that screening for antigen gave adequate protection, and that blood collection in prisons should be continued until the statistical significance of the figures in RTD(73)25<sup>102</sup> had been examined. [Name redacted] undertook to arrange this. It was agreed that if it were decided to discontinue bleeding prisoners, the Department should inform the Home Office before any local action was taken.<sup>103</sup>

<sup>95</sup> Ibid [DHF.002.8014] at 8020

<sup>96</sup> Revised minutes of meeting of 20 September [DHF.002.8022] at 8026 (Appendix 1)

<sup>97</sup> Wallace et al, 'Total screening of blood donations for Australia (Hepatitis Associated) Antigen and its Antibody', *British Medical Journal*, 11 March 1972 [SGH.002.9831]

<sup>98</sup> Minutes of Meeting [DHF.002.7960]

<sup>99</sup> Ibid [DHF.002.7960] at 7966

<sup>100</sup> Sheffield, Cambridge, Edgware, Brentwood, Tooting, Cardiff and Birmingham

<sup>101</sup> Newcastle, Leeds, Oxford, Bristol, Manchester, Liverpool and Wessex

<sup>102</sup> The Inquiry has been unable to identify this document. It seems likely, however, that it contained information similar to that contained in the appendix to the minutes of the previous meeting ie [DHF.002.8022] at 8026

<sup>103</sup> Minutes of Meeting [DHF.002.7960] at 7967

**26.70** At a meeting of the SNBTA Directors on 4 October 1973<sup>104</sup> it was noted, as a matter arising from the meeting of the English RTDs, that Dr William Maycock<sup>105</sup> 'had produced data on the incidence of Au positive blood among prisoner donors. The evidence was being re-examined and English directors were considering withdrawal of prison sessions'.<sup>106</sup> The minutes do not disclose any further discussion of the matter by the Scottish Directors.

**26.71** The English and Welsh RTDs met on 24 April 1974.<sup>107</sup> Dr Albert Bell attended on behalf of the SHHD and Dr Brodie Lewis, Director of the Aberdeen RTC, attended on behalf of the SNBTA. There was discussion of an article that had appeared in *The Sunday Times* in connection with a decision by the North London Blood Transfusion Service, Edgware, to suspend use of blood collected from donors from tropical areas who were considered to be a 'high risk' group as a result of having a higher incidence of Hepatitis B antigen.<sup>108</sup> It was agreed that an ad hoc group should be formed to consider 'what groups of donors can be identified, the use of whose blood should be given special consideration and whether any groups can be identified whose blood should be rejected'.<sup>109</sup>

**26.72** In July 1974 the NBTS in England and Wales compiled data for two periods: the year 1973 and January to March 1974.<sup>110</sup> The data for the whole year showed values for the incidence of HBsAg (Hepatitis B surface antigen) and anti-HBs (Hepatitis B antibody) in new general public and factory donors of 1:1107 and 1:772 respectively. In prisons, borstals etc, the relative values were 1:214 and 1:338 respectively. The incidence of infection in penal institutions in 1973 was relatively high.

### 1975–1979

**26.73** On 6 January 1975, Professor J Garrott Allen, Stanford University School of Medicine, wrote to Dr Maycock, Director, Elstree.<sup>111</sup> It appears from his letter that by the beginning of 1975 some practitioners in the United States of America were campaigning for a volunteer blood donation programme that would exclude high-risk donors in certain groups from giving blood. Professor Garrott Allen pointed out the increased risk of hepatitis from Factors VIII and IX produced by US commercial companies using blood taken from high risk donors. He also stated:

The other imponderable which has troubled most of us is the ineffectiveness in screening for the HB antigen ... Whatever this agent(s) may be, it still seems to be more frequently encountered in the lower socio-economic groups of paid and prison donors. It is minimal among volunteer donors. It seems that the most certain method we have for reducing the number of carrier donors at the present time is still to determine whether or not the donor has been paid in money or reduction of his prison sentence.<sup>112</sup>

<sup>104</sup> Minutes of Meeting [SNB.004.2488]

<sup>105</sup> Dr Maycock was Director of the Elstree, London, RTC and Chairman of the Advisory Group on Testing for the Presence of Hepatitis B Surface Antigen ('The Maycock Group') established by the then three territorial Health Departments in 1970.

<sup>106</sup> Minutes of Meeting [SNB.004.2488] at 2493, item 42(1)

<sup>107</sup> Minutes of Meeting [SGH.001.7096]

<sup>108</sup> Ibid [SGH.001.7096] at 7099–00. See also a memorandum dated 18 April 1974 from TE Cleghorn, Director of the North London BTC, Edgware, which explains the background to this issue [SNB.001.2494]. It is also noteworthy that Dr Cleghorn stated in the memorandum that 'the detection efficiency of IEOP is probably not much better than 50%'.

<sup>109</sup> Minutes of Meeting [SGH.001.7096] at 7100

<sup>110</sup> 'Frequency of HBAG and Anti-HBAG Exported by RTCs IN New General Public and Factory Donors and in Donors in Armed Forces and in Prison Borstals and Similar Institutions' [SGH.001.7095]. The numbers for prisoners in that quarter of 1974 were small.

<sup>111</sup> Letter [SGH.004.6061] BPL Elstree was the manufacturer of NHS concentrates in England

<sup>112</sup> Ibid [SGH.004.6061]

**26.74** Professor Garrott Allen had previously published a book in which he had reported the results of his studies into post-transfusion hepatitis in the USA and had stated:

The risk of serum hepatitis from transfusions derived from prison and Skid Row populations is at least 10 times that from the use of volunteer donors.

....

The most practical methods of reducing the hazard of serum hepatitis from blood are ... especially by excluding, if possible, all prison and Skid Row or commercial donors.<sup>113</sup>

**26.75** In his evidence to the Inquiry Professor Cash stated that he was not, at the time, aware of Professor Garrott Allen's letter to Dr Maycock but was aware of 'the whole issue of the dangers of paid donors'.<sup>114</sup> He commented that paid donation was not a phenomenon in the United Kingdom. Similarly, Dr McClelland was not aware of the letter but was aware of Professor Garrott Allen's book highlighting the risks associated with paid donors.<sup>115</sup>

**26.76** For his part, Professor Leikola was unaware of Professor Garrott Allen before being asked to assist the Inquiry as an expert witness. On being shown Professor Garrott Allen's letter to Dr Maycock he commented:

I think that it's very much in line with what we did in Finland. However, we were thinking at least at that time that these problems of prison conditions and drug addiction were quite different in America as compared to northern Europe and therefore we were not quite as anxious of these numbers as they were over there. However, I think that this statement here is very much in line with what was thought in our country.<sup>116</sup>

**26.77** In February 1975 the Advisory Group on Testing for the Presence of Hepatitis B Surface Antigen ('The Maycock Group'), established in 1970, produced a draft version of their second report.<sup>117</sup> In May 1974 a sub-group of the Advisory Group had considered the problem of certain parts of the population in whom the incidence of HBsAg was known to be high.<sup>118</sup> The report of the sub-group was included in an appendix to this version of the report of the main group.

**26.78** As regards blood collected in prisons, the appendix noted:

There is a relatively high risk of hepatitis being transmitted by the blood of prisoners. But there is probably an equally high risk in other groups of the population, e.g. drug addicts, who are not as easily identified in advance as prisoners. It is not necessary to discontinue the collection of blood at prisons and similar institutions provided all donations are subjected to one of the more sensitive tests referred to ... above [RPH or RIA].<sup>119</sup>

---

<sup>113</sup> Garrott Allen, J. *The Epidemiology of Post Transfusion Hepatitis, 1972*, Stanford University Medical Center, Stanford [PEN.012.0164] at 0165.

<sup>114</sup> Day 10, page 85

<sup>115</sup> Day 9, pages 70–73

<sup>116</sup> Day 13, page 42

<sup>117</sup> Second Report of the Advisory Group on Testing for the Presence of Hepatitis B Surface Antigen and its Antibody [SGH.003.0259]. Dr John Wallace, Director of Glasgow and the West of Scotland RTC was a member of the group.

<sup>118</sup> Second Report [SGH.003.0259] at 0265

<sup>119</sup> Ibid [SGH.003.0259] at 0286

**26.79** The appendix was not included in the final version of the second report of the Advisory Group, published in September 1975.<sup>120</sup> Instead, the conclusion reached by the sub-group on the continued collection of blood from donors in prisons was reflected in a letter dated 1 May 1975 from Dr Henry Yellowlees, Chief Medical Officer for England, to all Regional Medical Officers in England.<sup>121</sup> Dr Yellowlees noted that the DHSS had recently received advice from a group of experts<sup>122</sup> on the use of blood donations from certain categories of donors. The letter essentially repeated the wording of the appendix of the draft second report of the main group and, in relation to prisoners, stated:

There is a relatively high risk of hepatitis B being transmitted by the blood of prisoners. But there is probably an equally high risk in other groups of the population, eg drug addicts, who are not as easily identified in advance as prisoners, if they can be identified at all. The advice we have received is that it is not necessary to discontinue the collection of blood at prisons and similar institutions provided all donations are subjected to one of the more sensitive tests referred to above [that is, reversed passive haemagglutination (RPH) and radio-immunoassay (RIA)].<sup>123</sup>

**26.80** The issue of the use of prisoners as blood donors was determined for the time being for England and Wales by Dr Yellowlees' letter. That letter further noted that the *Memorandum on the Selection, Medical Examination and Care of Blood Donors*, issued for the guidance of RTDs, would be revised to take account of the advice received and that a copy of the letter was enclosed for each RTD.

**26.81** A copy of Dr Yellowlees' letter of 1 May 1975 was also sent to the SHHD. Dr Graham Scott, Deputy Chief Medical Officer, noted in a memorandum of 8 May 1975<sup>124</sup> that the Maycock Group had set up a small working group to consider 'geographical and racial factors' and produced recommendations in the form of an appendix which appeared in an early draft of the report, but that '[i]t was our view as soon as we saw it and indeed finally the view of the whole Advisory Group that the inclusion of such an Appendix could be inflammatory and the Appendix was therefore dropped'.<sup>125</sup> Dr Scott further noted that all he intended to do with Dr Yellowlees' letter was to ask Dr Archibald McIntyre, Medical Officer, SHHD, to discuss the recommendations with the National Medical Director of the SNBTS and to establish the practice in Scotland at that time and when the more sensitive methods of antigen screening had been instituted. He also indicated that if the practice recommended was not what the Scottish centres were doing, or intended to do, then all that would require to be done would be for the department to send a letter to the National Medical Director drawing his attention to the recommendations and asking him to take the matter up with the Regional Directors.

**26.82** On 16 May 1975 Dr McIntyre sent a copy of Dr Yellowlees' letter to Major-General Hugh Jeffrey, National Medical Director, SNBTS.<sup>126</sup> The emphasis in Dr McIntyre's letter was on blood from donors from endemic malarial areas and related to the risk of transmission of malaria. There was no discussion in Dr McIntyre's letter of donations from prisoners.

<sup>120</sup> Final version of Second Report [SGH.003.0079]. The recommendations may have exceeded the working party's terms of reference: Dr Wallace's letter to Dr McIntyre dated 5 March 1975 [SGH.003.0243]

<sup>121</sup> Letter [SGH.003.0187]

<sup>122</sup> That is, the sub-group of the Advisory Group on Testing for Hepatitis B Surface Antigen and its Antibody.

<sup>123</sup> Letter [SGH.003.0187] at 0188

<sup>124</sup> Memo [SGH.003.0185]

<sup>125</sup> Ibid [SGH.003.0185]

<sup>126</sup> Covering letter [SNB.002.5017]

**26.83** Dr Yellowlees' letter of 1 May 1975 was circulated to the SNBTS Directors and was considered at their meeting on 11 June 1975.<sup>127</sup> The discussion appears to have been restricted to the question of blood from donors from endemic malarial areas. The minutes do not record any discussion of donations collected from prisoners, including whether the practice should continue. Professor Cash had no recollection of the discussions which took place at that meeting but concluded that the SNBTS accepted the views of the CMO (England), which he suggested almost certainly enjoyed the support of the CMO (Scotland) and that of the Senior SNBTS Director, Dr John Wallace.

**26.84** Dr McClelland was not aware of Dr Yellowlees' letter at the time it was distributed. In giving oral evidence, he thought in retrospect that it was very strange and surprising advice from a CMO, a public health doctor. He did not know from the letter where the expert advice on transfusion came from but suspected it might have been from a committee chaired by Dr Maycock, a subgroup of that advisory group. He had never been privileged to see any of the deliberations of that subgroup. He repeated that it was 'a very surprising letter'.<sup>128</sup> He was asked to comment further on Dr Yellowlees' advice and said:

The change, obviously, here was all about suddenly having a test for Hepatitis B. I feel that the advice about prisons surprises me because it's wider than just hepatitis ... I would have expected an experienced public health expert to have been concerned about essentially the whole gamut of infection risks among prison donors and also about possibilities of ... prisoners being poorly nourished perhaps being rendered iron-deficient. There would be quite a lot of reasons why [in] what is essentially a pretty underprivileged community, one should think very carefully about asking them to donate blood, both from the safety of the patient and possibly also for the safety of the donor. I do find it surprising, despite that statement.

Q. So in 1975, if one was considering the practice of collecting blood from prisoners, should there have been any consideration of whether there was a higher risk of prisoners transmitting infection?

A. I think that's what I'm saying .... The focus here was on Hepatitis B, and I think there must have been a period after the discovery of the Australia antigen by Blumberg et al, which moved very rapidly on to having some really rather insensitive tests, when ... there was a sense that we have cracked the problem of hepatitis, and in the background these guys, particularly in the States, were very rapidly realising that they probably hadn't cracked the problem of hepatitis. Then, when the Hepatitis A tests became available and the importance of examining liver enzymes perhaps became more widely realised ... it very quickly became evident to people who were looking at all the facts that there was something else going on.

Q So again trying not to look back with the benefit of hindsight, do you think that any consideration between, let's say, 1975 and to the end of the 1970s, the second half of the 1970s, of whether it was appropriate to continue to collect blood from prisoners, or any such consideration to have included consideration of the question of non-A non-B hepatitis?

---

<sup>127</sup> Minutes of Meeting [SNB.002.4995] at 4999, para 9

<sup>128</sup> Day 9, page 74–75

A. I think to put it in those specific terms is probably asking for an incredibly quick knowledge transfer, to be quite honest. I mean, we are talking about these earliest inklings that there was another entity which are referred to here. It is perhaps a little unreasonable to expect that to move instantly into a completely different context and be considered carefully and reflected on and applied. Life's not like that.

Q. So not even between 1975 and, say, 1979?

A. That's a matter of opinion. This is conjecture, not evidence.<sup>129</sup>

**26.85** Dr McClelland did not know whether the view expressed in Dr Yellowlees' letter had ever been retracted. He accepted that it represented the government's advice and thinking at the time.<sup>130</sup> In some respects, however, his views were rather equivocal. He said he would have expected someone with an overview of some of the basic issues in public health to have paused and thought, 'Hang on, prisons can't be a very good idea'. It had been known for a long time, and he considered that common sense would tell one, that prison was a place where living hygiene standards were not very good, where there would be people who had difficult lifestyles and so on. All gathered together, it just did not make sense to him.<sup>131</sup>

**26.86** The second report of the Maycock Advisory Group was published in September 1975.<sup>132</sup> As noted above, the appendix that had appeared in an earlier version of the report setting out the views of the sub-group, on the collection of blood from donors from endemic malarial areas and from prisons, did not appear in the final report. The second report noted that blood and blood products could also transmit other forms of hepatitis which did not appear to be associated with the presence of HBsAg.<sup>133</sup> In a chapter on safety in laboratories the report noted that specimens from various categories of patient should be labelled 'high risk' at the time of collection, including specimens from drug addicts.<sup>134</sup> As noted above at paragraph 29.79, as a result of the procedures adopted the Advisory Group's views on prison collections were not published generally as part of its second report but were, rather, incorporated with advice to medical professionals issued by the Chief Medical Officer for England.

**26.87** In 1977 Dr Edward Follett and Dr Ajay Chaudhuri reported on the link between drug abuse and Hepatitis B Infection.<sup>135</sup> The authors compared the risk factors in cases of acute HBsAg in Greater Glasgow with the risk factors in such cases across the whole of Scotland and concluded:

It is apparent from these observations that drug abuse is giving rise to a very significant number of the total cases of acute hepatitis B in Scotland. The noted percentage for 1976 (27.2) is very likely an under-estimate as several patients may not be asked about or admit to drug abuse or association with drug abusers. It is also evident that this is not another problem peculiar only to the

<sup>129</sup> Ibid pages 87–89

<sup>130</sup> Ibid page 136

<sup>131</sup> Ibid page 76

<sup>132</sup> Second Report [SGH.003.0079]

<sup>133</sup> Ibid [SGH.003.0079] at 0083, para 12. (Para 7 notes the formal change in nomenclature at this time, late 1975, from 'Australia antigen' or 'hepatitis-associated antigen' to 'Hepatitis B surface antigen', HBsAg.)

<sup>134</sup> Second Report [SGH.003.0079] at 0100–01, para 68

<sup>135</sup> Follett and Chaudhuri, 'Drug abuse and Hepatitis B infection' [PEN.002.0515]



west of Scotland. It occurs throughout Scotland and what is seen in Glasgow reflects but does not magnify what occurs in the whole of Scotland.<sup>136</sup>

**26.88** In his book published in 1977, *Blood Transfusion for Clinicians*, Dr Wallace (Dr Mitchell's predecessor at Glasgow) commented, in a chapter on the collection and administration of blood:

Inmates of prisons and other institutions should be treated in the same way as other volunteers, provided the donation is proved to be HBsAg negative.

In respect of the transmission of viral hepatitis particular attention should be paid to volunteers who [are] suspected of being drug addicts or who have a tattoo. It is probably wise not to accept a volunteer who has been a drug addict.<sup>137</sup>

**26.89** In a chapter on the hazards of transfusion therapy Dr Wallace stated:

This is the appropriate time to consider certain controversial features of donor selection in respect of the transmission of hepatitis by transfusion. It has been established that within any potential donor population, certain groups have a higher than average incidence of HBs antigenaemia. In particular, HBs antigenaemia is more prevalent in male prisoners, and in volunteers from tropical areas. Some transfusion services have declined to accept volunteers in prisons and among immigrant populations. This ultracautious approach may be doubly undesirable. Few transfusion services have so much donor blood available that offers of substantial help can be refused in blanket fashion. Indeed visits to prisons to collect blood can often be arranged when the general intake of blood is low because of the holiday season. The incidence of HBs antigenaemia among male prisoners in Scotland is less than 1 per cent using the most sensitive techniques of testing, thus generous offers of useable donations would be lost by placing a total embargo on prison donors. Furthermore it is socially and psychologically undesirable to exclude prisoners and volunteers from tropical areas from the donor population. Acceptance of prisoners as donors helps to rehabilitate, and some of these volunteers become regular donors after their release.<sup>138</sup>

**26.90** Dr McClelland's general comments on Dr Wallace's book are noted in Chapter 14, *Knowledge of Viral Hepatitis 1*, paragraph 14.26. In his view the underlying assumption that, with the benefit of HBsAg screening and a low incidence of Hepatitis B infection, 'somehow non-A, non-B hepatitis just wasn't a problem in the UK', was inconsistent with the knowledge that only 25% of cases of post-transfusion hepatitis could be explained by Hepatitis B and that other causes, including Epstein-Barr virus, were not significant. He had similar difficulty with the conclusions of Dr Maycock's study which appeared to conclude that non-A, non-B Hepatitis was not a major transfusion problem.

---

<sup>136</sup> Ibid [PEN.002.0515] at 0516

<sup>137</sup> Wallace J, *Blood Transfusion for Clinicians*, 1977 [LIT.001.3058] at 3085. Later in the book Dr Wallace noted: 'Inevitably the offer of financial reward attracts drug addicts, alcoholics and the sexually promiscuous, who are more likely to be harbouring infective agents which may be transmitted by transfusion therapy'. at 3116.

<sup>138</sup> Ibid [LIT.001.3058] at 3106

**1980–1984**

**26.91** Research interest continued in to the 1980s. A workshop on hepatitis was held in Edinburgh on 8 January 1981 where Dr Brian Dow of the Department of Infectious Diseases, Glasgow University, gave a presentation on preliminary work he had carried out in Glasgow and the west of Scotland. A paper was later published.<sup>139</sup> The donor population studied included 352 prison donors, among whom Hepatitis B infection was known to be much more prominent than among the ordinary blood donor population and among whom it was expected that markers of NANB Hepatitis might also be more common, since NANB Hepatitis was a blood-borne virus assumed at the time to be similar to Hepatitis B.<sup>140</sup> SGPT/ALT<sup>141</sup> testing showed that of the 352 prisoners, eight had ALT levels exceeding the upper level of normal, at 35; six had levels greater than 42 and one had a level of 125. Of 164 other donors, only one exceeded 35 and one exceeded 42. Dr Dow would have expected more of the other donors to test positive. Even allowing for that, however, prison donors showed a higher level of elevated ALT compared to usual donor sessions.<sup>142</sup>

**26.92** In the discussion section the authors noted:

The index case of [NANB] hepatitis is usually in a haemophiliac, drug-abuser, or post-transfusion patient who may have developed jaundice as a result of a transfusion or a toxic reaction, and not from infection by an unknown agent.<sup>143</sup>

**26.93** In his evidence to the Inquiry, Dr Dow was asked what was meant by the words in the article, 'among whom it was expected that markers of [NANBH] might also be more common'. He replied:

It was basically because non-A, non-B Hepatitis was thought to be a blood-borne virus similar to Hepatitis B. We were just assuming that it was very similar to Hepatitis B.<sup>144</sup>

**26.94** Dr John Gillon's evidence (paragraphs 26.103–26.104 below) would indicate that the assumption was not necessarily well founded but the results, showing a higher incidence of elevated ALT, provided independent evidence of a higher prevalence of NANB Hepatitis (subject to all of the reservations about ALT testing explored later).

**26.95** At the same workshop Archibald Barr and others also presented data showing that the west of Scotland prison sessions had an increased incidence of both HBsAg and Hepatitis B antibodies compared to the general donor population.<sup>145</sup> Over 10 years more than a million donations had been tested for HBsAg. The incidence in institutionalised males was 1:145, compared with 1:693 in non-institutionalised males. In oral evidence, Dr Dow said:

That's about five times greater. It is also quite important to notice there as well that in the ten years, as far as donors tested for the first time, we only had

<sup>139</sup> Dow, Follett and Mitchell, 'Non-A, non-B Hepatitis markers in the west of Scotland', *Laboratory Sciences*, 1981; 38:359–363 [PEN.014.0074]. A final report was published in 1984.

<sup>140</sup> Dr Dow – Day 8, pages 131–132

<sup>141</sup> Alanine transaminase (ALT), sometimes referred to as serum glutamic-pyruvic transaminase (SGPT), is a protein synthesised in liver cells. Normally present in low levels in the blood, it becomes elevated when the liver is disordered by virus infection or other hepatic disorders.

<sup>142</sup> Day 8, pages 132–134

<sup>143</sup> Dow, Follett and Mitchell, 'Non-A, non-B Hepatitis markers in the west of Scotland', *Laboratory Sciences*, 1981; 38:359–363 [PEN.014.0074] at 0078

<sup>144</sup> Day 8, page 132. See also pages 149–150.

<sup>145</sup> Barr et al, 'Hepatitis B surface markers in blood donors in the west of Scotland', *Medical Laboratory Sciences*, 1981 [PEN.014.0068]

6234 institutionalised donors tested for the first time. And you would expect that sort of figure in roughly two years, when you think about it. So we had a lot of repeat donors from prisons. And they had obviously been screened and, you know, obviously if they had been screened they were negative.

....

What I'm trying to get across is when you go to prisons, they are not all new donors. When we go to prisons, some of them have actually given before. So what we are talking about in the 1 in 145 is that if you had, let's say 290 blood donors actually donated at a prison session, you aren't going to get two Hep B positives there, you are probably going to get maybe 0.5.<sup>146</sup>

**26.96** The authors of the west of Scotland paper further stated:

Despite the high incidence of HBsAg in male prisoners ... viral hepatitis is not a serious clinical problem in the institution surveyed, and the positive donors are not drug addicts. This high incidence is probably related to social habits and hygiene.<sup>147</sup>

**26.97** Dr Dow said of this study that he assumed intravenous drug users would have been excluded by the donation staff.<sup>148</sup> If that was correct, the total incidence of positivity would have been higher than found in those proceeding to donation.

**26.98** Dr Mitchell was asked in oral evidence if he knew the basis for the statement that 'the positive donors are not drug addicts' and replied:

Dr Crawford was one of my consultants at that time and he, of course, had a close interest in this work. And it's over a period of ten years ... And Bob actually made a point of interviewing some of these people at the Prison Service, and saying, "Have you had any cases of hepatitis among the inmates since they were screened and do you have any evidence of any of these men being addicts?"<sup>149</sup>

**26.99** Dr Mitchell suggested that the reference to 'social habits and hygiene' did not refer to injecting drug use but may have included habits such as tattooing. He also stated that in the early days of blood transfusion intravenous drug use wasn't much of a problem and was something that came in 'much later'.<sup>150</sup>

**26.100** In oral evidence Dr Dow explained that 'social habits and hygiene' may have been a reference to homosexuality and the sharing of razors and toothbrushes, etc.<sup>151</sup> He was asked, with the benefit of hindsight what he thought was the likely explanation for the higher prevalence of Hepatitis B in male prisoners. He replied, 'Probably drug abuse of some sort'. That link was not made at the time and Dr Dow could not give an explanation for that, other than to say, as far as he was concerned, he was unaware of the amount of intravenous drug use among prisoners until seeing a newspaper report to that effect in March 1984.<sup>152</sup> Professor Urbaniak pointed out that some prisoners are liable to tattoo themselves, or others, and are likely to do so in unhygienic circumstances. He opined that,

---

<sup>146</sup> Day 8, page 137

<sup>147</sup> Barr et al, 'Hepatitis B surface markers in blood donors in the west of Scotland', *Medical Laboratory Sciences*, 1981 [PEN.014.0068]

<sup>148</sup> Day 8, pages 137–140. Cf Dr Wallace's paper [SGH.002.9831]

<sup>149</sup> Day 9, pages 151–152

<sup>150</sup> Ibid page 156

<sup>151</sup> Day 8, pages 99 and 141

<sup>152</sup> Ibid pages 142–143 and 150–151

before the marked increase in intravenous drug use in the early 1980s discussed below, tattooing was a more likely explanation for the increased prevalence of Hepatitis B in the prison population than intravenous drug use.

**26.101** In his evidence to the Inquiry Professor Cash stated that his impression was that the problem of drug use in UK prisons in 1983 was not the problem it is now.<sup>153</sup> While Professor Cash had no recollection of having seen the paper at the time, his view now was that the assertion that the positive donors were not drug addicts and that the higher prevalence of Hepatitis B probably related to social habits and hygiene, was an error and that the most likely explanation for the higher prevalence was drug use and needle sharing.<sup>154</sup>

**26.102** Professor Leikola was of the view that if he had read the paper by Barr and colleagues in 1981 he would have considered the explanation for the higher prevalence of Hepatitis B in donors being due to 'social habits and hygiene', as 'possible, but not probable'. He explained:

[A]fter seeing Dr Helske's article in 1975, and after having discussed this problem briefly, when the people from the prison administration approached Dr Koistinen, I think that these explanations brought forward by Dr Helske – that was illegal use of intravenous drugs, needle sharing and then tattooing – were probably more plausible explanations than this one. And if I would have read this very carefully, I would have really questioned whether the explanation here is correct.<sup>155</sup>

**26.103** Dr Gillon, Consultant Physician at the Edinburgh and South East Scotland BTS from 1985, having heard other witnesses discuss the situation at this time, drew a distinction of some importance based on the relative infectivity of the diseases. He said that there is a gradation from Hepatitis B being highly infectious through HIV being pretty infectious to Hepatitis C, as it came to be known, being not very infectious. In the mid 1970s it was known that in any sort of residential setting Hepatitis B was likely to spread: unlike with Hepatitis C, close family members of people with acute Hepatitis B or high level carriers of Hepatitis B are at risk, just through everyday contacts and excluding sexual contacts as a factor. The assumption that the reference to 'social habits and hygiene' was code for homosexuality was not necessarily correct. He thought that in situations like a prison, a residential school, or any institutionalised situation like the armed forces, Hepatitis B could spread quite readily.<sup>156</sup>

**26.104** Dr Gillon's observations made a particularly helpful contribution to understanding the evidence about infection in the prison population as a whole. On the one hand, they gave added weight to the risk of Hepatitis B transmission inherent in the institutional setting, tending to explain a high prevalence of infection among prisoners and, together with the known ineffectiveness of HBsAg testing, tending to reinforce the case against using prison donations. On the other hand, his evidence warned against the suggestion that a high rate of Hepatitis B transmission in the institutional setting necessarily implied a high rate of NANB Hepatitis transmission among prisoners. That would have to be investigated independently and, indeed, research proceeded to do so.

---

<sup>153</sup> Day 10, page 68

<sup>154</sup> Ibid page 83

<sup>155</sup> Day 13, pages 78–79

<sup>156</sup> Day 11, pages 69–71

**26.105** In 1982 the appropriateness of collecting blood from prisons in Scotland was questioned by the Medicines Inspectorate. The Inspectorate interpreted widely its remit for monitoring the implementation of processing and manufacturing standards for pharmaceutical products. While the licensing regime did not apply to state bodies such as the SNBTS because of the doctrine of Crown Immunity, the policy of the NHS in Scotland at the time was to aim to comply with good manufacturing practice, as if Crown Immunity did not apply.<sup>157</sup>

**26.106** The Medicines Inspectorate visited the Edinburgh and South East Scotland BTS on 10-11 March and 10-12 May 1982. A report was subsequently issued, to which the Edinburgh and South East of Scotland BTS responded, as already noted, on 12 January 1983.<sup>158</sup> The report queried whether prisons and borstals were appropriate places to recruit donors.

**26.107** On 25 March 1982 the Medicines Inspectorate inspected the Dundee BTS.<sup>159</sup> The Regional Director, Dr Ewa Brookes, raised the question of prison donations with the Inspectorate. In her previous employment in London she had met them and regarded them as helpful critics, believing that they were likely to be supportive of her concerns. She advised the Inspectors that she understood that prison collection was in line with government policy but expressed her concern about the practice, as she had previously done whilst working in London. Her concerns were reflected in the Inspector's report.<sup>160</sup>

**26.108** The Inspectors' report of their visit to the Dundee BTS stated:

Brief discussions were ... held on sources of donated blood. At the time of this visit the Inspectorate had not visited donor sessions with Mobile Teams. However, it would seem most unlikely that we could continue to endorse the continued collection of blood from places such as Prisons and Borstals.

This recommendation is based on the following:

- (a) Prison Medical Officers are often not involved in assessing the suitability of donors.
- (b) The increased risk of infection associated with prison populations and the increased risk of transmitting disease through such donations.
- (c) The unreliable answers to the pre-donation questionnaire that can occur in such environments as well as the motivation of some of the donors.<sup>161</sup>

---

<sup>157</sup> The advice of Scottish Law Officers from 1979 was that Crown privilege applied to the CSA (see footnote 169) and Health Boards in Scotland, altering advice previously given. In practice, licences granted prior to 1979 were allowed to become time expired: letter from DHSS to SHHD dated 14 February 1983 [SNB.008.7481]. See a paper by Professor Cash, written in 1984 in which the position (after 1979) was set out, 'Medicines Inspectorate/SNBTS activities: current unresolved problems', dated January 1984 [SGH.001.3012] at 3013.

<sup>158</sup> Report [SGF.001.0351]; Response [SNB.008.6721]

<sup>159</sup> Report [SGF.001.0086]

<sup>160</sup> See witness statement of Dr Brookes, [WIT.003.0057] at 0060-0061: 'I regarded MI as a helpful critic and expressed my concerns. These were later reflected in their general report...'. Dr Brookes' experience of collecting blood from prisons in London is noted above at paragraph 26.53.

<sup>161</sup> Report [SGF.001.0086]

**26.109** The Inspectors' reports of their visits to the Glasgow and West of Scotland BTS on 8–9 March 1982<sup>162</sup> and the Inverness and North Scotland BTS on 5 May 1982<sup>163</sup> made no mention of the practice of collecting blood in prisons, though clearly the practice continued in the West of Scotland at least.<sup>164</sup>

**26.110** By letter dated 4 June 1982, Mr David Haythornthwaite of the Medicines Inspectorate sent a copy of the draft reports of the visits to Professor Cash.<sup>165</sup> Mr Haythornthwaite made a number of observations 'which may be "disconnected" but nevertheless apply to many centres'. In respect of 'source material', the selection and management of blood donors, Mr Haythornthwaite stated:

I have not observed donor sessions under the worst conditions however, I wonder whether certain 'high risk' areas are necessary or desirable. Prisons and Detention Centres would seem to come under this category and I would be interested in your views on this.<sup>166</sup>

**26.111** Professor Cash wrote to Mr John Watt, Scientific Director, PFC, on 5 July 1982 in respect of the Medicines Inspectorate's inspections.<sup>167</sup> Professor Cash noted that there were one or two items arising that deserved 'our collective (national) attention'. He further noted that 'We need to consider, formally, in the not too distant future, the question of Sessions in Prisons etc. I would very much welcome your comments as to whether we should abandon this practice'.

**26.112** In November 1982 Professor Cash prepared a General Response<sup>168</sup> in the name of the Common Services Agency (CSA)<sup>169</sup> to the inspection of SNBTS RTCs by the Medicines Inspectors. It was noted that a more detailed response would follow as soon as possible. The General Response referred to various steps that were under way including building works, the purchase of new equipment, staffing, improved record keeping and a quality assurance programme. There was no mention of the practice of collecting blood in prisons.

**26.113** The Edinburgh and South East Scotland BTS also prepared a response to the Medicines Inspectors' report, dated 12 January 1983.<sup>170</sup> It commented, in respect of the practice of collecting blood in institutions: 'Prisons and Borstals. We do not visit these regularly. No such sessions have been held for two years. These donors will only be used in an emergency'.<sup>171</sup> The response noted that the new comprehensive guide to donor selection, which had been prepared and sent to the Medicines Inspectorate, was in routine use by donor selection staff.<sup>172</sup> It did not distinguish the treatment of prison donors from donors in the general public.

<sup>162</sup> Report [SGF.001.0362]

<sup>163</sup> Report [SNB.008.8095]

<sup>164</sup> Although that may not be entirely surprising given that the Glasgow report stated: 'This visit was restricted to the manufacturing activities conducted at the Centre along with the Quality Control activities. No donor services were visited ...'. [SGF.001.0362] para 4, and the Inverness report stated: 'Insufficient time was available for an examination of all activities'. [SNB.008.8095] para 2.

<sup>165</sup> Letter enclosing draft reports [SNB.008.7582]

<sup>166</sup> Ibid [SNB.008.7582] at 7583

<sup>167</sup> Letter [SNB.005.6703]

<sup>168</sup> General Response [SGH.003.5165]. The General Response appears to have been approved by the CSA's BTS Sub-Committee before being forwarded to the Medicines Division on 2 June 1983 [SGH.001.3012] at 3013, para (a).

<sup>169</sup> Section 19 of the National Health Service (Scotland) Act 1972 provided for the constitution of the Common Services Agency for the Scottish Health Service (the CSA) with effect from 1 April 1974. Amongst its several responsibilities was the operational management of the blood services. See Chapter 17, *Blood and Blood Products Management*, paragraphs 17.23–17.27.

<sup>170</sup> Response [SGH.003.5059]

<sup>171</sup> Ibid [SGH.003.5059] at 5063

<sup>172</sup> Ibid [SGH.003.5059] at 5063. (As noted in paragraph 26.42 of this chapter, the last prison donor session had taken place on 22 December 1981.)

**26.114** Although collection from prisons had been raised by the Medicines Inspectorate in their draft reports sent to Professor Cash in June 1982, there is no minuted discussion of the matter at the meetings of the SNBTS Directors between June 1982 and March 1983.<sup>173</sup> Nor does the topic appear to have been discussed at the meetings of the Ad-Hoc Medicines Inspectorate Steering Group of the CSA.<sup>174</sup>

**26.115** Dr McClelland did not recall the topic of the collection from prisons having been discussed at any Directors' meeting prior to March 1983.<sup>175</sup> Similarly, Professor Cash did not recall having ever given the collection of blood from prisons any consideration prior to it being raised by the Medicines Inspectors in 1982. As Professor Cash put it in his evidence to the Inquiry: 'There were some big, big other issues and I suspect this was a casualty .... A major issue developed within the Scottish Office that major investment, capital investment, was going to be required [at PFC] to keep us on track with self-sufficiency'.<sup>176</sup> Professor Cash explained that during this time the SNBTS was 'heavily committed' to addressing the problems of plasma and haemophilia, in particular, 'the problem of national self-sufficiency in plasma products', which was 'a monumental task'.<sup>177</sup>

**26.116** The issue of prison collections became live in March 1983. The minutes of the Directors' meeting on 29 March<sup>178</sup> include comments on 'Blood Collection in Prisons and Borstals':

Dr Cash reported that the Medicines Inspector had commented adversely on the practice of collecting blood in prisons and borstal institutions, and he invited Directors to comment on the practices in each region and to give their views on the Medicines Inspector's criticism.

It was reported by all Directors present that sessions were held in penal institutions in all regions, although Dr Brookes and Dr Urbaniak intended to review the situation in their regions.

It was not possible for the Directors to agree on future policy, but it was agreed that Dr Brookes, as the Scottish representative, should ask the Working Party on the Selection and Care of Blood Donors to consider this issue. In the meantime, Dr Cash agreed to inform the Medicines Inspectorate of these SNBTS discussions and conclusions.<sup>179</sup>

**26.117** In oral evidence Professor Cash was asked if he had any recollection of the meeting on 29 March 1983 and replied:

My main recollections were that I was not the boss, that all consultants are equal, that I was merely there to co-ordinate and chair; that individual regional directors had the authority to stick to their view and so on and so forth. That was one of the main things.

<sup>173</sup> That is, at the Directors' meetings on 16 March 1982 [SGH.001.0119], 15 June 1982 [SGH.001.0101], 14 September 1982 [SGH.001.0055] and 14 December 1982 [SGH.001.0027]

<sup>174</sup> The Steering Group was set up in response to a report issued by the Medicines Inspectorate in relation to the PFC in November 1981. It met on 5 May 1982 [SNB.008.7309], 26 May 1982 [SNB.008.7393], 21 July 1982 [SNB.008.8235], 16 September 1982 [SGH.002.4287] and 11 November 1982 [SNB.008.8342] and produced a draft report in October 1982 [SNB.008.7278]

<sup>175</sup> Day 9, page 39

<sup>176</sup> Day 10, page 35

<sup>177</sup> Ibid page 75. Professor Cash further stated that he had no recollection of whether he was aware between 1974 and 1982 of the evidence suggesting that there was a higher prevalence of Hepatitis B among prisoners in the west of Scotland: Day 10, page 81

<sup>178</sup> Minutes of Meeting [SGF.001.0234]

<sup>179</sup> Ibid [SGF.001.0234] at 0238, para 7

I remember it being very heated because ... Dr Mitchell was very concerned that if this was precipitously implemented, he would run into problems of blood supply. These were regarded as local matters and we respected his position at that time.<sup>180</sup>

**26.118** This attitude to regional autonomy was common. In his written statement to the Inquiry Professor Cash explained that:

Without SNBTS Directors' consensus, there was no national management process for considering issues related to the location of blood collection sessions in the regions. Throughout the UK: this issue was strictly left to the RTDs and their teams and their priority was maintenance of supply. This management practice and the operational priorities enjoyed SHHD/DOH support.<sup>181</sup>

**26.119** Professor Cash was asked what his personal view was at the time about the appropriateness of continuing to collect donations in prisons and replied, 'I am as sure as I can be but not absolutely certain that my view was we should get out of that'. When asked why he was of that view he replied, '[o]n the grounds that the inspectors had raised, this is an issue, and for all of the reasons that they had stated'.<sup>182</sup>

**26.120** Professor Cash went on to say:

I don't think ... Dr Mitchell was totally opposed. I think the notion he felt of suddenly stopping when his donor programme had been planned for 12 months ahead and he foresaw major problems with shortages – we didn't second guess that, we accepted his point of view and it is very interesting that even by 1984 it had dropped from 2500 donors down to about 400.

So they were clearly, in 1983, as the others switched off finally, the West team were making strenuous efforts to detach at the same time ... Ruthven Mitchell found himself, he felt, in a very difficult position.<sup>183</sup>

**26.121** In her written statement to the Inquiry Dr Brookes stated, in relation to the meeting:

In discussion, I expressed my strong view that I thought the prison and young offenders sessions should be stopped, on the basis of my experience in London.

Although opinion was divided, it became evident that those Directors who wished to discontinue prison sessions, could do so.

....

In Dundee, immediately following the ... meeting of 29/3/83 I asked the Organising Secretary to phase out prison and young offenders sessions over the coming year.

The Centre's programme of donor sessions was generally confirmed for one year ahead, and outlined for the coming year.<sup>184</sup>

---

<sup>180</sup> Day 10, page 42

<sup>181</sup> Professor Cash's Witness Statement [WIT.003.0120] at 0124

<sup>182</sup> Day 10, page 46

<sup>183</sup> Ibid pages 94–95

<sup>184</sup> Dr Brookes' Witness Statement [WIT.003.0057] at 0061–62



**26.122** Professor Urbaniak succeeded to the post of Director for the North East Region, his predecessor, Dr Brodie Lewis, having retired on 3 March 1983. Professor Urbaniak attended the meeting on 29 March 1983 and formed the view that prison collection was undesirable and decided to review the practice in the NE region.

**26.123** By letter dated 12 April 1983,<sup>185</sup> Professor Cash advised Mr Haythornthwaite that the practice of donor sessions at prisons and borstals had been discussed at length by the SNBTS Directors at the meeting. He noted that '[o]pinion was strongly divided and it was not possible, at this time, to obtain a consensus view'; that, nevertheless, the Directors recognised that the problem would require further discussions; and, to that end, that Dr Brookes had agreed to raise the matter at the next meeting of the UK Working Party which was currently considering the whole question of donor selection and care.

**26.124** On 6 May 1983 Mr John Davies, Assistant Secretary, SHHD, sent a minute to the Private Secretary of Mr John MacKay, Under Secretary of State for Scotland, on the subject of AIDS.<sup>186</sup> The minute noted that there had been recent media comment about AIDS, that the DHSS had prepared briefing material for the Prime Minister and that there were a few Scottish points to be made, including:

Donation Policy

The Blood Transfusion Directors in Scotland are very aware of the problem and have it under constant consideration. They are currently considering:-

....

(d) Avoiding collection in high risk locations such as prisons or where there is known to be a high proportion of homosexuals or drug abusers in the population.<sup>187</sup>

**26.125** On 27 July 1983 Mr JB Brown, Medicines Division, DHSS, sent a minute to his DHSS colleagues on the use of blood from prisons.<sup>188</sup> In the minute he explained that, at a recent meeting of Medicines Division's Inspection Action Group, concern had been expressed about the collection and use of blood from borstal institutions and prisons. Blood Transfusion Centres in Scotland were making use of these sources, particularly prisons, and some, at least, of the English Blood Transfusion Centres were also understood to be doing so. He went on:

The Group considered this practice to be highly questionable because of the incidence of homosexuals and homosexual activity in prisons and the present unease about the incidence of AIDS among this group of people.

The Group asked to be advised of Departmental policy on the practice of collecting and using blood from borstals and prisons and I shall be grateful if you will let me have a note about this which I can pass on.

**26.126** A handwritten note on Mr Brown's minute records that Mr Winstanley, DHSS, was to consult with Dr Diana Walford and respond. An SHHD note dated 11 August 1983<sup>189</sup> recorded that Mr Winstanley had contacted the SHHD in respect of the Medicines

---

<sup>185</sup> Letter [SNB.002.6408]

<sup>186</sup> Minute [SGH.002.6764]

<sup>187</sup> Ibid [SGH.002.6764]

<sup>188</sup> Minute [SGH.001.0575]

<sup>189</sup> Note [SGH.001.0572]

Inspectorate's query relating to departmental policy on donor sessions in prisons and borstals 'given there is now AIDS'. Mr Winstanley told the SHHD: 'England and Wales have tended to shy-off in part because of Hepatitis' but he wondered what the Scottish practice was. The SHHD official referred to the discussion at the SNBTS Directors' meeting on 29 March 1983 in that regard. It was also noted that Mr Winstanley 'made the point that if policy was to be withdrawal, would probably need to consult Home Office in view of the importance placed on the social responsibility aspect of such sessions'.<sup>190</sup>

**26.127** By letter dated 23 August 1983,<sup>191</sup> Dr Brookes advised Professor Cash that the Working Party on the Selection of Donors/Notes for Transfusion had met for the first time on 30 June 1983. Dr Brookes had raised the matter of donor sessions at prisons and borstals but noted that '[i]n fact, no discussion was necessary since as far as England and Wales are concerned these sessions have already been stopped. It is now left to the Scottish regions to decide whether they will do the same'.

**26.128** In her written statement to the Inquiry Dr Brookes explained that:

[I]n 1983, the SNBTS National Director had asked me to raise the matter of prison sessions in the working party on Selection of Donors and when I did, I was advised by the chairman that there was nothing to discuss, it being his understanding that all English Transfusion Centres had stopped holding prison sessions. After the meeting I reported this to the Scottish National Director who asked me to ring round informally to check. I contacted 12 of the 14 Directors. In the minutes of the SNBTS Directors meeting of 8 December 1983 ... it is recorded that of the 12 Directors I had contacted, 11 were not holding prison donor sessions.<sup>192</sup>

**26.129** By minute dated 23 August 1983 Mr Winstanley, DHSS, replied to Mr Brown. He stated:

It is difficult to advise any particular Departmental policy on the collection of blood from borstals and prisons at the moment. It is for individual Regional Transfusion Directors to determine how and from where donations are sought in the light of the targets they need to achieve and the numbers of donors on their panels.

However, Transfusion Directors have been aware of the dangers of relying too heavily on prisons as a source of donations for some time i.e. prior to the advent of AIDS as a cause of concern, because of the risk of hepatitis in prisons, (also connected with the higher incidence of homosexuality) which can be spread through blood transfusion. Nevertheless, although most Regions, especially those with no shortage of donors, may not need to use prisons, there is at least one which has to view them as a major source of donations in order to meet targets.

AIDS has now of course called the wisdom of continuing to view prisons as a source of blood even further into question and the Directors are due to discuss it at their next meeting in September.<sup>193</sup> If the risks are now considered

<sup>190</sup> The note [SGH.001.0572] is as quoted: it does not indicate who would have the obligation to consult the Home Office.

<sup>191</sup> Letter [SNB.002.6554]

<sup>192</sup> Dr Brookes' Witness Statement [WIT.003.0057] at 0070

<sup>193</sup> In fact, the minutes of the meeting of the English and Welsh BTS Directors on 22 September 1983 contain no reference to the collection of blood from prisons having been discussed [SNB.001.3412]

too great to justify the continued collection from prisons, some measures will be needed to compensate for the loss of that source of donors, perhaps, for example, a system whereby Regions with no need to rely on prisons can take extra blood to be transferred to those Regions for whom the loss of prisons as a source of blood will cause difficulties ....

[I] gather that this problem has been debated by Transfusion Directors in Scotland, but no particular policy line emerged. We shall obviously need to liaise closely with Home Office also since they have in the past been very much in favour of blood donation by prisoners.<sup>194</sup>

**26.130** The SNBTS Directors met on 13 September 1983.<sup>195</sup> As regards the Working Party on the Selection of Donors/Notes for Transfusion, the minutes state:

On the matter of collection in prisons and borstals it was noted that the Medicines Inspector had expressed concern at this practice. Owing to different circumstances in the Transfusion Regions the Directors had been unable to reach a consensus. The Chairman of the Working Party thought that the practice was diminishing in all regions in England and Wales. Dr Brookes felt strongly that donations should not be collected from prisoners because of the uncertainty about replies to questions concerning health.

It was reported that the practice had been raised at the Medicine Inspectors' Action Group who had referred it to the DHSS Administrative Division who confirmed that some Transfusion Centres in England still collected from prisons and borstals and that cessation of this practice would place them in difficulty. The NBTS Directors were due to discuss the matter and the DHSS would wish to consult the Home Office who had been anxious previously to encourage donation in prisons.

It was acknowledged that prisons and prisoners differed greatly from one place to another and some Directors felt that a blanket decision to cease visiting prisons would be a mistake. Dr Mitchell in particular felt that it would be unfortunate if such a recommendation was to be included in the "Red Book".

Dr Brookes undertook to circularise the English/Welsh Transfusion Directors and report back to the meeting.<sup>196</sup>

**26.131** A note of the meeting by an SHHD observer recorded that:

The details in Mr Winstanley's minute of 23 August were reported to the meeting of RTDs on 13/9/83.

With the exception of the West of Scotland, RTDs were ceasing collection of blood at prison sessions.

The subject would be kept under review, particularly to hear of developments in England which might be influenced by Home Office views.<sup>197</sup>

<sup>194</sup> Minute [SGH.001.0574]

<sup>195</sup> Minutes of Meeting [SNF.001.0072]

<sup>196</sup> Ibid [SNF.001.0072] at 0077, para 8. The 'Red Book' was shorthand for the *Standards for the Collection and Processing of Blood and Blood Components and the Manufacture of Associated Sterile Fluids* (see paragraphs 26.21 above) compiled by the Medicines Division of the DHSS in conjunction with the UK Blood Transfusion Services, BPL, PFC and SHHD.

<sup>197</sup> Note [SGH.001.0571]. In a written statement provided to the Inquiry, Mr Wastle, an SHHD administrative officer who attended the meeting, stated: 'The Director of East of Scotland RTC was strongly against collecting donations from prisoners but some Directors considered that a total ban would be a mistake, with the Director of the Glasgow and West of Scotland RTC strongly opposed to a formal ban'. [PEN.010.0316] at 0319.

**26.132** The UK Blood Transfusion Services' Working Party on Transfusion Associated Hepatitis met on 27 September 1983.<sup>198</sup> Discussion was dominated by AIDS. In respect of donor sessions in prisons the minutes record:

Members asked if the chairman could provide details of which Centres took donations at Prisons. They realised that the definition of 'prison' ranged from 'closed' to 'open' prisons. The working party felt that prisons should be considered in the context of a 'high risk' population in terms of several of the transfusion-transmitted infections and as such should be avoided as a donor source.<sup>199</sup>

**26.133** The SNBTS Directors met on 8 December 1983.<sup>200</sup> As regards the Working Party on the Selection of Donors/Notes for Transfusion, the minutes state:

Reporting her consultation with the English/Welsh Transfusion Directors concerning collections in prisons and borstals Dr Brookes explained that only one of the 12 which she had consulted was attending prisons. It was noted that the only Scottish region to continue holding sessions in prisons was the West.<sup>201</sup>

**26.134** On 9 February 1984 a meeting on the infectious hazards of blood products was held at the National Institute for Biological Standards and Control (NIBSC), attended by Professor Cash and Dr McClelland.<sup>202</sup> There was discussion of AIDS and hepatitis. The minutes note:

The policies adopted in Scotland to minimise the risk of transmission of infection were explained. The three main strategies were 1) avoidance of high risk communities (such as prisons, known homosexual areas, etc.); 2) detection of clinical abnormalities by examination and careful questioning; 3) exclusion of the high risk donor, or his blood, always allowing an 'escape route' for the donor who is deemed unsuitable. Dr McClelland pointed out that it is essential to have well established and well documented procedures in order to carry out these fairly simple strategies.<sup>203</sup>

**26.135** In his evidence to the Inquiry Dr McClelland explained that AIDS 'was on top of everybody's mind at that period'<sup>204</sup> and led to a 'step change in the rigour of the donor selection procedures'.<sup>205</sup>

**26.136** In July 1984 Drs Dow and Follett produced a Final Report on their study into NANB Hepatitis in the west of Scotland.<sup>206</sup> The study period had been 1 September 1980 to 31 August 1983. The main aim of the study was to determine whether 'unrecognised viruses are circulating in the Scottish population resulting in cases of hepatitis which at present cannot be categorised' (ie NANB Hepatitis).<sup>207</sup> A total of 10,655 west of Scotland

---

<sup>198</sup> Minutes [SNB.014.3030]. Drs McClelland and Mitchell were members of the Working Party as was Dr Bruce Cuthbertson, Microbiology Manager, PFC.

<sup>199</sup> Ibid [SNB.014.3030] at 3037, para 7

<sup>200</sup> Minutes of Meeting [SNF.001.0178]

<sup>201</sup> Ibid [SNF.001.0178] at 0181

<sup>202</sup> Minutes of Meeting [SNB.004.8628]

<sup>203</sup> Ibid [SNB.004.8628] at 8633–34

<sup>204</sup> Day 9, page 82

<sup>205</sup> Ibid page 23

<sup>206</sup> Report [SGH.002.8040]

<sup>207</sup> Ibid [SGH.002.8040] at 8043

blood donors had been tested for elevated ALT levels. It was noted that ‘screening sessions in prisons detected 10 times more donations with grossly elevated [ALT] levels compared to other sessions’.<sup>208</sup> The report commented that among the prisoners with high ALT levels, nine were found to be known drug users. In a section of the report on ‘Drug Abusers’ it was noted that ‘[t]he vast majority of users with elevated ALT levels admitted being heroin addicts and a considerable proportion were prisoners’.<sup>209</sup>

### 1985 onwards

**26.137** The Dow/Follett study formed the basis for Dr Dow’s PhD thesis, ‘Non-A, Non-B Hepatitis in West Scotland’, completed in October 1985.<sup>210</sup> In a discussion on ALT testing of blood donors the thesis commented:

Around one third of those with raised [ALT] levels were known to be drug abusers (ie they did not admit being drug abusers at the time of giving blood, but were found to be drug abusers when specimens were received from them at the HRL)<sup>211</sup>.... It must be assumed that this is a minimum number of drug abusers as many more are known to exist in prisons and many will not readily admit abuse. In a Scottish newspaper (Sunday Post, 1984)<sup>212</sup> it was reported that Scotland’s prisons are now the country’s largest drug treatment centres. In 1973 only 6 individuals were diagnosed as being dependent on drugs on admission to prison whereas in 1983 around 300 (6% of the prison population) were drug abusers. These results have led to the [SNBTS] refraining from visiting prisons to obtain blood for transfusion purposes.<sup>213</sup>

**26.138** On 24 March 1986, in a reply to a Parliamentary Question on blood donations from prisoners, Baroness Trumpington, Under-Secretary of State, DHSS, stated:

Regional Transfusion Directors [in England and Wales] have clinical responsibility for the acceptance of blood donors. They do not collect blood from groups known to be at risk from certain diseases.

I am advised that RTDs in England started to phase out collecting blood from prisoners in 1980. Among the factors which they took into account was the large number of donations from prisoners which routine screening for hepatitis showed could not be used. The available tests are not able to screen for all types of hepatitis virus or the presence of the virus in the early stages of the disease. The primary concern of the [NBTS] must be to protect recipients of donated blood.<sup>214</sup>

<sup>208</sup> Ibid [SGH.002.8040] at 8045

<sup>209</sup> Ibid [SGH.002.8040] at 8051

<sup>210</sup> Dr Dow’s PhD thesis [LIT.001.3300]

<sup>211</sup> Hepatitis Reference Laboratory

<sup>212</sup> ‘Drug Boom in Prisons’, *The Sunday Post*, 11 March 1984 [PEN.016.0456]

<sup>213</sup> Dr Dow’s PhD thesis [LIT.001.3300] at 3434

<sup>214</sup> Extract from *Hansard*, 24 March 1986 [DHF.002.1163]

### **Evidence relating to drug use among prisoners**

**26.139** The chronological review of the evidence available to the Inquiry discloses a belief, expressed from time to time in the later 1970s and early 1980s, and perhaps most clearly by Dr Mitchell in a passage quoted later, that prisoners were ‘not in the drug addict class...’. There were drug addicts among paid blood donors, hence their exclusion from donation for example in the USA. There were drug addicts among young adult males, as reported for example by Dr Helske in Finland. In 1972, however, in England and Wales and in Scotland, even among those prisoners who were HBsAg-positive, it appears that none were thought to be drug addicts. A similar picture was presented as late as 1983. There could have been an issue over the classification of an individual as a drug ‘addict’. Custodial sentences for possession of controlled drugs, with or without intent to supply, were not uncommon after the commencement of the Misuse of Drugs Act 1972, however, and a frequent plea heard in courts where an intent to supply was admitted or proven, was that the individual had been dealing to ‘feed a habit’. Anecdotal evidence suggested that drug use among prisoners might have been a material factor. The belief that prisoners were not in ‘the drug addict class’ appeared counterintuitive and it was necessary to investigate the official reporting of data.

### ***Annual Reports by the Secretary of State for Scotland***

**26.140** The Secretary of State for Scotland presented annual reports to Parliament on prisons and other penal institutions in accordance with section 5 of the Prisons (Scotland) Act 1952. The annual reports dealt with various matters including the health of prisoners and the incidence of drug dependency among prisoners.<sup>215</sup> The reports generally, but not invariably, gave numbers for those prisoners with a continuing dependency on drugs at the time of admission, rather than those prisoners who had ever used drugs intravenously. The reports are therefore likely to have underestimated the numbers presenting risk of transmission of infection for that among other reasons, such as those given by Dr Brookes based on her previous experience.<sup>216</sup>

---

<sup>215</sup> For a full list of the matters covered in the annual reports, see the contents page of the 1975 report [PEN.012.0535] at 0538.

<sup>216</sup> Letter dated 18 July 2011 from Ms Robson of the Scottish Government Legal Directorate to the Inquiry [PEN.012.1904] at 1905, para 3, in response to a list of questions by the Inquiry [PEN.012.1782]

**26.141** The data returned for the years 1970 to 1985 were:

**Table 26.4: Secretary of State’s Annual Report to Parliament of recorded cases of dependence on drugs in prisons and other penal institutions**

Reference period and date	Hard drugs			Other drugs
	Males	Females	Total	
1970: June 1978 <sup>217</sup>	[16]		16	
1971: June 1978 <sup>218</sup>	[16]		16	
1972: June 1978 <sup>219</sup>	[12]		12	
1973: June 1978 <sup>220</sup>	[6]		6	
1974: June 1978 <sup>221</sup>	[6]		6	
1975: June 1978 <sup>222</sup>	[5]		5	
1976: June 1978 <sup>223</sup>	21	11	32	
1977: December 1978 <sup>224</sup>	7	8	15	
1978: December 1979 <sup>225</sup>	11	8	19	
1979: October 1980 <sup>226</sup>	5	9	14	
1980: November 1982 <sup>227</sup>	6	12	18	51
1981: August 1982 <sup>228</sup>	51	35	86	35
1982: September 1983 <sup>229</sup>				
1983: November 1984 <sup>230</sup>			1163	
1984: November 1985 <sup>231</sup>			1160	

- The 1976 report did not distinguish males and females for the earlier years.
- The 1982 report did not disclose figures but noted ‘steadily increasing numbers of admissions ... who have been abusing drugs’.

<sup>217</sup> 1976 Report [PEN.012.0605] at 0607

<sup>218</sup> Ibid [PEN.012.0605]

<sup>219</sup> Ibid [PEN.012.0605]

<sup>220</sup> Ibid [PEN.012.0605]

<sup>221</sup> Ibid [PEN.012.0605]

<sup>222</sup> Ibid [PEN.012.0605]

<sup>223</sup> Ibid [PEN.012.0605]

<sup>224</sup> 1977 Report [PEN.012.0612] at 0615

<sup>225</sup> 1978 Report [PEN.012.0619] at 0621

<sup>226</sup> 1979 Report [PEN.012.0625] at 0627

<sup>227</sup> 1980 Report [PEN.012.0631] at 0640

<sup>228</sup> 1981 Report [PEN.012.0669] at 0673 and 0674

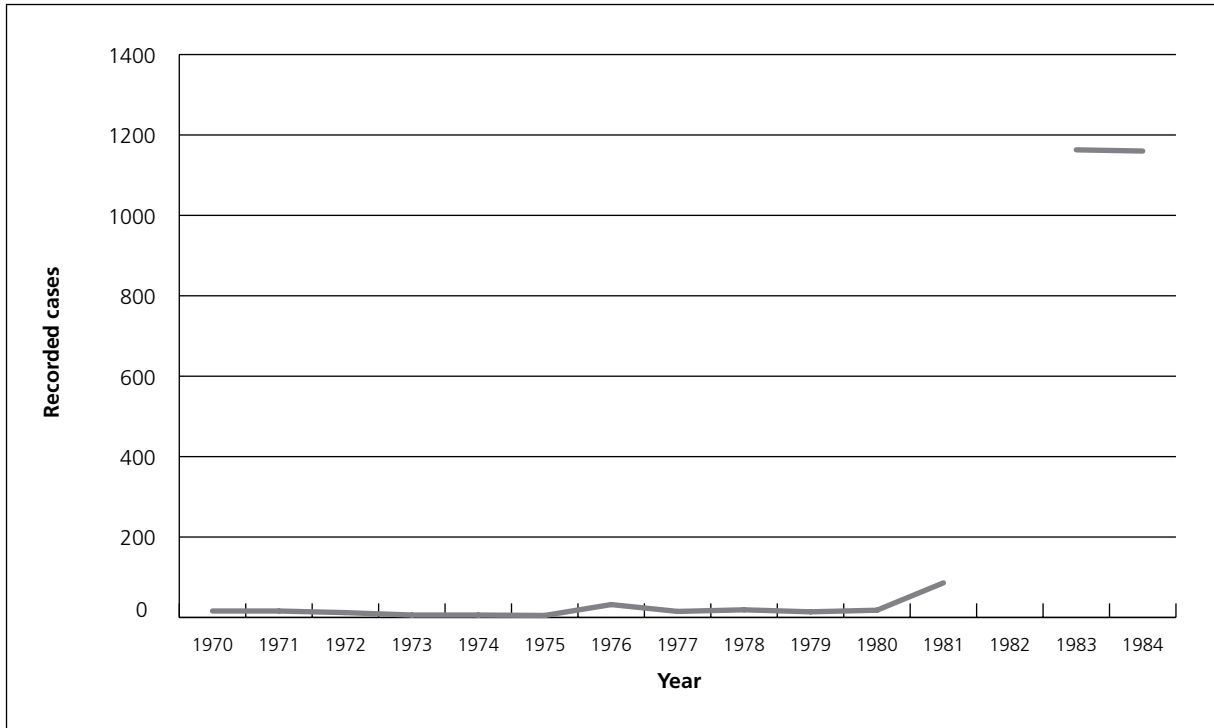
<sup>229</sup> 1982 Report [PEN.012.0693] at 0696. Although figures were not disclosed, the Report noted the ‘steady increase’ in admissions of those using drugs. ‘Nearly all’ of these prisoners were reported to have been using heroin or other opiates.

<sup>230</sup> 1983 Report [PEN.012.0715] at 0718. Again, ‘nearly all’ of these prisoners were reported to have been using heroin/opiates.

<sup>231</sup> 1984 Report [PEN.012.0734] at 0740

**26.142** The data were not returned consistently and only the broadest of pictures is painted by the totals of all cases.

**Figure 26.1: Recorded cases of drug dependence in Scottish Penal Institutions, 1970–1985**



**26.143** It appears that it was not until the early 1980s that the reports showed a significant and continuing increase in drug dependence among prisoners. In the final two years, growth was exponential. There was no evidence before the Inquiry that the contents of these reports, including in particular the evidence of drug use by prisoners, were shared by the SHHD with the SNBTS. The narrative comment in the reports is instructive as to changing perceptions, however.

**26.144** The annual report for 1976 (presented to Parliament in June 1978) commented that all but one of the prisoners dependent on hard drugs were adult inmates.<sup>232</sup> The 1977 report (presented to Parliament in December 1978) stated that the number of recorded cases of dependence on hard drugs had fortunately not continued to show the marked increase recorded in the previous year.<sup>233</sup> The 1978 report (presented to Parliament in December 1979) recorded numbers without comment.<sup>234</sup> The 1979 report (presented to Parliament in October 1980) stated:

Drug dependency diagnosed within Scottish penal establishments, fortunately, does not present a serious problem and there has been little change in the numbers requiring treatment in recent years.<sup>235</sup>

<sup>232</sup> 1976 Report [PEN.012.0605] at 0607

<sup>233</sup> 1977 Report [PEN.012.0612] at 0615

<sup>234</sup> 1978 Report [PEN.012.0619] at 0621

<sup>235</sup> 1979 Report [PEN.012.0625] at 0627



**26.145** The 1980 report (presented to Parliament in November 1981) commented:

The diagnosis of dependence on hard drugs shows little variation over recent years, 18 ... of which 6 ... were males and 12 ... females. However, 51 ... were recorded as dependent on other drugs. There are many more admissions who, if not actually dependent, have a clear history of drug abuse.<sup>236</sup>

**26.146** The impression conveyed to Parliament by the reports to this date was that drug dependence among inmates of penal institutions was not a serious problem in Scotland. Only in the 1980 report was there an indication that the recorded data may not have represented the full extent of the problem of past or current use of drugs by prisoners.

**26.147** The 1981 report (presented to Parliament in August 1982) stated:

The large reservoir of hepatitis infectivity in the world is now appreciated and medical, dental and nursing staff in penal institutions are aware of the special risk categories which come under their care.<sup>237</sup>

....

The increasing misuse of drugs throughout the country is well publicised and prison medical officers are reporting an increase in the number of admissions who have been abusing drugs. There has, this year, been a marked increase in the number of inmates recorded as being dependent on hard drugs such as heroin, 86 ... of which 51 ... were male and 35 ... female. There has, conversely, been a slight fall in the number of cases recorded as being dependent on other drugs, 35 ... 7 ... male and 28 ... female.<sup>238</sup>

**26.148** The 1982 report (presented to Parliament in September 1983) did not provide figures but commented in general terms on the growing problem:

There is no doubt that over the past few years we have seen steadily increasing numbers of admissions to local prisons who have been abusing drugs. These drugs have, unfortunately, usually been hard drugs such as heroin and diconal [a different opioid drug]. In many cases there are obvious signs of self injection and others willingly give a relevant history. This reflects the well publicised, regrettable and dangerous pandemic of drug abuse taking place at present.<sup>239</sup>

**26.149** The 1983 report (presented to Parliament in November 1984) stated:

- The general health of inmates has been satisfactory, but the number who seek medical attention is large and has shown a steady increase over the past few years, almost doubling over the past 10 years ....<sup>240</sup>
- These rising numbers are not the result of any marked changes in disease pattern, but they do perhaps reflect the increasing number of inmates with personality disorders, with a history of alcoholism and, over the past 2 years, the rapidly increasing number who have been misusing drugs of addiction

---

<sup>236</sup> 1980 Report [PEN.012.0631] at 0640

<sup>237</sup> 1981 Report [PEN.012.0669] at 0672

<sup>238</sup> Ibid [PEN.012.0669] at 0673–74

<sup>239</sup> 1982 Report [PEN.012.0693] at 0696

<sup>240</sup> 1983 Report [PEN.012.0715] at 0716

prior to admission. The psychological and physical morbidity associated with these conditions lead to considerable demands upon medical and nursing staff.<sup>241</sup>

- Drug Abuse: 490 inmates were recorded as being dependent upon drugs at the time of reception or had recently misused drugs of addiction. The dramatic rise in misuse of narcotic drugs in the UK has been well publicised and this is mirrored in the admissions to our local establishments. Nearly all have been using heroin and most have been multiple drug abusers, involving combinations of heroin, morphine, methadone and sometimes cocaine. Misuse of cannabis, amphetamines and barbiturates is often reported, as is the misuse of dipipanone [another name for diconal] and LSD.<sup>242</sup>
- *Infective Hepatitis*:... The incidence of carriers and suspected carriers of Hepatitis B infection in the general community is well recognised and it is realised that penal establishments, with an increasing number of admissions who are drug abusers, will contain their share of possible carriers.<sup>243</sup>

**26.150** The 1984 report (presented to Parliament in November 1985) stated:

- The alarming increase in the use of narcotic drugs in the United Kingdom is mirrored in the number of persons admitted to penal establishments who are identified as having recently used dangerous drugs of addiction. In 1984 some 1160 persons admitted to Scottish penal establishments had been involved in drug abuse compared with 490 in 1983. Almost all had been using heroin, although many had also been abusers of other drugs.<sup>244</sup>
- Of this number recorded, 935 were males and 228 females. Almost all had been using heroin, although many had also been multiple drug abusers.<sup>245</sup>
- The increase in the incidence of hepatitis over the past few years is, of course, associated with the increase in intravenous drug abuse. Wherever possible potential carrier states are identified and all sensible precautions to protect staff and inmates are taken.<sup>246</sup>

**26.151** Taken together these reports express the impression conveyed by the figures quoted. They do so particularly in the comments made. They also represent a sudden and rapid increase in the incidence of recorded illicit drug use beginning in the first half of the 1980s. For present purposes there are some obvious concerns about the relevance of the data, especially for the earlier periods. Drug dependency on admission may give a poor indication of a history of relevant drug use up to that point in the individual's life. Reported drug dependency may have been less than actual drug dependency (especially before methadone was readily available on prescription as a substitute for heroin). A drug habit that did not require medical intervention would not have been captured in clinical records. The data appear to have been the best available in official records at the time, however.

<sup>241</sup> Ibid [PEN.012.0715]

<sup>242</sup> Ibid [PEN.012.0715] at 0718

<sup>243</sup> Ibid [PEN.012.0715] at 0718

<sup>244</sup> 1984 Report [PEN.012.0734] at 0740

<sup>245</sup> Ibid [PEN.012.0734] at 0749. The total number referred to in this paragraph was 1163.

<sup>246</sup> Ibid [PEN.012.0734] at 0750

### *Annual reports by HM Chief Inspector of Prisons for Scotland*

**26.152** The post of Her Majesty's Chief Inspector of Prisons for Scotland was created in 1980 and the Inspectorate of Prisons for Scotland began operations in 1981. The Chief Inspector's 1981 report (presented to Parliament in August 1982) contained no reference to drug use among prisoners,<sup>247</sup> nor did the 1982<sup>248</sup> or 1983<sup>249</sup> annual reports. The Chief Inspector's 1984 annual report (presented to Parliament in October 1985) contained only a brief reference to drug use, in particular in relation to smuggling drugs into prisons during prison visits.<sup>250</sup>

**26.153** On the face of the official records, they appear to give some support for the views expressed by Dr Mitchell and others that until the AIDS era there were no, or at least few, drug addicts in Scottish prisons. With the benefit of hindsight one might question the accuracy and the relevance of the data published and to look at collateral sources of information, such as records of criminal proceedings related to drug use and trafficking for insight into the actual level of use giving rise to the risk of transmission of infection. Later studies were to show that recreational drug use in the United Kingdom increased steadily in the 1960s and into the 1970s.<sup>251</sup> Given the relatively high prevalence of viral infection among prisoners, this would have been significant information in the 1970s and early 1980s. This was not known at the time, however. Based on the official records, drug use could not be shown to have been a material factor aggravating the risks associated with collecting blood in Scottish prisons. The desirability or undesirability of collecting blood in prisons has to be judged on more general grounds.

### *Blood supply and prison collections*

**26.154** As noted earlier, the percentage of total blood donations in Scotland collected from prisons fell from 2.38% in 1975 (5915 of 248,558 donations) to 0.11% in 1984 (342 of 308,617 donations), with an annual average over that period of 1.097%.<sup>252</sup> In view of the international guidance that need and supply were factors that might affect local choices, a question arises whether an adequate supply of blood could have been maintained had collection from prisons stopped at any time between 1975 and 1984.

**26.155** In general, in Edinburgh and the south east of Scotland there was a surplus of red cells, at least in the early 1980s, as a result of the drive to collect plasma for fractionation.<sup>253</sup>

**26.156** In contrast, in Glasgow and the west of Scotland, which accounted for almost one half of all of the blood collected in Scotland, there were problems from time to time, in particular during holiday periods, in collecting enough blood from local supplies to meet clinical demand.<sup>254</sup> As the evidence of Mrs Prior indicated, prison visits in Glasgow took place principally during holiday periods.

<sup>247</sup> 1981 Report [PEN.012.0645]

<sup>248</sup> 1982 Report [PEN.012.0677]

<sup>249</sup> 1983 Report [PEN.012.0701]

<sup>250</sup> 1984 Report [PEN.012.0720] at 0728

<sup>251</sup> See paragraph 26.201 below.

<sup>252</sup> In fact, these figures are likely to be slightly higher as the number of prison donations collected from the North of Scotland RTC (Inverness) are not available as a result of records being destroyed in a flood – see para 1 of the SNBTS paper 'Blood collection 1975–1991' [PEN.010.0003]

<sup>253</sup> Dr McClelland – Day 64, pages 51–52

<sup>254</sup> See, for example, Professor Cash's letters to Dr Mitchell of 30 December 1982 [SNB.003.7020], 16 January 1987 [SNB.011.3355] and 15 January 1990 [SNB.013.6496]

**26.157** In a letter dated 30 December 1982 to Dr Mitchell, Professor Cash suggested that any difficulties in ensuring a sufficient supply of blood for cardiac surgery in Glasgow could be met by obtaining red cell concentrates, or even whole blood, from other SNBTS Regional Centres. Professor Cash noted:

Whilst I recognise that figures can be misleading, particularly in the context of fluctuating supply and demand for blood and blood products, the facts are that in the year ending 31st March, 1983 the SNBTS as a whole outdated more than 40,000 donations of whole blood and 35,000 donations of red cell concentrates. It may well transpire that the periods in the year when the West is short and the periods when other regions are short are identical. This topic, however, has not been explored and, in view of the significant potential implications contained in your letter to David Wheatley, I believe the time has come for me to place the matter on the Agenda for our next Co-ordinating Group meeting.

....

Common sense demands, previous experience points to fact, that real co-operation between the Regional Centres of the SNBTS is an essential option that needs to be explored continuously. The public, not to mention the Scottish blood donors, would be disturbed to discover that because of management failings patients in one part of Scotland were suffering because of a lack of blood and in an adjacent city blood was being discarded.<sup>255</sup>

**26.158** However, when the matter was considered at the meeting of the SNBTS Directors' Co-ordinating Group on 22 February 1983, it was noted that Dr Mitchell indicated that he preferred to cope from within his own region.<sup>256</sup>

**26.159** In a letter dated 28 January 1985 to Dr Bell, SHHD, Professor Cash noted that:

The SNBTS currently outdates 30% of its shelveable blood intake (90,000 donations/year). The reasons for this are well known to you – it reflects, primarily, the fact that we are largely plasma driven.

The SEBTS (with the knowledge of the CSA) is now regularly supplying the Edgware RTC [in London] with red cell concentrates.<sup>257</sup>

**26.160** The themes of occasional blood shortages in Glasgow, excess blood products in Edinburgh and Glasgow's communication with other centres arose again in the winters of 1986–87<sup>258</sup> and 1989–90.<sup>259</sup>

**26.161** By way of explanation for the situation in the west, Professor Cash stated in his written evidence to the Inquiry that:

[I]t is worth pointing out that the annual blood collection figures per million of population in the West was significantly below all other regions in Scotland throughout the 1980s. Thus supply difficulties for red cell was [sic] a not

---

<sup>255</sup> Letter [SNB.003.7020]

<sup>256</sup> Minutes of Meeting [SNB.003.6988] at 6990

<sup>257</sup> Letter [SNB.013.4238]

<sup>258</sup> See letter dated 16 January 1987 from Professor Cash to Dr Ruthven Mitchell [SNB.011.3355]

<sup>259</sup> See letter dated 15 January 1990 from Professor Cash to Dr Mitchell [SNB.013.6496] and subsequent letters between Dr RJ Crawford, Glasgow BTS, and Professor Cash dated 29 January 1990 [SNB.014.1589] and 6 February 1990 [SNB.005.2159]

infrequent anxiety for colleagues in the West where poverty and deprivation were significant challenges for those responsible for the blood collection programmes. It is almost certain that it was never a problem for Edinburgh or any other SNBTS region.<sup>260</sup>

**26.162** In his evidence to the Inquiry Dr Mitchell was asked to comment on the particular benefit to the West in collecting donations from prisons. He replied:

Well, it depended at what time of the year. Clearly, every transfusion centre that I have ever worked in has shortages. There is no question that that does occur. It occurs for a variety of reasons. Sometimes it is due to ... holiday times, especially festive seasons, certainly around the West of Scotland. It may also be due to problems with transport, problems with weather and so on. These can easily upset a session or a set of sessions.

So when people are going away or things don't happen then you are left with a major problem and that's one of the reasons that one went to prisons during times when you could anticipate that there might well be shortages.<sup>261</sup>

**26.163** In his evidence to the Inquiry, Dr McClelland was asked whether stopping collection from HMP Saughton caused any problems to supplies in the region. He replied:

It did not, and we would not have expected it to do so because our blood collection programme at that time was firmly driven by the requirement for plasma to be used in the preparation of Factor VIII, you know, in the effort to achieve self-sufficiency with an ever rising utilisation of Factor VIII.

So we actually had a superabundance of red cells. The reason for that is that the majority of the plasma which was provided from our centres to the fractionation plant was collected, at that time, in the form of whole blood from which it was then separated. So we had had a lot of red cells and we shipped the plasma off. Over this sort of period we quite frequently supplied red cells to centres south of the border. We regularly supplied them to one of the London centres for quite a period because we were concerned about ... inappropriate wastage of cells that had been donated.

So it didn't cause a problem in the south east region.<sup>262</sup>

**26.164** Dr Mitchell was asked whether stopping the collection of blood from prisons in the west of Scotland in early 1984 caused any difficulties in respect of shortages of blood and replied, 'I think the answer to that is: yes from time to time. Most of the time one could cope. In fact, pretty well all of the time you could cope'.<sup>263</sup> Dr Mitchell agreed with the suggestion put to him that stopping collection from prisons did not cause any insurmountable problems with the blood supply.<sup>264</sup>

**26.165** Professor Cash was asked whether a decision in 1975 to stop prison collections in Scotland was likely to have caused any insurmountable problems in the supply of blood. He replied:

---

<sup>260</sup> Professor Cash's Witness Statement [WIT.003.0120] at 0122

<sup>261</sup> Day 9, page 162

<sup>262</sup> Ibid pages 67–68

<sup>263</sup> Ibid page 163

<sup>264</sup> Ibid page 164

[I]t would in my experience have required a little less autonomy, a little more cross-regional support, when times got difficult. But if you take the total input of red cells to the whole of Scotland, I don't believe that 1 per cent would have – we could easily have coped with it.<sup>265</sup>

### *The role of government*

**26.166** It appears that the Home Office favoured the collection of blood in prisons. That seems clear from the minutes of the meeting of the English directors on 26 September 1973,<sup>266</sup> discussed above, where it was noted that the Home Office should be informed before any action was taken to discontinue collection in prisons, and from the DHSS memo dated 23 August 1983 which referred to the need for close liaison with the Home Office, 'since they have in the past been very much in favour of blood donation by prisoners.'<sup>267</sup>

**26.167** In addition, in her written evidence to the Inquiry Dr Brookes stated that, when she arrived in Scotland in 1981 as Director of the Dundee RTC, she understood, based on her experience working in England, that it was long-standing government policy that the BTS should visit prisons to 'permit prisoners to make some restitution to society' and to 'do something which many of the community did, to help their return to normal life after release'.<sup>268</sup>

**26.168** Dr Graham Scott, former Deputy Chief Medical Officer, SHHD, was asked about the consideration, if any, given by the SHHD between 1975 and 1984 to the practice of collecting blood from penal institutions, the risk of NANB Hepatitis from such donations and whether the practice of collecting blood from such institutions should continue. In his written response to the Inquiry he stated, 'I do not know whether SHHD gave any consideration to this issue; I do not recall being asked to consider it. In any event, I would not have considered it appropriate to interfere with SNBTS practices'.<sup>269</sup> During his oral evidence to the Inquiry he was asked what he meant by the statement that he would have not considered it appropriate to interfere with SNBTS practices and replied:

I wouldn't have considered it appropriate to question their decisions about taking donations from prisons. I considered them to be excellent scientific individuals and well able to judge what they were doing in their individual circumstances and their individual reason. And in their areas, they would know what was going on. I would not have interfered with that.<sup>270</sup>

**26.169** Despite the evidence that the Home Office in London had been in favour of collecting blood from prisons, Dr Scott was not aware that the SHHD had expressed any views in favour of collection in prisons, which he considered to be 'a matter for the SNBTS Directors'<sup>271</sup> who were 'in the best position to make informed decisions based on local circumstances'.<sup>272</sup> He was asked whether, in the 1970s and early 1980s, the SHHD or ministers encouraged donations in prisons and replied in the negative. Dr Scott was also asked whether between 1975 and 1984 he or the SHHD had any view on the practice

<sup>265</sup> Day 10, page 73. See also Professor Cash's Written Statement on blood shortages [PEN.011.0066]

<sup>266</sup> Minutes of Meeting [DHF.002.7960] at 7967

<sup>267</sup> Memo [SGH.001.0574]

<sup>268</sup> Dr Brookes' Witness Statement [WIT.003.0057] at 0059

<sup>269</sup> Dr Scott's Witness Statement [WIT.003.0019] at 0020

<sup>270</sup> Day 11, page 130. That answer requires to be considered against the background that Dr Scott, like his other medical colleagues at SHHD, was a public health doctor, and was not an expert in any one medical discipline such as transfusion medicine.

<sup>271</sup> Day 11, page 134

<sup>272</sup> Dr Scott's Witness Statement [WIT.003.0019] at 0021

of collecting blood from prisons. He replied, 'I don't have a view on this. In my opinion, this was a matter for SNBTS'. Nor was he prepared to offer a view on the practice with the benefit of hindsight.<sup>273</sup> He stated, 'if I had told the SNBTS directors what to do with regard to ... donors selection, I would have been told to mind my own business'.<sup>274</sup> SNBTS Directors, as Consultants in the NHS, 'were in the position to make their own decisions'.<sup>275</sup> In Dr Scott's view, the SNBTS Directors could not expect to get a lead from either the SHHD or the DHSS on whether the practice of collecting blood from prisons was acceptable.<sup>276</sup>

**26.170** In his written statement to the Inquiry, the position of Dr McIntyre, Principal Medical Officer (PMO) was similar to that of Dr Scott.<sup>277</sup> Dr McIntyre stated:

The collection of blood from penal institutions was an established practice by the time I took responsibility for blood policy as PMO in charge of the public health group.

....

I did not take part in any discussions regarding the continued collection of blood from penal institutions. I am not aware of my colleagues having been involved in such discussions. This was really an issue for the Regional Transfusion Directors to address.

....

We knew that SNBTS were running the show and there was felt to be no need for us to interfere. SHHD did not set policy for SNBTS in this area.

....

I do not remember SHHD or Ministers encouraging donations in prisons.<sup>278</sup>

**26.171** In a written statement provided to the Inquiry, Mr John Wastle, an administrative officer in the SHHD, stated:

I was aware that the Home Office had encouraged the collection of blood from prisons in England but I was never aware that the "Home" side of SHHD (which was roughly the Scottish equivalent of the Home Office) had sought to give such encouragement in the 1970s and early 1980s. Similarly, I am not aware that the "Health" side of SHHD or Ministers ever gave such encouragement. My understanding in 1982-83 was that this was an operational consideration for the individual RTC Directors and this, I think, is reflected in the differing positions which they had taken on the issue.<sup>279</sup>

**26.172** Professor Cash was asked whether the SHHD ever sought to influence or encourage the collection of blood in prisons in Scotland and replied, 'No, I'm not aware ... Encouraged? No, I'm not aware. Nor am I aware that they discouraged either'.<sup>280</sup> He went on:

---

<sup>273</sup> Ibid [WIT.003.0019] at 0022; Day 11, pages 156–157

<sup>274</sup> Day 11, page 158

<sup>275</sup> Ibid page 161

<sup>276</sup> Ibid page 159

<sup>277</sup> Dr McIntyre's Witness Statement [WIT.003.0013]

<sup>278</sup> See, generally, Dr McIntyre's Witness Statement [WIT.003.0013]

<sup>279</sup> Mr Wastle's Witness Statement [PEN.010.0316] at 0323–24

<sup>280</sup> Day 10, page 65

I would add that there is this strong tradition ... that these matters were under very much the governance of DHSS and I suspect, to be fair to my Civil Service colleagues in Scotland ... that they were waiting for a judgment to come up from London on this and they waited.<sup>281</sup>

**26.173** Professor Cash was further asked who he thought was best placed to consider whether it was appropriate to collect blood from prisons in Scotland. He replied:

In retrospect, I have no doubt it should have been SNBTS but at that time these matters – we broke away eventually in Scotland at that time. These matters, the question of donor selection, were very much in the hands of the DHSS and I think we eventually recognised that this wasn't right.<sup>282</sup>

**26.174** Dr McClelland was asked if he was aware whether the SHHD ever sought to influence or encourage the SNBTS in the collection of blood from prisons. He replied:

I'm not aware of the [SHHD] expressing a view either way, either for or against .... [T]he transfusion directors' meetings were regularly attended by a senior person, a medical person, from the department and they received all the papers and so on. They would have been party to any discussions and would have had ample opportunity to express a departmental view, had they wished to do so.<sup>283</sup>

**26.175** Dr McClelland was asked who was best placed to decide on matters of donor selection policy, the SHHD or the SNBTS, and replied:

I think it probably was primarily an issue for the [SNBTS]. Had there been a view that there was, as it were, a non-medical, like a sociological or welfare reason, to encourage donations in prisons, which certainly is the strand that emerged from the consultations in London, that, I think, would have been an issue for the Department of Health because it certainly is not a health issue for the transfusion service.<sup>284</sup>

### *Why prison collections stopped*

**26.176** In his evidence to the Inquiry Dr McClelland was asked why his region stopped prison collections in 1981. He explained that he had recently spoken with his former regional donor organiser who had reminded him that the donor organiser:

[A]ctually felt it was just an unsuitable environment in total.

It was almost more that concern, plus the specific concerns that really, for lots of very good reasons, we could not rely on getting completely clear transparent answers from prisoners ....

So it would not be correct for me to say that we were worried about hepatitis in the prisons. We were worried about the totality of the environment and I was certainly aware that infection with hepatitis and related viruses was a problem in prisons. I was certainly aware of that information in the United States. So it was a sort of complex of things that led us to this decision.<sup>285</sup>

---

<sup>281</sup> Ibid pages 65–66

<sup>282</sup> Ibid page 67

<sup>283</sup> Day 9, page 83

<sup>284</sup> Ibid pages 83–84

<sup>285</sup> Ibid pages 32–33



**26.177** In answer to a question as to whether the concerns of his regional donor organiser centred on it being unfair on the blood transfusion service staff to expect them to conduct sessions in prisons, Dr McClelland replied, 'I think the BTS found it quite a threatening environment'.<sup>286</sup>

**26.178** Dr McClelland also explained that he could find no evidence that a policy decision was taken by his region not to visit prisons again. Indeed, his response to the Medicines Inspectors in January 1983 had been to the effect that while no sessions in prisons or borstals had been held for two years, such collections might be used in an emergency.<sup>287</sup> He gave the following evidence:

We never did go to prisons again. Having tried to reconstruct this, I find no evidence that we recorded a policy decision that we will stop collecting blood in penal institutions; we just stopped doing it. We informed the contact person, who I think was the Director of Saughton ... that we were not making any further appointments, and in fact we had several representations from them subsequently to come back and run sessions and we did not do that.

I honestly cannot remember now why we did not, as it were, make it a formal policy. I have tried very hard to find any evidence of that, but, as I say, the actions are that we did not ever return and we did not book any further sessions and we never felt any need to do so.<sup>288</sup>

**26.179** In his evidence to the Inquiry Dr Mitchell stated that 'the question that tipped the balance, as far as Glasgow was concerned, was the advent of an incurable disease at that time, called HIV'.<sup>289</sup>

**26.180** Professor Urbaniak decided to attend the collection sessions scheduled, before his tenure, for HMP Craiginches on 7 July 1983 and HMP Peterhead on 28 July 1983. Following his visits he concluded that in the light of the potential for undesirable peer pressure, the potential for an unreliable medical history to be provided and difficulties with confidentiality, the practice should end in the NE region. He also had concerns, on behalf of his all-female donor staff team, at their working in such an environment. No further prison sessions took place in the NE region after 28 July 1983. A cluster analysis, subsequently undertaken by him, revealed both prisons to be HBV 'hotspots'.

### *Evidence relating to the question whether prison collections should have stopped earlier*

**26.181** While Dr Gillon was not working in the field of blood transfusion at the time, his impression was that 'the focus on prisons had been largely in relation to Hepatitis B and the feeling was that testing had reached the level of sensitivity that took that off the radar to some extent'.<sup>290</sup> That appears to have been the position by about 1975 when the third generation tests for HBsAg was thought to have significantly reduced HBV infection among blood transfusion recipients. Relatively sensitive and accurate tests for HBV were beginning to be widely available at that time and tests for HAV soon followed.<sup>291</sup> Several

---

<sup>286</sup> Ibid page 33

<sup>287</sup> Response to Medicines Inspectors Report [SGH.003.5059] at 5063

<sup>288</sup> Day 9, pages 35–36

<sup>289</sup> Ibid pages 157–158

<sup>290</sup> Day 11, page 73

<sup>291</sup> A practical test for HAV was not available in Scotland until 1978.

groups reported in the following year that the majority of patients with clinically diagnosed post-transfusion hepatitis tested negative for infection with HAV and HBV.<sup>292</sup>

**26.182** From 1976 to 1977, the focus began to change towards NANB Hepatitis. However, tests for HBsAg continued to improve. In 1976, there was controversy between Dr Wallace and SHHD over the relative effectiveness of Reverse Passive Haemagglutination and Radioimmunoassay, two widely available HBsAg tests,<sup>293</sup> against a background of growing confidence in the effectiveness of the screening process to reduce, if not totally eliminate, the risk of transmission of HBV. Doubts began to emerge as the investigation of chronic liver disease widened in the later 1970s. For example, the Haemophilia Centre Directors' Hepatitis Working Party report dated 20 August 1978 on the pilot project to investigate the incidence of chronic liver disease in patients treated with Hemofil in 1974–75, expressed doubts about the screening tests for HBsAg.<sup>294</sup>

**26.183** It is necessary to keep a sense of historical perspective in discussing the question of the exclusion of prison donors. A view that might have been taken on the basis of understanding of the accuracy of assays before NANB Hepatitis was known would require revision after that stage.

**26.184** Dr Mitchell was asked whether, with the benefit of hindsight, blood should have been collected from prisons in Scotland in the late 1970s and early 1980s and replied:

I don't think there was any major reason not to do it .... It was quite clear that prisoners are human beings. They have a right to give blood like anybody else. It is a civic duty. Many of them felt that it was important that they should do that. Many of them continued when they left prison. Some had been giving before they went into prison. Nothing very much had happened in the interval to suddenly decide against one particular group, it would be difficult to sustain against the idea "Well, why are you discriminating against us?"<sup>295</sup>

**26.185** Dr Mitchell was asked whether the following factors altered his view: namely, the higher prevalence of Hepatitis B in the prison population, the likelihood that the initial Hepatitis B tests did not detect all donations that were positive for Hepatitis B and, in the late 1970s/early 1980s, the emergence of NANB Hepatitis and there being no tests to exclude that disease. He replied:

No, not really. I think the question of the advent of [NANB Hepatitis] was something which was badly understood in the UK. Something which wasn't entirely – the whole epidemiology of it wasn't understood. And whether it would be confined to prisoners who we already knew were not in the drug addict class and so on, like anybody else, we had no reason to believe that they were any different, except for the statement that's made that there were social differences between prisoners, for reasons of close contact with others, incarceration and so on.

....

[NANB Hepatitis] was a diagnosis of exclusion in most cases. There are very few cases in the UK that I was aware of at that time. We seldom got reports from

<sup>292</sup> Alter et al, 'Clinical and serological analysis of transfusion-associated hepatitis', *The Lancet*, 1975; 2:838–841 [PEN.002.0836]

<sup>293</sup> See Letter dated 22 June 1976 from Regional Director to Dr McIntyre [SGF.001.2836]

<sup>294</sup> See Report of the Haemophilia Directors Hepatitis Working Party – 1978 [SNB.001.7192]

<sup>295</sup> Day 9, pages 164–165

hospitals, “Oh, we have got a case of post-transfusion hepatitis” of any kind. That was unusual. They knew to report that.

....

So I’m sure they would have let us know but they didn’t and you would take it, well, it wasn’t all that important.<sup>296</sup>

**26.186** Dr Mitchell’s evidence on the reported incidence of NANB Hepatitis was similar to the evidence of Professor Hayes. (See Chapter 15, *Knowledge of Viral Hepatitis 2 – 1975 to 1985*, paragraph 13.34.)

**26.187** Dr McClelland joined the SNBTS in 1977 and became a Regional Director in 1979. He was not aware of Dr Yellowlees’ letter of 1 May 1975 when he joined the service. His observations on reading the letter later have been set out in paragraphs 26.84–26.85 above. He found the letter surprising but later he qualified that evidence by saying: ‘That is a personal view. It says absolutely nothing about what I might or might not have thought about it had I read it 30 years ago ...’.<sup>297</sup>

**26.188** Dr McClelland was asked why he continued to collect blood from prisons until 1981 if he found the advice contained in Dr Yellowlees’ letter of 1 May 1975 ‘surprising’ and replied:

I think that we should have stopped. I think we should have stopped sooner. I think it was a matter of focussing on, you know – you come to a complicated new job, you have to decide on which bit of it you are going to focus on and there were many, many preoccupations, like – as will be evident from the medicines inspector’s report, the facilities in Edinburgh were deeply unsatisfactory. There was a huge pressure within the organisation. Really the driving pressure within the organisation was collecting plasma to meet haemophilia requirements, and I think that I, as a director there, was slow off to the mark in realising this.

I don’t wish to defend that but, as you say, you end up not paying attention to all the potential problems simultaneously. This was one that came a little bit later but I think we responded to it. I think that once we sort of started to think about the issue, it became quickly very obvious that we were going to stop.<sup>298</sup>

**26.189** Later, Dr McClelland was asked whether the collection of blood from prisons had been a real issue for him before his regional donor organiser raised it with him and replied:

I don’t think it had. I think I had probably accepted it as the way things were done and probably not directed a great deal of attention to it because I was probably directing my attention to other things.<sup>299</sup>

**26.190** Dr McClelland was asked what his view would have been at the time, had he been asked between 1975 and 1981 whether it was appropriate to collect blood at prisons. He replied:

I think that’s almost impossible to answer. I can’t unlearn. I mean, what may have happened at that time was I would have consulted my colleagues, as

---

<sup>296</sup> Ibid pages 165–166

<sup>297</sup> Ibid page 146

<sup>298</sup> Ibid pages 76–77

<sup>299</sup> Ibid page 79. There, Dr McClelland also agreed with the suggestion that he hadn’t really applied his mind to the collection of blood from prisons as an issue until his new regional donor organiser raised it as an issue when she arrived.

transfusion directors, many of whom had been in post for a long [time] and were highly experienced, and I would have perhaps consulted what, you know, the recommendations from the CMO, or whoever, were. And I might have concluded that, because it was normal practice, because everybody else was doing it and because the CMO said it was fine, I might well have continued – I can't put myself back 25 years in any meaningful way.<sup>300</sup>

**26.191** Dr McClelland gave the following written evidence in respect of the state of knowledge of NANB Hepatitis in 1975:

The importance of the condition [ie NANB Hepatitis] had not at this time been fully appreciated by many concerned with these decisions. Because no causative agent could be identified there was no specific test for NANB and knowledge of the natural history and the epidemiology was lacking. It was not possible to know that individuals could become infected without having evidence of jaundice or indeed any clinical features. Nor could it be known that once an individual was infected their blood could continue to contain the infectious agent for many years in the absence of any symptoms or that some forms of chronic liver disease would eventually be discovered to be caused by chronic infection.<sup>301</sup>

**26.192** Dr McClelland was taken to the international guidance documents discussed earlier and was asked whether the international guidance was consistent or inconsistent with the practice of collecting blood in prisons. He replied:

I think it certainly calls the practice into question, that some of the guidance in these documents would, I think, fairly clearly identify [the] prison population as potentially at least a population from which it is inadvisable to collect blood donations.<sup>302</sup>

**26.193** Professor Cash agreed with five propositions that were put to him. These were that: (i) initially, Hepatitis B screening tests were relatively insensitive in the sense that they did not detect all or perhaps even most positive donors; (ii) there came a point, perhaps around the mid 1970s, when Hepatitis B screening tests were more sensitive and probably did detect most Hepatitis B positive donors; (iii) around that time, there appeared to be a blood-borne non-A, non-B Hepatitis agent or agents; (iv) there was an increased prevalence of Hepatitis B among prisoners; and, (v) Hepatitis B is a blood-borne virus.<sup>303</sup> Professor Cash was asked whether it followed from these five propositions that there may also have been an increased prevalence of NANB Hepatitis among prisoners and replied, 'I agree that there may have been, yes'. He agreed with the suggestion that these five propositions should at least have given pause for thought in the mid to late 1970s as to whether blood should continue to be collected from prisons.<sup>304</sup>

**26.194** Professor Cash was asked, if one had regard to those five propositions and had paused for thought in the mid- to late-1970s to consider whether blood should continue to be collected from prisons, whether he could say what the likely conclusion ought to have been. He replied:

---

<sup>300</sup> Ibid pages 77–78

<sup>301</sup> Dr McClelland's Witness Statement [WIT.003.0072] at 0085

<sup>302</sup> Day 9, page 130

<sup>303</sup> Day 10, pages 106–108

<sup>304</sup> Ibid page 108

I find that very difficult to answer .... I really don't honestly know ... in 2011. Again, with the power of the retrospectoscope [ie the benefit of hindsight] I would probably say they should have got out of that and the whole of the transfusion world should have moved, including the commercial people, collecting plasma. But that's a very retrospective view ....<sup>305</sup>

**26.195** Professor Leikola had not seen Dr Yellowlees' letter of 1 May 1975 prior to being asked to assist the Inquiry. On being sent the letter and asked for his comments he replied:

To me, when I read this particular paragraph here on prisons, I agreed with the first sentence. I also agreed with the second sentence that there are various groups with high risks that are extremely difficult to identify. But somehow I don't see that this fact that we can't identify some risk groups would lead to the decision that one group that we can identify should not be excluded from the donor pool. This means that if there are a number of things that we can't do, that doesn't mean that if there is something that we can do, it should not be done. If that group can be clearly identified, as stated here, the prisoners were a group with risk.<sup>306</sup>

**26.196** Professor Leikola confirmed that the introduction of more sensitive Hepatitis B screening tests around 1975 did not alter his opinion that a donor group which was known to carry a greater risk of Hepatitis B should still have been avoided.<sup>307</sup> He was asked whether this was an area in which different experts could reasonably hold different views or whether he considered that it simply would not be a reasonable view that collection in prisons should continue. He replied:

I think that the meaning of introduction of a more sensitive test was interpreted differently by different countries, notably in France, the donations in prisons continued and therefore I think that experts could interpret this differently. However, in the light [of] what was known at that time about Hepatitis B and possibly other viruses, I think this advice of, "Yes, go ahead with prison donations", was probably not correct.<sup>308</sup>

**26.197** He went on:

I would refer to the practice in Finland, where we decided to stop that because the significance of prison donations ... to the blood supply was not significant and therefore we decided to, so to say, play safe and therefore from our perspective this particular recommendation, "Yes, go ahead with prison donations", was not reasonable.<sup>309</sup>

**26.198** Professor Leikola was asked a number of specific questions relating to this topic, which are best set out in turn:

- Asked whether he considered that the practice in Scotland of collecting blood in prisons ought to have been reconsidered at any point in the 1970s or early 80s, he replied:

I think my feeling is that the matter should have been taken on the table and discussed in a logical way. Seeing what are the cons and pros of continuing this

---

<sup>305</sup> Ibid page 109

<sup>306</sup> Day 13, page 46

<sup>307</sup> Ibid page 48

<sup>308</sup> Ibid page 49

<sup>309</sup> Ibid page 50

long practice .... However, the impression that I have received from reading these different documents that you sent me is that this matter was really not taken into serious consideration during the late 1970s up until 1981 and of course then 1983.

So my impression – and this is just my impression from reading these documents – is that this tradition went on without really being seriously considered whether it should now be stopped because of various facts that had been published during the 1970s.<sup>310</sup>

- Asked what the conclusion ought to have been had the matter been considered in the 1970s and early 80s, he replied:

In my opinion, that should have been stopped, not necessarily ... from one day on, but sort of faded away, so that it would not have caused very much publicity and the impression of not taking prisoners as human beings. But the conclusion would be that I think it would have been reasonable to stop this old practice.<sup>311</sup>

- Asked whether it was reasonable to continue the practice in the 1970s and early 80s, he replied:

In these circumstances, where, if I'm not mistaken, it was not seriously discussed, then I think that it was reasonable to understand that it went on, even though in my opinion it should have been seriously discussed and then made the conclusion that, no, it's much better not to go to prisons.<sup>312</sup>

- Asked, given that Hepatitis B and NANBH were considered to be blood-borne viruses and studies had shown a higher prevalence of Hepatitis B among prisoners, whether could one reasonably have predicted in the late 1970s that there might also be an increased prevalence of NANBH among prisoners, he replied:

At least in retrospect one would say that one could have seen this connection and drawn that kind of conclusion.

....

Just because it appeared then, on the basis of the American studies, that the non-A non-B, at least in 1977/78, is a blood-borne virus or viruses and very likely to be a virus. So if Hepatitis B is a blood-borne virus, then it is reasonable to think that the inmates would have also higher prevalence of this new, unknown virus.

....

Because the ways of acquiring the virus seemed to be quite similar.<sup>313</sup>

- Asked, given that the initial understanding was that NANB Hepatitis was a clinically benign disease, whether that was a material consideration when deciding whether collection in prisons should continue, he replied:

---

<sup>310</sup> Ibid pages 80–81

<sup>311</sup> Ibid page 81

<sup>312</sup> Ibid page 81

<sup>313</sup> Ibid page 82

I think that it influenced, in the background, the decision.

....

But once it became clear that it is a blood-borne virus and so on, and as was shown in the late 1970s, that indeed it does cause disease and this disease is not necessarily mild, then I think that in a case where there is a possibility to prevent that, even if the measure is not very effective but still if that is possible, then I think it should have been done.<sup>314</sup>

**26.199** Dr McClelland was asked whether there were any lessons that could be learned going forward. He replied that various expert groups had been formed which had worked extremely hard to be aware of information about new or emerging infections and populations at risk and to push for action to be taken quickly. He went on:

What I think is much more difficult is to deal with the problem where you have within a community, a professional communal, a sort of very powerful sort of dome of received opinion, which is sitting over everybody and they have a belief system that this isn't a problem. And therefore even when perhaps some individuals sort of stand up and make a noise and say, "I think there is a problem", there is a very good history of you know, people who actually do see a little bit further ahead, clearly not being – actually they seem to be a nuisance because they get in the way of what we are doing at the moment, and that's really a sort of sociological problem, I'm sure not unique to blood services and it is actually very difficult to deal with.

So I think that the best that we can do ... is wherever possible to encourage attitudes that permit and encourage questioning of things that "everybody knows" and more specifically to look at the mechanisms that we have now and that would include the ... advisory committee on the safety of blood ... the national body charged with informing the ministers of health for UK countries about precisely this type of issue, and try to see that that group is well supported, well resourced, has access to the best intelligence, the best connections for picking up, assessing the importance of things and then making a big noise about it so that somebody does something.

I think these are not exactly revolutionary mechanisms but I don't know that I'm in a position to invent any better solutions. Challenging the received wisdom – because no doubt the received wisdom in the UK was that these things weren't a problem. We were okay because we didn't have paid blood donors and somehow that just made everybody feel – I think it would not be unfair to say that there was a slight sort of sense of superiority because we didn't have paid blood donors in the UK. And that may well have been a factor that sort of blinded people to the fact that we need to look at the totality of our donor populations and be sure that we were sensitive and aware of where perhaps there were risks that were greater and should be seriously questioned.<sup>315</sup>

---

<sup>314</sup> Ibid pages 95–96

<sup>315</sup> Day 9, pages 132–134

***Evidence in respect of the incidence of Hepatitis C among drug users and prisoners following the availability of Hepatitis C tests***

**26.200** As discussed elsewhere in this Report (see Chapter 16, *Knowledge of Viral Hepatitis 3 – 1986 Onwards* and Chapter 31, *The Introduction of Screening of Donated Blood for Hepatitis C*), the Hepatitis C virus (HCV) was identified in 1988, scientific details of the discovery were published in 1989, tests for HCV subsequently became available and screening of all blood donors for HCV was introduced throughout the UK in September 1991. In short, once tests for HCV became available, studies showed a higher incidence of HCV among those who injected drugs and a higher incidence of HCV among prisoners compared with the general public.

**26.201** In Scotland, all blood donors who were found to be infected with HCV in the first six months of routine testing of all donations for anti-HCV were followed up. Of those HCV-positive donors, intravenous drug use was found to be the most common risk activity (in 39% of the HCV positive donors).<sup>316</sup>

**26.202** In 1999 Dr Sheila Gore and others reported on a study carried out between 1994 and 1996 into the incidence of Hepatitis C among prisoners in five Scottish prisons.<sup>317</sup> Overall, the study found a prevalence of antibodies to Hepatitis C in 20% of inmates, with a prevalence of anti-HCV in 49% of inmates who reported having injected drugs and a prevalence of 3% in inmates who reported not having injected drugs. The study also found that those who began injecting in 1992–96 were less likely to be positive for anti-HCV than those who started before 1992 (31% compared to 55%).<sup>318</sup> The paper noted that:

International data, including from Scotland, suggested that between 60% and 90% of injectors might have hepatitis C antibodies, with between 50% and 90% of them being also RNA positive.<sup>319</sup>

**26.203** In 2002 Dr M. Adekoyejo Balogun and others reported on a study to ‘estimate the background population prevalence of hepatitis C in England and Wales, observe the prevalence over time and assess the extent of infection outside of known risk groups’.<sup>320</sup> In the study, residual sera from samples sent to laboratories for routine diagnostic examination in 1986, 1991 and 1996 were tested for the presence of antibodies to the Hepatitis C virus (anti-HCV).<sup>321</sup> Testing of the serum samples in each of the years gave an estimation of the overall anti-HCV prevalence in the general population of 1.07% in 1986, 0.55% in 1991 and 0.70% in 1996.<sup>322</sup> Having regard to the HCV genotype<sup>323</sup> distribution

<sup>316</sup> Crawford et al, ‘Prevalence and epidemiological characteristics of hepatitis C in Scottish blood donors’, *Transfusion Medicine*, 1994; 4:121 [PEN.002.0582]

<sup>317</sup> Gore et al, ‘Prevalence of hepatitis C in prisons: WASH-C surveillance linked to self-reported risk behaviours’, *Quarterly Journal of Medicine*, 1999; 92:25–32 [LIT.001.3258]. The five prisons were Barlinnie, Perth, Cornton Vale, Low Moss and Aberdeen, and held approximately one half of the adult prisoner population in Scotland. The test used was a ‘recently validated method for detecting antibodies to hepatitis C in saliva (HepCAbs) which had been shown to correlate with the presence of hepatitis C RNA in blood, and thus with hepatitis C carrier status’.

<sup>318</sup> The authors commented that ‘It is possible that the establishment of harm minimization interventions for injectors in the late 1980s, particularly needle or syringe exchange, has led to a reduction in needle sharing, and thus in hepatitis C transmission’. [LIT.001.3258] at 3262

<sup>319</sup> Gore et al, ‘Prevalence of hepatitis C in prisons: WASH-C surveillance linked to self-reported risk behaviours’, *Quarterly Journal of Medicine*, 1999; 92:25–32 [LIT.001.3258] at 3259. The paper listed 20 references, published between 1992 and 1998, in support of this statement.

<sup>320</sup> Balogun et al, ‘The prevalence of hepatitis C in England and Wales’, *Journal of Infection*, 2002; 45:219–226 [PEN.002.0822]

<sup>321</sup> Pooled serum specimens of 12 were tested using the Ortho HCV 3.0 eSAVE ELISA and reactive samples were further tested by the Monalisa anti-HCV Plus system.

<sup>322</sup> Balogun et al, ‘The prevalence of hepatitis C in England and Wales’, *Journal of Infection*, 2002; 45:219–226 [PEN.002.0822] at 0824

<sup>323</sup> HCV exhibits considerable genetic heterogeneity, with six major genotypes identified exhibiting important biological differences. See Chapter 13, *Knowledge of Viral Hepatitis Now*, paragraph 13.14.



in the study samples, the authors considered that their findings were ‘consistent with the majority of infections having been acquired by injecting drug use’.<sup>324</sup> In the discussion section the authors commented:

Most of the HCV infections in the population studied in this survey were probably acquired before 1986, mainly amongst people born between 1946 and 1970. The low prevalence in the more recent birth cohorts, implies that the incidence of HCV infection has declined. This epidemic is probably primarily associated with acquisition of HCV through injecting drug use. Seroprevalence studies both in the UK and Europe have found prevalence levels ranging from 50% to 90% in injecting drug users and the importance of drug use as a major risk factor for infection has been well documented. The use of recreational drugs in the UK increased steadily during the 1960’s and into the 1970’s. During this time, non-therapeutic heroin misuse emerged in London and spread to neighbouring counties. More widespread injecting of other illicit drugs, such as barbiturates, also increased during this period. The age profile of persons now presenting with HCV liver complications who have acquired HCV through injecting drug use reflects these historical patterns of injecting drug use.<sup>325</sup>

### **Other possible higher risk donors – the collection of blood from US military personnel in Scotland**

**26.204** The suggestion that the Inquiry should address the position of US military personnel as ‘higher risk’ donors was raised in correspondence from Messrs Thompsons, the solicitors acting for the patients, relatives and Haemophilia Society core participants, on 18 March 2011.<sup>326</sup>

**26.205** The Inquiry did not discover any research conducted in Scotland. As noted above (paragraph 26.66), an early English study (in 1972) found that there were no antigen or antibody positive results found – hence prevalence was 0% – on testing armed forces donors, including US Air Force personnel. Technology was not well developed at that time but the results offered some reassurance that there was no significant problem in this population.

**26.206** The Inquiry received evidence that blood was collected from US military personnel in Scotland at RAF Edzell between 1963 and 1996 and from the US naval base at Holy Loch from an unknown date until 1990.<sup>327</sup>

<sup>324</sup> Balogun et al, ‘The prevalence of hepatitis C in England and Wales’, *Journal of Infection*, 2002; 45:219–226 [PEN.002.0822] at 0827

<sup>325</sup> Ibid [PEN.002.0822] at 0828

<sup>326</sup> Correspondence from Messrs Thompsons [PEN.017.0942]

<sup>327</sup> SNBTS response dated 19 April 2011, ‘Collection of blood from US military’, [PEN.017.0966]

**26.207** The number of donations collected at RAF Edzell is shown in the following table:

**Table 26.5: Collection of Blood at RAF Edzell by the East of Scotland Regional Transfusion Centre (Dundee)**

Date	No. of donations	Date	No. of donations	Date	No. of donations
09.04.1963	73	13.05.1975	214	26.02.1987	320
14.11.1963	92	10.11.1975	201	14.09.1987	237
07.05.1964	67	17.06.1976	217	01.02.1988	233
10.12.1964	105	03.12.1976	197	07.06.1988	207
20.05.1965	79	07.06.1977	214	28.02.1989	201
07.04.1966	93	08.11.1977	243	22.06.1989	240
27.10.1966	137	13.06.1978	221	27.02.1990	164
04.05.1967	120	14.11.1978	179	14.06.1990	312
12.10.1967	108	17.05.1979	160	06.11.1990	241
14.05.1968	124	30.10.1979	119	18.04.1991	212
10.10.1968	164	17.06.1980	157	15.10.1991	159
01.05.1969	178	28.10.1980	198	03.03.1992	162
17.11.1969	146	19.05.1981	185	23.07.1992	120
21.05.1970	219	22.10.1981	174	02.02.1993	190
24.11.1970	228	06.05.1982	172	28.09.1993	110
25.05.1971	234	15.11.1982	162	07.04.1994	150
09.11.1971	194	26.05.1983	198	17.10.1994	254
30.05.1972	129	31.10.1983	266	06.06.1995	183
14.11.1972	231	28.06.1984	183	05.10.1995	135
26.04.1973	139	20.11.1984	175	27.02.1996	117
13.11.1973	191	11.07.1985	143		
14.05.1974	132	13.03.1986	280		
12.11.1974	206	02.09.1986	262	Total	11,856

**26.208** The number of donations collected from the US naval base at Holy Loch is shown in the following table:

**Table 26.6: Collection of blood at the Holy Loch US Navy base by the West of Scotland Regional Transfusion Centre (Glasgow) 1982–86; 1989–90**

Date of session	Number of donations
21.10.82	179
10.03.83	119
07.10.83	166
08.03.84	165
04.04.85	102
02.10.85	61
19.05.86	16
13.02.89	142
14.02.89	245
21.02.90	71
22.02.90	131

**26.209** Between 1982 and 1990, an approximate average of 600 donations a year was collected from US military personnel in Scotland. There were approximately 300,000 donations collected annually in Scotland during that period.<sup>328</sup> The donations collected from US military personnel in Scotland between 1982 and 1990 therefore represented approximately 0.2% of the total number of donations collected annually in Scotland.

**26.210** The Inquiry has also considered whether there was evidence to suggest that blood collected from US military personnel in Scotland carried a higher risk of transmission of NANB Hepatitis/Hepatitis C. Reference has been made to some data collected by the Transfusion Directors in the early 1970s. On a more general level, the Inquiry's attention was drawn to three papers in that regard that were suggested to have particular relevance.

**26.211** The first relevant source of information was a paper by Albert Sabin on the incidence of viral hepatitis among US military personnel published in 1976 in the *Yale Journal of Biology and Medicine*.<sup>329</sup> While the author concluded that the incidence of reported cases of icteric viral hepatitis (hepatitis, that is, associated with clinical observation of jaundice) was much higher in US military personnel than in comparable age groups in the civilian population, the author went on to state that the preliminary data strongly suggested that Hepatitis B (rather than Hepatitis A or the 'hypothetical' Hepatitis C) was the predominant viral cause of hepatitis among US military personnel throughout the world and that sexual promiscuity, rather than drug use, appeared to be a more likely explanation for that higher incidence.<sup>330</sup> The paper did not suggest or establish that US military personnel stationed in Scotland were likely to have a higher incidence of NANB Hepatitis than in the general population.

<sup>328</sup> SNBTS Blood Collection, 1975–1991 [PEN.010.0026] at 0029

<sup>329</sup> Sabin, 'Viral hepatitis: problems of incidence and control in military personnel', *Yale Journal of Biology and Medicine*, 1976; 49:259 [PEN.017.0944]

<sup>330</sup> *Ibid* [PEN.017.0944] at 0948–49

**26.212** Secondly, a paper by Kenneth Hyams and others on viral hepatitis in the US navy was published in the *American Journal of Epidemiology* in 1989.<sup>331</sup> The authors reported that, from 1974 to 1984: total first hospitalisations of US naval personnel for viral hepatitis declined, that there was a significant decrease in the incidence of confirmed cases of Hepatitis B and NANB Hepatitis and that the incidence of confirmed cases of Hepatitis A increased after 1980 when a commercial serologic test for acute Hepatitis A became available.<sup>332</sup> During each of the 10 study years, confirmed cases of Hepatitis B were the most frequent hepatitis diagnosis overall. Again, the study did not suggest or establish that US naval personnel stationed in Scotland were likely to have a higher incidence of NANB Hepatitis than the general Scottish population. Indeed, because the study was based on hospital admissions for cases of acute hepatitis and it is now known that most cases of Hepatitis C are non-icteric, the cases of viral hepatitis in the study are more likely to have been caused by Hepatitis A or Hepatitis B than by Hepatitis C.

**26.213** Finally, there was a short article by Michael D Parkinson and others on viral hepatitis in the US Air Force in the period 1980–89, published in the journal *Vaccine* in 1993.<sup>333</sup> It is apparent that no meaningful conclusions can be drawn from the very brief narration of the results of the study reported in the article. In any event, the article was published at a time when all blood collected by the SNBTS, including blood collected from US military personnel, was screened for HCV.

**26.214** In summary, the amount of blood collected from US military personnel in Scotland was minimal (about 0.2%) compared with the total amount of blood collected in Scotland. In addition, the Inquiry is unaware of any evidence to suggest that the SNBTS, the UK Government or any responsible Scottish agency knew or ought to have known during the 1970s or 1980s that blood collected from US military personnel in Scotland carried a higher risk of transmitting NANB Hepatitis, Hepatitis C or, indeed, HIV than blood collected from the general donor population.

## Discussion

### *Use of drugs*

**26.215** As indicated in the first part of this chapter, a current or recent history of injecting drugs, or physical evidence of having injected drugs, were seen throughout the reference period as grounds for deferment from donation for specified periods, or for exclusion from donation altogether. While the general policy may have been clear as it evolved from time to time, prior to 1983 the SNBTS did not provide uniform directions or recommendations for Regional Transfusion Directors and their staff to ensure, as best might be achieved, the application of that policy, for example, by asking prospective donors directly about drug use and/or including a question to that effect in the health check questionnaire.

**26.216** With the passage of time, oral evidence of practice in the 1970s and early 1980s is inherently unreliable, especially in the case of Regional Transfusion Directors and more senior officers of the SNBTS who would not, in the general run of things, be involved regularly in routine donor session work. However, the evidence on this matter does tend to suggest that direct questioning of the donor on their drug use may not then have been

<sup>331</sup> Hyams et al, 'Viral hepatitis in the US navy, 1975–1984', *American Journal of Epidemiology*, 1989; 130:319 [PEN.017.0952]

<sup>332</sup> Ibid [PEN.017.0952] at 0953–54. The authors recognised, however, that 'the decline in reported cases of [NANB] hepatitis, which was most pronounced after a test for acute hepatitis A became available, was probably due in part to more accurate diagnosis of hepatitis A'. At 0958.

<sup>333</sup> Parkinson et al, 'Viral hepatitis in the US Air Force, 1989–1989', *Vaccine*, 1993; 11(5):516 [PEN.019.0861]

routinely used as a means of enforcing that policy. That evidence is limited. Mrs Prior ceased working as a MTA in the west of Scotland in 1974. Dr Mitchell thought that there was no questioning on injecting drugs in the 1970s but thought that it might have come in later in the consideration of AIDS. Dr McClelland was only confident that the majority of the staff would have questioned donors about drug use from the early 1980s onwards.

**26.217** Observation by donor session staff, short of a thorough and structured examination backed up by relevant and detailed questioning, might not have uncovered the full extent of intravenous drug use among prospective donors. The 1971 WHO Guide seems to have been excessively optimistic in suggesting that medical officers should be able to pick out 'drug addicts' in distinguishing acceptable from unacceptable donors. However, it may have envisaged a more thorough medical examination than typically happened in Scotland in the 1970s.

**26.218** In any event, injection of controlled drugs by a donor might have ceased long before the examination and have left no surviving traces either on the donor's body or in their behaviour. As was to become clear after tests for Hepatitis C became available, infection could remain asymptomatic, but transmissible, for decades in individuals who had ceased to be IVDUs and who may never have been addicted to intravenous drugs. The true nature of the risk was not known in the 1970s and early 1980s.

**26.219** The principal guidance available to the Regional Directors of the SNBTS prior to 1983 appears to have been the 1977 *Memorandum on the Selection, Medical Examination and Care of Blood Donors*. Until the arrival of AIDS, neither international nor UK produced guidance seems to have contained any explicit advice emphasising the need to question blood donors about their drug usage, in particular, any intravenous drug usage. In June 1983, the South East BTS introduced donor questions about risk factors including intravenous drug use and by early 1984, at the latest, this had become SNBTS practice. Professor Juhani Leikola of the Finnish Red Cross Blood Transfusion Service confirmed that the donor questionnaires used in Finland in the late 1970s/early 1980s did not include a question as to whether the donor had ever injected or used drugs. He also indicated that it was not until 1983 when 'AIDS came into the picture' that questioning of donors about intravenous drug use started in Finland. The numbers of those who were drug dependent within prison and other penal institutions remained relatively stable until the early 1980s. The upward trend in drug use outside such institutions was modest until 1980. In and after 1981 the rate of growth in drug abuse accelerated.<sup>334</sup> This may also assist in explaining the relative lack of emphasis on the questioning of donors up until the early 1980s. A number of the Regional Directors were concerned about the sensitivities of the donor population and this was, plainly, a legitimate consideration given that the blood supply depended upon voluntary donation. In both Finland and Scotland AIDS seems to have been the catalyst for the introduction of the routine questioning of donors about the injecting of drugs.

### *Prisons and other penal establishments*

**26.220** By the mid-1970s there was some international guidance tending towards advice that blood should not be collected for transfusion from those detained in penal institutions. It was emphasised, however, that decisions on the designation of high risk groups was

---

<sup>334</sup> See the data appended to the Schnier, Goldberg paper on the Estimated Number of individuals Infected and Alive in 2011 as a Consequence of Blood Transfusion in Scotland 1970–1991: [PEN.019.0899] at 0902.

a matter for local decision in the light of circumstances obtaining from time to time and having regard to the need for and availability of blood. As noted at the beginning of this chapter, international practice varied widely in respect of collecting blood from penal institutions. National circumstances clearly varied considerably. The policy and practice in Scotland must be considered in the light of local circumstances here.

### ***Responsibility for policy***

**26.221** When, at a meeting on 26 September 1973, the incidence of Australian antigen in prison donors was reported to be higher than in the general public, the English and Welsh Regional Transfusion Directors agreed that, if it were decided to discontinue accepting blood donations from prisoners, the Home Office should be informed before any local action was taken.<sup>335</sup> There is, however, no evidence that there was a similar concern within the Scottish administration at the time. As discussed in Chapter 17, *Blood and Blood Products Management*, policy was a matter for ministers and their civil service advisers.

**26.222** The letter dated 1 May 1975 by Dr Yellowlees, referred to earlier, was a clear example of government giving advice on donor selection, at least in England and Wales. Equally, Dr Wallace's comments in his 1977 publication, that it was socially and psychologically undesirable to exclude prisoners from the donor population, acknowledged that the collection of blood required to be seen not only in the context of the adequacy and safety of the blood supply. He referred to the role of blood donation in prisoner rehabilitation, observing that some prison donors became regular volunteers after their release. The DHSS document, published in 1979 and applicable throughout the UK, *Standards for the Collection and processing of Blood and Blood Components and the Manufacture of Associated Sterile Fluids*, also provided government advice on this matter. Dr Brookes' experience in London before moving to Dundee in 1981 had informed her that it was long-standing UK Government policy that the BTS should visit prisons to permit prisoners to make some restitution to society and to do something, which many in the community did, to help their return to normal life after release. Dr McClelland's evidence that the Director of HMP Saughton made several representations to the Edinburgh and South East of Scotland BTS to return to the prison and resume sessions after Dr McClelland had terminated the practice in 1981, indicated in a practical way that the rationale for the practice included policy relating to prison management rather than exclusively to SNBTS management.

**26.223** The wider policy aspects of the question were clearly recognised by the UK government. The minute sent by Mr JB Brown, Medicines Division, to his DHSS colleagues on 27 July 1983 on the use of blood from prisons, sought departmental guidance on the issue at the request of the Medicines Division's Inspection Action Group.<sup>336</sup> Mr Winstanley commented on the need to consult the Home Office in view of the importance placed on the social responsibility aspect of prison sessions. The SHHD manuscript file note dated 11 August 1983 recorded the outcome of Mr Winstanley's contact with the SHHD in respect of the Medicines Inspectorate's query.<sup>337</sup> It recorded that the situation in Scotland would be kept under review, 'particularly to hear of developments in England which might be influenced by Home Office views'.

---

<sup>335</sup> Minutes of Meeting [DHF.002.7960] at 7967

<sup>336</sup> Minute [SGH.001.0575]

<sup>337</sup> File Note [SGH.001.0571]

**26.224** By the date of his minute of 23 August 1983, quoted in paragraph 26.128, Mr Winstanley had clearly identified the problem presented by the risk of transmission of AIDS. His view reflected the position common at the time, that it was difficult to advise on Departmental policy on the collection of blood from borstals and prisons since it was for individual Regional Transfusion Directors to determine how and from where donations were sought. However, his observation on the need to liaise closely with the Home Office underlined the wider policy issue. The Home Office had in the past been in favour of blood donation by prisoners as an aspect of policy unrelated to the risk of transmitting disease. It was clearly understood at the meeting of SNBTS Directors on 13 September 1983 that the DHSS would wish to consult the Home Office on account of that department's previous wish to encourage donation in prisons.<sup>338</sup>

**26.225** The letter dated 1 May 1975 by Dr Yellowlees referred to earlier was a clear example of government giving advice on donor selection, at least in England and Wales, as was the document published by the DHSS in 1979 and applicable throughout the UK, on the *Standards for the Collection and Processing of Blood and Blood Components and the Manufacture of Associated Sterile Fluids*. The intervention of the Medicines Inspectorate in 1982 clearly had an impact on the thinking of the Working Party on the Selection of Donors. Among other considerations, it undermined further the notion within the SHHD that the selection of donors was wholly a matter for transfusion directors.

**26.226** It is implicit that there will be issues affecting the portfolios of more than one government Minister or, in the case of Scotland before devolution, more than one department of the Scottish Office. Resolution of any differences of substance was ultimately a matter for political office holders rather than officials. The exchanges between UK departments were appropriate. However it was arrived at, the decision communicated by Dr Yellowlees in May 1975 removed from the NBTS direct responsibility for continued prison collections, notwithstanding the relatively high risk of transmitting Hepatitis B.

**26.227** Dr Wallace's view was not a policy consideration for the SNBTS. The social factors that entered into the debate – whether it was socially or psychologically desirable to exclude prisoners, whether blood donation assisted rehabilitation and similar formulations – were issues for government. In deciding on social policy, it was for ministers to determine whether the incidental benefits to prisoners of giving blood should prevail over risks to the safety of recipients of the blood. That would have required advice on whether there was a risk and, if so, on its magnitude. Social cost and benefit might not have been easy to balance, though the safety and well-being of NHS patients would on any view have been a high priority. It was clearly, however, not a matter for a transfusion specialist such as Dr Wallace to decide. The emphasis in the documents on the views of the DHSS was a reflection of the political reality: collection in prisons was not exclusively a matter appropriately devolved to technical specialists. It engaged wider social values and was properly a matter for ministers and government policy.

**26.228** If that was recognised at UK level, it was appropriate that it should be recognised at local level in Scotland. As set out in Chapter 17, *Blood and Blood Products Management*, paragraph 17.20, it was the statutory duty of the Secretary of State for Scotland, and now the Scottish Ministers, to provide effective health care in Scotland, including promoting the effective provision of blood transfusion services, and the Scottish Ministers have

---

<sup>338</sup> Minutes of Meeting [SNF.001.0072] at 0077

operational control of health care policy. The CSA had delegated responsibility for the operational management of blood services but was subject to, and obliged to act in accordance with, such directions as might be given by the Secretary of State. Devolving management responsibility to the CSA could not remove ultimate responsibility from ministers for wider social policy.

**26.229** The evidence of Dr Scott, Dr McIntyre and Mr Wastle, that it was for SNBTS Transfusion Directors to deal with the issue, to the extent that they did not know whether the SHHD had ever considered it, was clearly a true reflection of officials' attitude at the time and is accepted as a reliable account of their own views and practices. While there is evidence that the Home Office in England and Wales encouraged donations in prisons, there was no evidence before the Inquiry that the SHHD encouraged donation in prisons in Scotland. Instead, the SHHD took a passive role, noting without demur Dr Yellowlees' letter dated 1 May 1975 and otherwise leaving it for the SNBTS to decide whether prison collection was appropriate.

**26.230** The Regional Transfusion Directors were an appropriate group to advise government on the medical and technical aspects of this question. Individually they may have held different views on the answer from time to time but the Inquiry heard no evidence that would have cast doubt on their competence to assess risk according to the standards of the time and to contribute to the debate. It was not, however, the appropriate group to advise on, much less to determine, the social issues raised. On the other hand, there was no evidence before the Inquiry that the SNBTS Directors advised the SHHD of any concerns regarding collection from prisons.

*When and how was the issue raised?*

**26.231** It is appropriate for the Inquiry to discuss the questions that arise in relation to timing and the presentation of the issue of prison donations with reference to relevant medical and technical aspects.

**26.232** Regional Transfusion Directors were free to follow their own practices. Dr McClelland's decision in 1981 to discontinue prison sessions was prompted by the views of the regional donor organiser.<sup>339</sup> Her reasons – related to the threatening prison environment, the difficulty of obtaining clear, transparent answers and other social factors – would have been of similar weight in any region. Dr McClelland responded to her views without reference to other Regional Transfusion Directors, a clear example of the exercise of the local autonomy that characterised the service at the time. Similarly, Dr McClelland received, but did not respond positively to, representations by the Director of HMP Saughton to return and run further sessions. It would not be appropriate to draw general conclusions relating to other regions from the timing or circumstances of his decisions. They were not prompted by apprehensions relating to transmission of infection and they were not supported by any well-formulated policy.

**26.233** Dr Brookes was opposed to prison collections before she came to Scotland and clearly articulated her concerns after she arrived in Dundee in 1981. After she took up her post, she vetoed a proposal for additional prison sessions. The last prison session in her region was 2 August 1983. She deliberately raised her concerns with the Medicines Inspectors and was well informed of the practice of her Welsh and English colleagues. After

---

<sup>339</sup> Day 9, page 79



the meeting on 29 March 1983 Dr Brookes asked the organising secretary in Dundee to phase out prison and young offenders' sessions over the coming year, accommodating the Centre's programme of donor sessions which was generally confirmed one year ahead.<sup>340</sup>

**26.234** It is clear from Dr Brookes' evidence that it was at the meeting on 29 March 1983 that it became evident to her that, although the Directors were divided, individual Directors who wished to discontinue prison sessions could do so. At that same meeting Professor Urbaniak had indicated that he intended to review the situation in his region and, like Dr Brookes, he concluded that the practice was undesirable and terminated it. It seems reasonable to conclude that for the Scottish regions as a whole, excluding Edinburgh and the South East, the issue became live in March 1983. By then, the Directors were, effectively, solely responsible for implementing their individual decisions and discontinuing or not according to their individual assessments of the needs of their regions.

**26.235** As in other areas, Professor Leikola's insight into the position up to that point was helpful. There had been a long standing practice of collecting blood in prisons. He said:

[T]he impression that I have received from reading these different documents that you sent me is that this matter was really not taken into serious consideration during the late 1970s up until 1981 and of course then 1983.

So my impression – and this is just my impression from reading these documents – is that this tradition went on without really being seriously considered whether it should now be stopped because of various facts that had been published during the 1970s.<sup>341</sup>

**26.236** Once the equilibrium in a static society is disturbed, the potential for change may be unlimited. Disturbing the established position is not necessarily easy, however. Dr McClelland's observation was pertinent. Again, as noted above, he spoke of:

[T]he problem where you have within a community, a professional communal, a sort of very powerful sort of dome of received opinion, which is sitting over everybody and they have a belief system that this isn't a problem. And therefore even when perhaps some individuals sort of stand up and make a noise and say, "I think there is a problem" ... actually they seem to be a nuisance because they get in the way of what we are doing at the moment, and that's really a sort of sociological problem, I'm sure not unique to blood services and it is actually very difficult to deal with.<sup>342</sup>

**26.237** The difficulty of challenging the status quo of entrenched opinion perhaps explains most cases of prolonged practices after they are or should be challenged. One can exclude conspiracy: there was no decision to continue to accept donations in the face of contrary indications. The practice simply continued until it stopped.

***Should the practice have been discontinued earlier than it was?***

**26.238** On the evidence there is an obvious question whether prison collections were at all necessary in the reference period to secure the blood supply. The issue relates to demand for blood components and in particular for red cells. Packed red cells were produced in

---

<sup>340</sup> Dr Brookes' Witness Statement [WIT.003.0057] at 0061–62

<sup>341</sup> Day 13, pages 80–81

<sup>342</sup> Day 9, pages 131–134

the course of preparation of plasma for fractionation at PFC and surplus production was sent to England. The preference in the west of Scotland appears to have been for blood components produced locally (mainly at Law Hospital) and that provides the principal context for discussion.

**26.239** Prison collection was not necessary in Edinburgh and south east Scotland: discontinuation of the practice caused no supply problems. The dedication of a high proportion of whole blood collections to the preparation of plasma for supply to PFC ensured an ample supply of red cells for surgical and other medical applications. Apart from some very general observations that there were occasional shortages during local holidays and other periods for example, the only region that consistently sought to justify prison collections on supply grounds was the west of Scotland.

**26.240** It has to be accepted that there were occasional issues over supply in the west of Scotland but it cannot be accepted that those problems were necessary (or, at least, insurmountable). Professor Cash's observation on this issue is pertinent: it would have required a little less autonomy and a little more cross-regional support when times got difficult. Given the total input of red cells in the whole of Scotland, the loss of prison donations could easily have been coped with.<sup>343</sup> The continued practice cannot, on the evidence, be justified on the grounds that without prison donations there would have been shortages of red cells for surgical or other medical applications that could not be made good from Scottish sources. Dr Mitchell's comment that he preferred to cope from within his own region<sup>344</sup> was at odds with the need for more collaborative working.

**26.241** The impact of the AIDS epidemic finally led to a change of mind in Glasgow and the west of Scotland.<sup>345</sup> The risk of transmission of HIV 'tipped the balance' as far as Glasgow was concerned. Implicitly, the risk of transmission of Hepatitis B and NANB Hepatitis had not tipped the balance and collections did not cease until 25 March 1984, about the time of Dr Gallo's publication of the discovery of HTLV-III. (See Chapter 11, *HIV/AIDS Aetiology*.)

**26.242** There was ample evidence before March 1984 that Hepatitis B and NANB Hepatitis presented threats to recipients of blood, blood components and blood products. In the case of Hepatitis B, there was ample evidence that there was a relatively high prevalence of infection in the prison population. The paper by Dr Wallace and colleagues published in March 1972 represented a major advance in the collection and analysis of relevant data: overall, the incidence of Hepatitis B positive donations among prison donors (0.65%) was just under seven times higher than that in the general public (0.10%). The English and Welsh Directors' researches yielded similar data when they completed their exercise in July 1974: in 1973 the incidence of Hepatitis B antigen in new general public and factory donors was 0.09% whereas the incidence of Hepatitis B antigen in donors in prisons, borstals and similar institutions in 1973 and Jan-March 1974 was 0.43%.<sup>346</sup> The validity of the data did not depend on whether prisoners were drug addicts or how they came to be infected. The numbers defined the relative seriousness of the problem prison donors presented. The Dow/Follett report of July 1984 showed that raised ALT in the prison population was ten times the incidence found in the general population.

<sup>343</sup> Day 10, page 73. See also Professor Cash's Written Statement on blood shortages [PEN.011.0066]

<sup>344</sup> Minutes of BTS Co-ordinating Group held on 22 February 1983 [SNB.003.6988] at 6990

<sup>345</sup> Dr Mitchell – Day 9, pages 157–58

<sup>346</sup> Frequency of HBAg and Anti-HBAg Exported by RTCs New General Public and Frequency Donors and in Donors in Armed Forces and in Prison Borstals and Similar Institutions [SGH.001.7095]

**26.243** In earlier chapters of this Report, the Inquiry has discussed:

- The effectiveness of basic collection procedures to identify the risks presented by potential donors. The discussion showed that the procedures were not effective in the case of a person unwilling or unable to provide information on the risks arising from his or her medical history, such as a history of hepatitis/jaundice or blood transfusion. They were equally ineffective in the case of a person with a past or current history of injecting drug use who was unwilling to disclose that practice and who either did not have signs of current drug use or had taken pains to conceal track marks from investigators.
- The effectiveness of screening technology to identify blood that presented risk of transmission of infection. HBsAg screening was very ineffective until the mid-1970s in identifying blood infected with Hepatitis B. It was totally ineffective in identifying blood infected with NANB Hepatitis.

**26.244** If it is known that there is a real risk of transmitting serious infection; that identification of that risk as presented by donors is beset by procedural and technological problems; and that a particular group presents risk of transmitting infection of an order of magnitude greater than the general population, there appears at first blush to be good reason to avoid that population.

**26.245** The position is complicated by a number of factors, however. HBsAg assays were initially very ineffective: a detection rate of 25–30% would have suggested that a population with a relatively high prevalence of infection should have been avoided. The tests became more efficient with time, however, and that factor became less significant.

**26.246** The issue was thought to have diminished by the mid-1970s. Dr Yellowlees' letter of 1 May 1975 shows the official UK response to the perception of risk at that stage, when confidence in screening for HBsAg was at its peak.

**26.247** There were, however, good scientific and medical grounds for terminating prison collections by the early 1980s. The time frame for consideration of the issue is defined roughly by these dates. By the early 1980s concerns about prison collections were being articulated by Directors such as Dr Brookes and they were probably shared by Professor Cash and others. Dr McClelland acted alone in not collecting blood from prisons in his region after December 1981: others might have taken a similar step. There was still no consensus even in 1983. The role of a specialist service such as the SNBTS was to express a view that might have persuaded government to act. While the SNBTS could not alter UK Government policies understood to be in place that were opposed to termination on social or rehabilitation grounds, it would have been reasonable for the SNBTS to have formulated a collective view for communication to the SHHD on whether there were medical and scientific reasons to suggest that the continuation of the practice presented an unnecessary risk to patients. In the absence of the SNBTS bringing the potential health risks of collecting blood from prisons to the attention of the SHHD, one can perhaps understand why SHHD officials did not consider the issue or bring it to the attention of ministers. By way of example, the Finnish Red Cross had considered the matter and had taken the decision, in 1975, to cease collection in penal institutions having regard to the results from the introduction of more sensitive Hepatitis B screening tests around that time. The SNBTS Transfusion Directors could have given similar advice to the SHHD as Dr Helske gave to his government agencies, although it must be borne in mind that

Finland had a highly centralised service. It appears that it was not exposed to differences of opinion such as existed between Dr Wallace and Dr Brookes.

**26.248** Although by March 1983 Professor Cash, the National Medical Director, appears to have been of the view that the practice of collecting blood in prisons should cease, he could not bring about the end of that practice in Scotland. Regional Directors did not report to, or accept review by, the National Director. If a Regional Director considered that the practice should continue in his region, he was free to follow that course. One of the effects of this limitation in the effective powers of the National Medical Director of the SNBTS was that, in the absence of consensus amongst the Regional Directors, collective action could not be taken.

**26.249** Even if the Scottish Transfusion Directors had tried to reach a collective view before 1983 on the practice of continued collection in penal institutions, it is not obvious that agreement would have been reached given the differences of professional opinion among them. It is important to avoid colouring the evidence that has been gathered, with the benefit of hindsight. A speculative proposition about ‘what should have been obvious’ would be easily made and might be superficially attractive; there is, however, no basis on which it could be suggested that the differences of opinion among experts were other than genuinely held and honestly and reliably reported. Given the evidence that has been narrated, including the lack of a uniform practice among the transfusion regions in England and Wales or in other European countries, there is no point in the chronology at which it can be said that the SNBTS Directors should have delivered a consensus opinion to government that prison collections should be terminated before 1983 when they voluntarily began to withdraw from prison collections (with the exception of Dr McClelland who, prompted by his regional donor organiser, had stopped earlier).

## Conclusions

### *Intravenous drug use*

**26.250** The International Society of Blood Transfusion (ISBT) Guide *Criteria for the selection of blood donors* of 1976 identified individuals suspected to be parenteral drug addicts among those who should be excluded from donating blood.

**26.251** In 1977 the BTS produced the *Memorandum on the Selection, Medical Examination and Care of Blood Donors*. It was used as guidance by all Scottish RTCs in developing their local policies. It stated that ‘Illicit drug taking if admitted or suspected should debar’. Similar wording was contained in the *Standards for the Collection and Processing of Blood and Blood Components etc* published by the DHSS in 1979.

**26.252** Before the advent of AIDS in the early 1980s, therefore, it was known that drug taking by a potential donor and, in particular, intravenous drug taking, should exclude the potential donor from donating blood. The measures implemented within the SNBTS in order to exclude such individuals from donating blood included inspection, assessment and, to a limited extent, interview. However, up until the advent of AIDS in the early 1980s it seems likely that there was no uniform policy within the organisation in order to ensure that donors were routinely and directly questioned on their drug use.

**26.253** In any voluntary donation system there would always have been (and there continue to be) limitations on the procedures that might reasonably be followed to exclude the risk of accepting blood from a prospective donor with a history of intravenous drug

use. Full medical examination was, and remains, impractical. The health questionnaire forms used in current practice contain questions focused on risk associated with ‘ever’ having injected drugs and the forms must be signed by prospective donors in the presence of a member of staff. The requirement for signature was an important step forward. However, the effectiveness of the collection system to exclude or reduce risk related to parenteral drug use (in particular, in relation to risks arising from blood-borne viruses for which sensitive screening tests are not yet available) still depends on the reliability of the prospective donor and, at the end of the day, in some cases at least, on the donor’s honesty. Notwithstanding the risk of upsetting some prospective donors, there is no alternative to emphasising in direct interview the prohibition on donation associated with a history of injecting drugs, so as to limit the scope for error or the provision of inaccurate information.

### *Collection of blood from prisons*

**26.254** The evidence obtained by the Inquiry indicates that blood was collected from penal institutions in Scotland from at least 1957 until the last prison session took place in each individual region.<sup>347</sup> The last prison donor sessions took place respectively in the south east (Edinburgh) on 22 December 1981; north (Inverness) on 24 February 1983; north east (Aberdeen) on 28 July 1983; east (Dundee) on 2 August 1983; and west (Glasgow) on 25 March 1984.<sup>348</sup>

**26.255** The ISBT *Criteria for the Selection of Blood Donors* in 1976 proposed that prospective donors should be excluded if they are ‘inmates of a correctional institution’. However, in this as in other matters, individual Transfusion Directors exercised a high degree of autonomy in donor selection and it is not possible to state that there was uniform practice.

**26.256** Practice among European blood transfusion services in respect of collecting blood from prisoners clearly differed. In particular:

- Some countries never collected blood from prisoners (Denmark, the Netherlands<sup>349</sup> and Eire).
- In the 1970s some countries introduced a permanent or temporary deferral of blood collected from prisoners (Switzerland, 1970<sup>350</sup>; Belgium, mid-1970s; Finland 1975).
- Some countries ceased the collection of blood from prisons in the 1980s (England and Northern Ireland, 1983; Scotland, 1984; Luxembourg, 1985; France, 1985–89).<sup>351</sup>
- Other countries did not introduce a permanent or temporary deferral of blood donation by prisoners until the 1990s (Portugal, 1990; Austria, 1995; Germany, 1996; Norway, 1997).<sup>352</sup>

<sup>347</sup> The commencement of the practice of prison collection in 1957 is taken from the SNBTS paper, ‘Collection of Blood in Prisons’ [PEN.018.1521] at 1525.

<sup>348</sup> SNBTS Blood Collection 1975–1991 [PEN.010.0003] at 0012. The prisons visited by each RTC are listed in SNBTS Blood Collection 1975–1991 – further response [PEN.010.0026] at 0028

<sup>349</sup> It was also Professor Leikola’s understanding, based on discussion with Professor van Aken of the Netherlands Red Cross Blood Transfusion Service, that the Netherlands never collected blood in prisons: Day 13, pages 58–59

<sup>350</sup> See also the evidence of Professor Leikola: Day 13, pages 59–62

<sup>351</sup> Ibid pages 62–64

<sup>352</sup> See also the discussion in the SNBTS paper ‘Collection of Blood in Prisons’ [PEN.018.1521] at 1529

**26.257** There was no evidence before the Inquiry that any additional steps were taken at prison donor sessions in Scotland to seek to screen out higher risk donors such as those who had ever injected drugs.

**26.258** Dr McClelland's decision in 1981 to discontinue prison sessions was prompted by the views of the regional donor organiser. The decision was based more on the fact that prisons were felt to be an unsuitable environment in which to conduct donor sessions, than on concerns that prisoners' blood was thought to carry an increased risk of infectious diseases, including NANB Hepatitis. It was open to other Regional Transfusion Directors to have done the same.

**26.259** It appears that Regional Transfusion Directors in Scotland collectively did not apply their minds to whether collection from penal institutions carried a greater risk of transmission of infectious disease and whether, therefore, the practice should continue until the matter was raised by the Medicines Inspectorate in 1982. However, the Medicines Inspectorate appear to have raised the matter at that juncture because Dr Brookes had informed them of her concerns about the practice of prison collection when they inspected Dundee in March 1982. The matter was first discussed by the Scottish Transfusion Directors, collectively, at their meeting on 29 March 1983.

**26.260** It is unfortunate that consideration was not given by the Scottish Transfusion Directors, collectively, as to the appropriateness of continuing with prison collection prior to the matter being raised by the Medicines Inspectorate in 1982. There was evidence in the 1970s showing an increased prevalence of Hepatitis B in the prison population, knowledge that tests for Hepatitis B were not completely sensitive and emerging knowledge of an additional hepatitis disease, NANB Hepatitis, from about 1974 onwards which, like Hepatitis B, was also transmitted by blood.

**26.261** Had the Transfusion Directors applied their minds to the practice, however, it cannot be said that they are likely to have decided to stop collecting in prisons or that it was unreasonable for the practice to have continued until the early 1980s. In particular:

- While there was evidence in the 1970s of an increased prevalence of Hepatitis B among the prison population in Scotland, it was reasonable to think that by the mid-1970s available tests for Hepatitis B had become sufficiently sensitive to detect most, if not all, carriers of that virus.
- While knowledge of NANB Hepatitis emerged and developed from around 1974 onwards, the disease was considered in the late 1970s and early 1980s to be clinically mild in most cases.
- It does not seem to have been suggested in the late 1970s and early 1980s that there may have been an increased prevalence of NANB Hepatitis in the prison population in Scotland (and had such a suggestion been made it could only have been a tentative one given the absence of any tests for NANB Hepatitis with which to establish the hypothesis).

**26.262** Against that background, and in the absence of any instruction or direction from government in Scotland, it cannot be said that the Scottish Regional Transfusion Directors acted unreasonably in continuing to collect blood from prisons until the early 1980s.

**26.263** In addition, given the variation in practice in transfusion regions in England and Wales and in other European countries, it cannot be said that the practice in Scotland in the 1970s and early 1980s to collect blood from penal institutions was out of step with generally accepted practice elsewhere.

**26.264** With the benefit of hindsight, it seems likely that there was a higher prevalence of Hepatitis C in the prison population in Scotland in the 1970s and early 1980s than among the general donor population, probably as a result of a higher proportion of prisoners with a history of injecting drug use. It is not possible so long after the event and given, in particular, the lack of data on the incidence of NANB Hepatitis/Hepatitis C among prisoners in Scotland in the 1970s and early 1980s (and indeed the lack of data on the incidence of NANBH/Hepatitis C in the general population and general donor population at that time) to estimate the extent to which blood collected from penal institutions carried an increased risk of transmitting HCV. All that can be concluded, with the benefit of hindsight, is that blood collected from prisoners during that period is likely to have had an increased risk of transmitting HCV, albeit the chance of receiving blood collected from prisoners was, overall, relatively low given that only approximately 1% of all donations collected in Scotland between 1975 and 1984 was collected from penal institutions.

#### *US Military Personnel*

**26.265** The amount of blood collected by the SNBTS from US military personnel based in Scotland was even smaller, ie approximately 0.2% of all donations collected in Scotland. In any event, there is no support in the evidence before the Inquiry for the suggestion that American service personnel presented a higher risk of transmitting HCV (or indeed HIV) than the general Scottish or UK donor population.

## Appendix to Chapter 26

Table 26.1: Blood donation and prisoners, Synopsis of the answers by EBA members, September 2004

	Mandatory deferral	Reason for deferral	Mode of deferral	Time of introduction	The measure challenged?	Ethical issues
Austria	Yes	Epidemiological HBV, HCV	Permanently?	~1995	Never	Not voluntary
Belgium	Yes	Epidemiological HBV	One year	Mid 1970s	Never	None
Denmark	Yes	Epidemiological	One year	Never been used as blood donors	Never	None
England	Yes	Epidemiological HBV, IV drug abuse		1980s	Never	None
Finland	Yes	Epidemiological HBV		1975	Prisoners' organisation	None
France	Yes	Epidemiological HBV, HIV	Not permanently	1985/1989	Prison administration	Rehabilitation of prisoners
Germany	Yes	Epidemiological	Permanently	1996	Prison administration	None Rehabilitation?
Ireland	Yes	Epidemiological HBV, HCV	One year after release	Never		None
Luxembourg	Yes	Epidemiological HIV		1985	Never	None
Netherlands	No	Evaluation of individual risk behaviour		Early 1980s. No blood collection in prisons	Never	True volunteer status
Northern Ireland	Yes	"high risk"		1983	Prisoners' representatives	"True volunteers?"
Norway	Yes	Epidemiological	One year after a 72-hour arrest	1997	Never	None
Portugal	Yes	Epidemiological		1990	No	None
Scotland	Yes	Epidemiological		1983		None
Sweden	No		Risk evaluation of the individual. Deferral of 6 months after 72 hours in prison			
Switzerland	Yes	Epidemiological HBV; drug abuse	Only persons in prison	1970	Never	None
Wales	not deferred		Those serving a custodial sentence cannot donate			



**Table 26.2: Donations collected in each Scottish RTC 1971–84**

Year	Total number of donations in each region					Total Scottish donations	Total prison donations*	Prison donations (% Total)
	Edinburgh	Aberdeen	Inverness	Glasgow	Dundee			
1971	n/a	n/a	8500	107,251	24,654	n/a	1126	n/a
1972	n/a	21,156	9000	107,462	25,258	n/a	902	n/a
1973	n/a	21,960	9500	107,249	26,207	n/a	875	n/a
1974	n/a	22,612	10,000	113,312	27,551	n/a	5125	n/a
1975	59,326	23,364	10,482	124,701	30,685	248,558	5915	2.38
1976	62,239	27,125	10,632	130,022	32,531	262,549	2633	1.00
1977	69,878	29,089	11,505	133,736	33,564	277,772	2710	0.98
1978	75,302	29,841	12,697	133,203	32,263	283,306	3436	1.21
1979	77,318	30,565	13,701	135,831	32,663	290,078	4371	1.51
1980	75,639	32,252	14,033	135,008	32,392	289,324	3064	1.06
1981	74,537	33,434	14,388	139,546	31,596	293,501	3360	1.14
1982	73,985	34,803	15,256	142,056	31,751	297,851	2356	0.79
1983	74,146	34,373	16,226	145,944	31,544	302,233	3120	1.03
1984	81,232	33,863	14,539	148,909	30,074	308,617	342	0.11

\* Excluding prison donations from Inverness RTC for which records were lost in a flood.

## CHAPTER 27

### SURROGATE TESTING OF DONATED BLOOD FOR NON-A, NON-B HEPATITIS

**27.1** This chapter deals with the topic of surrogate testing of blood donors for non-A, non-B Hepatitis (NANB Hepatitis) in the late 1980s. The chapter is divided into four parts: (i) an introduction to the topic, (ii) detailed narrative of events in the USA, Europe and the UK, (iii) discussion of the main issues that arise and (iv) the conclusions reached by the Inquiry.

#### Introduction

**27.2** As indicated at the end of the last chapter, in the second half of the 1970s and early 1980s the existence of non-A, non-B viral hepatitis was first postulated and then established.<sup>1</sup> There was, however, no serological or other test available for screening donated blood for markers of infection. In the USA a debate emerged as to whether to introduce tests for 'surrogate' (or 'indirect') markers of NANB Hepatitis infection and a programme of surrogate testing was eventually introduced there. Surrogate testing, described below, was not adopted in the UK generally or in Scotland in particular and the reasons for that became one of the issues for discussion at the Inquiry's public hearings of evidence. This chapter incorporates the Inquiry's discussion and findings related to that topic.

**27.3** As more fully discussed elsewhere in this Report, the Hepatitis B virus (HBV) was identified in 1963,<sup>2</sup> and screening of blood donors in Scotland for the Hepatitis B surface antigen (HBsAg) was introduced in the early 1970s. The Hepatitis A virus (HAV) was identified in 1973<sup>3</sup> but was not associated with the transmission of hepatitis by transfusion. In 1974, however, a US study reported that an agent that was neither HAV nor HBV seemed to be responsible for a substantial proportion of cases of post-transfusion hepatitis.<sup>4</sup> The term non-A, non-B Hepatitis came to be used for cases of hepatitis in which Hepatitis A and Hepatitis B were excluded.<sup>5</sup>

#### *Surrogate testing: ALT and anti-HBc as indirect markers of possible infection*

**27.4** Despite work by many researchers in the late 1970s and early 1980s, the virus responsible for most cases of NANB Hepatitis, the Hepatitis C virus (HCV), was not identified until 1988.<sup>6</sup> In the meantime, research groups in the USA reported a correlation between elevated alanine aminotransferase (ALT)<sup>7</sup> levels in donors and an increased risk of transfusion recipients developing NANB Hepatitis.<sup>8</sup> The same research groups later reported

<sup>1</sup> See also Chapters 13–16 generally.

<sup>2</sup> Blumberg et al, 'A serum antigen (Australia antigen) in Down's Syndrome, Leukemia and Hepatitis', *Annals of internal Medicine*, 1967; 66:924 [PEN.002.0792]. See Chapter 14, *Knowledge of Viral Hepatitis 1*, paragraph 14.1.

<sup>3</sup> Feinstone et al, 'Hepatitis A: detection by immune electron microscopy of a virus like antigen associated with acute illness', *Science*, 1973; 182:1026 [PEN.010.0110]. See Chapter 14, *Knowledge of Viral Hepatitis 1*, paragraph 14.63.

<sup>4</sup> Prince et al, 'Long-incubation post-transfusion hepatitis without serological evidence of exposure to hepatitis B virus', *The Lancet*, 1974:241 [LIT.001.0363]. See Chapter 14 *Knowledge of Viral Hepatitis 1*, paragraph 14.64.

<sup>5</sup> Typically, the term NANB Hepatitis also depended upon the exclusion of diseases such as Cytomegalovirus (CMV) and Epstein-Barr Virus (EBV), both of which are known to cause hepatic disorder.

<sup>6</sup> A 1986 paper, for example, stated: 'There are more than 40 published reports of specific NANB hepatitis assays, many of which have been reviewed. Not a single test, however, has been reproducibly and independently confirmed, not a single test has successfully distinguished proved NANB hepatitis infectious sera from control sera when tested under independent code, and not a single test has moved from the research laboratory to the point of practical application.' Dienstag and Alter, '[NANB] Hepatitis: Evolving Epidemiologic and Clinical Perspective', *Seminars in Liver Disease*, 1986; 6:67 [LIT.001.1675] at 1682

<sup>7</sup> This protein, synthesised in liver cells and normally present in low levels in the blood, becomes elevated when the liver is disordered by virus infection or other hepatic disorders.

<sup>8</sup> Aach et al, 'Serum [ALT] of donors in relation to the risk of [NANB] hepatitis in recipients: the TTV study', *New England Journal of Medicine*, 1981; 304:889 [LIT.001.0753] (the TTV study, discussed below) and Alter et al, 'Donor transaminase and recipient hepatitis', *Journal of the American Medical Association*, 1981; 246:630 [LIT.001.1817] (the NIH study, discussed below).

an association between the presence of antibody to Hepatitis B core antigen (anti-HBc) in donors and an increased risk of NANB Hepatitis in recipients.<sup>9</sup> It was therefore suggested that elevated ALT and/or anti-HBc might be useful 'surrogate markers' for NANB Hepatitis. A surrogate marker is a directly measurable physical entity (usually measured in a blood test) that correlates (has a statistical association) with a disease, where it is not possible to test directly for the disease or where any direct test would be problematic.

**27.5** There were, however, difficulties with the use of either raised ALT or the presence of anti-HBc as surrogate markers for NANB Hepatitis.

**27.6** The underlying difficulty with the use of surrogate tests to identify donors with NANB Hepatitis was twofold. First, such tests were by their very nature non-specific<sup>10</sup> – there would be many 'false positives' where the test result for the surrogate marker (ALT or anti-HBc) was positive but the NANB Hepatitis virus (HCV) was not in fact present. Secondly, such tests also lacked sensitivity<sup>11</sup> – there would be many 'false negatives' where the virus was in fact present, but was not detected because the test was not sensitive enough, precisely because it was not directly testing for HCV.

**27.7** Despite the problems associated with using surrogate tests for the mass screening of donations, with the AIDS crisis and increasing knowledge of the potential seriousness of NANB Hepatitis infection, the arguments for introducing surrogate screening gained ground in the USA. The result was that surrogate screening of donors was first introduced in some centres in 1986 and very widely by 1987. The introduction of surrogate testing in the USA led to further consideration of the issue in Europe, including in the UK. While some European countries introduced surrogate testing of blood donors, most European countries, including the UK, did not.

**27.8** In the event, the issue of surrogate testing was eventually superseded by the identification of the Hepatitis C virus – the virus responsible for most cases of NANB Hepatitis – in 1988 and the subsequent availability of a direct test which detected antibodies to that virus.

## Events in the USA

**27.9** This section sets out in detail the main events in the history of surrogate testing for NANB Hepatitis. Since developments in the USA formed a major element of the background to what happened elsewhere, and in the UK in particular, they are discussed first.

### *Developments in the USA to the end of 1985*

**27.10** Extensive research relating to the aetiology and natural history of NANB Hepatitis in the mid-1970s is discussed in Chapter 15, *Knowledge of Viral Hepatitis 2*. The debate on the effectiveness of screening of blood for ALT elevation and for the presence of anti-HBc as possible indicative markers of NANB Hepatitis infection emerged from that research. The debate took on added significance with the publication in 1978 of an

---

<sup>9</sup> Stevens et al (the TTV study group), 'Hepatitis B virus antibody in blood donors and the occurrence of [NANB] hepatitis in transfusion recipients', *Annals of Internal Medicine*, 1984; 101:733 [LIT.001.3755] and Koziol et al (the NIH study group), 'Antibody to hepatitis B core antigen as a paradoxical marker for [NANB] hepatitis agents in donated blood', *Annals of Internal Medicine*, 1986; 104:488 [LIT.001.1869]

<sup>10</sup> 'Specificity' is a function of a test's ability to identify only the target pathogen.

<sup>11</sup> 'Sensitivity' is a function of a test's ability to capture all cases of infection with the target pathogen.

interim report by the Transfusion Transmitted Viruses (TTV) study group,<sup>12</sup> a project which arose in 1973 from an initiative of the Division of Blood Diseases and resources of the United States National Heart, Lung and Blood Institute, to assess the incidence and cause of post-transfusion viral hepatitis.

### The Transfusion Transmitted Viruses study group

**27.11** The TTV study was a major research exercise that began in 1974.<sup>13</sup> The investigation was initially undertaken at blood transfusion centres in Los Angeles, St Louis and Houston and, from 1976, at the New York Blood Centre.<sup>14</sup> Specimens from all patients enrolled in the study were tested for ALT activity following a standardised protocol and using the same reagents and standards. The same samples were also screened for markers of HBV infection, including anti-HBc.

**27.12** The TTV group's interim report discussed the study of 1307 patients, followed between July 1974 and December 1976. There were 75 episodes of hepatitis among transfused patients, 10 of whom had been infected with HBV. The Inquiry's Terms of Reference did not require detailed discussion of the aetiology or natural history of HBV. The insensitivity of the available tests for Hepatitis B was a significant factor at this time, however, and a number of transfused patients still became infected despite screening. By about 1980 tests for HBV were more sensitive and this problem was materially reduced, though not eliminated. In analysing outputs from their research, the group used sophisticated techniques to identify potential correlations between specific cohorts of donors and recipients, and the ALT and other biometric values found. Volunteer donors alone were selected for this part of the study. Of the various outputs examined, it was found that only the highest donor ALT levels correlated with the development of post-transfusion NANB Hepatitis in recipients and that that correlation was more striking than the relationship with transfusion volume. It was tentatively concluded that there was a possible correlation between donors with markedly elevated ALT and an increased risk of recipients developing post-transfusion NANB Hepatitis.

**27.13** The authors stated:

Since the TTV study is an on-going effort our sample size will continue to grow. Although our study suggests that screening donor units for ALT levels might be useful in reducing the incidence of non-A/non-B posttransfusion hepatitis, the data must be interpreted with caution since the number of patients analyzed to date is small. Also, there are a number of causes for an elevated ALT other than viral hepatitis, one possible reason why 41 of the 75 patients given blood with an abnormal ALT level did not develop evidence of hepatitis in serial follow-up. Furthermore, 30 of the 65 non-A/non-B cases received blood with normal ALT values.

....

Screening volunteer donor units for ALT may be useful in reducing the incidence of hepatitis although further study is warranted.<sup>15</sup>

<sup>12</sup> Aach et al, 'Transfusion-Transmitted Viruses: interim analysis of hepatitis among transfused and nontransfused patients' in Vyas et al (eds), *Viral Hepatitis*, The Franklin Institute Press, 1978, pages 383-396 [PEN.017.0870]

<sup>13</sup> Ibid [PEN.017.0870]

<sup>14</sup> Blood from volunteer donors was used exclusively at the centres in St Louis, Houston and New York. From 1974 to 1976 the Los Angeles centre acquired most of its blood from volunteers but some units were also used from commercial agencies that depended on paid donors.

<sup>15</sup> Aach et al, 'Transfusion-Transmitted Viruses: interim analysis of hepatitis among transfused and nontransfused patients' in Vyas et al (eds), *Viral Hepatitis*, The Franklin Institute Press, 1978, pages 383-396 [PEN.017.0870] at 0882-83

**27.14** In 1978, Dr Harvey Alter and colleagues, who were conducting research at the US National Institutes of Health (NIH) into data on post-transfusion hepatitis from a number of countries, commented on the TTV study:

A finding of potentially great practical import was the observation in the TTV study that 30% of patients with [NANB] hepatitis received one or more blood units with an ALT of greater than 60 International Units/liter. This raises the possibility that donor screening for ALT might prevent some cases of [NANB] hepatitis, but it must be remembered that 70% of non-A/non-B cases received only blood with normal ALT and that 3% [*sic* – 56%<sup>16</sup>] of blood units with elevated ALT did not result in hepatitis. This observation has vast implications for blood banks in that it will increase the time and cost of donor screening and will exclude a significant number of donors who probably do not represent a hepatitis risk. Nevertheless it is a provocative finding ....<sup>17</sup>

**27.15** Alter's group compared the donor ALT levels in their study group of patients with known cases of post-transfusion NANB Hepatitis transmission. They had limited data but commented that their initial findings did not substantiate the correlation suggested by Dr Aach in the TTV paper.

**27.16** Before 1980 therefore, there was no consensus in the USA that ALT testing of donor blood would provide protection against the transmission of NANB Hepatitis.

**27.17** A further report from the TTV study group, entitled 'Serum Alanine Aminotransferase of Donors in Relation to the Risk of Non-A, Non-B Hepatitis in Recipients, The Transfusion-Transmitted Viruses Study,' was published in the *New England Journal of Medicine (NEJM)* on 23 April 1981, ensuring wide circulation of the findings.<sup>18</sup> This second article by Dr Aach and colleagues set out the history of earlier research and the controversy over whether ALT screening would provide an effective, routine method of donor evaluation. In common with other commentators,<sup>19</sup> the TTV study had recognised that the exclusion of HBsAg-positive donors did not eliminate all cases of post-transfusion hepatitis, necessarily implying that an agent other than HBV was responsible for some cases of post-transfusion viral hepatitis. The report stated:

That observation directed the attention of the Study Group back to ALT screening of donors as one approach to reducing further the incidence of hepatitis in recipients ....

....

Systematically collected data for the period 1974 through 1979 now provide substantial evidence that the level of donor ALT is related to the occurrence of [NANB] hepatitis in transfusion recipients. The extent of the association is sufficient to raise the question of whether ALT screening of donors should be reconsidered.<sup>20</sup>

<sup>16</sup> The source of this 3% figure is unclear from the Aach report and appears to be a misprint. The reported data (41/75) suggest that the correct figure was 56%.

<sup>17</sup> Alter et al, 'Non-A/Non-B Hepatitis: a Review and Interim Report of an Ongoing Prospective Study' in Vyas et al (eds), *Viral Hepatitis*, The Franklin Institute Press, 1978, pages 359-369, [PEN.019.0863] at 0868

<sup>18</sup> Aach et al, 'Serum [ALT] of donors in relation to the risk of [NANB] hepatitis in recipients: the TTV study', *New England Journal of Medicine* 1981; 304:889 [LIT.001.0753]

<sup>19</sup> See chapter 25, *Screening of Donated Blood for Hepatitis B* at paragraphs 25.82–25.87

<sup>20</sup> Aach et al, 'Serum [ALT] of donors in relation to the risk of [NANB] hepatitis in recipients: the TTV study', *New England Journal of Medicine*, 1981; 304:889 [LIT.001.0753] at 0753-0754

**27.18** The 1978 findings on ALT were confirmed. The article noted that, by this time, 1513 US transfusion recipients had been followed between 1974 and 1979 to evaluate the incidence of post-transfusion hepatitis and factors influencing its occurrence. The prevalence of post-transfusion NANB Hepatitis was 10%. At lower (low to normal) ALT levels the NANB Hepatitis 'attack rate'<sup>21</sup> was 6% or lower. At higher ALT levels (definitely abnormal) the attack rate rose to 45%. The issue was clearly focused. The authors concluded that ALT testing was a potentially useful method of screening donors to reduce the incidence of post-transfusion NANB Hepatitis. The TTV group stated:

The observations in this report suggest that about 40 per cent of the cases of [NANB] post-transfusion hepatitis among recipients in this study could have been prevented by discarding units with an ALT level in the upper 3 per cent of the distribution (i.e.  $ALT \geq 45$  IU).<sup>22</sup>

**27.19** Having noted that the implementation of ALT testing would reduce the volume of blood available for transfusion, the authors continued:

Consequently, the benefits of initiating ALT screening must be carefully weighed against the number of potential donors that would be excluded, the overall incidence of hepatitis in recipients, and the severity of the disease.

....

Other considerations must be taken into account if widespread ALT testing of blood donors is to be initiated. These include the uncertainty about how long to defer a donor whose blood was rejected, as well as the problems that might occur in the quality control and proficiency of ALT testing on a nationwide basis. Advising donors of the implications of the ALT level would also pose a special problem. In addition, adjustments might have to be made for the observed differences between ALT levels in male and female donors and for the ages of donors. Nonetheless, it appears from this study that screening donor blood to eliminate units with elevated ALT levels would result in a substantial reduction in [NANB] post-transfusion hepatitis.<sup>23</sup>

**27.20** The paper concluded:

Although ALT screening lacks the sensitivity to detect all infectious units and lacks the specificity to detect only infectious units, the high correlation between an elevated ALT level and infectivity of transfused blood provides a compelling argument that such screening should be instituted.<sup>24</sup>

**27.21** In this paper, apart from noting that advising donors of the implications of findings posed a special problem (precisely because the test was a *surrogate* test that might *indicate*, but could not conclusively demonstrate, infection with NANB Hepatitis), little consideration was given to communication with, and care of, donors who were found to have elevated ALT levels.<sup>25</sup>

<sup>21</sup> 'Attack rate' is the cumulative incidence of infection, calculated by dividing the number of people infected by a particular disease by the total number of people in the group being studied.

<sup>22</sup> Aach et al, 'Serum [ALT] of donors in relation to the risk of [NANB] hepatitis in recipients: the TTV study', *New England Journal of Medicine*, 1981; 304:889 [LIT.001.0753] at 0757

<sup>23</sup> Aach et al, 'Serum [ALT] of donors in relation to the risk of [NANB] hepatitis in recipients: the TTV study', *New England Journal of Medicine*, 1981; 304:889 [LIT.001.0753] at [LIT.001.0753] at 0757

<sup>24</sup> *Ibid* at [LIT.001.0753] at 0757

<sup>25</sup> The American approach to donor care was discussed in an article entitled 'Duties to Donors' originally submitted in January 1990 and published in 1992 but said to reflect American policy goals dating from 1973: Sayers, 'Duties to Donors', *Transfusion* 1992; 32:465-466 [PEN.017.0649] See Chapter 30, *Screening of Donated Blood for HIV*, paragraphs 30.16-30.17

## The NIH Study

**27.22** The proposal to introduce ALT screening did not meet with unqualified agreement. In an editorial in the same edition of the *NEJM*, Dr Paul Holland and colleagues (from the Clinical Centre Blood Bank, NIH: Dr Alter's group) argued against the immediate introduction of ALT testing.<sup>26</sup> They acknowledged that the TTV study had presented the best evidence to date that blood donors with elevated ALT levels had a significantly increased likelihood of transmitting post-transfusion NANB Hepatitis but argued that the data did not support routine testing. 63% of patients receiving blood with elevated ALT did not get NANB Hepatitis and 7% of patients who received blood with below normal levels of ALT did apparently become infected. Predicting the outcome of implementation was problematical. They concluded that the 'manifold effects' of ALT testing had to be 'thoroughly considered' before wide-spread adoption of what would be an interim measure until specific tests for NANB Hepatitis viruses became available. The editorial commented:

The question is whether ALT testing of all blood donors should become routine. Is the expected benefit to the patient worth the drawbacks, especially to the donors and to the blood-service complex? In other words, what is the practicality of setting up ALT testing, and what is its impact? A number of questions have to be answered before adoption of the ALT test is to be recommended: How can the test be made uniform from one blood bank to the next? Above what level should donors be excluded? What should they be told when rejected, and should they be rejected permanently? Blood banks would have to add the cost of ALT testing to the cost of blood and recruit more donors to replace those rejected. Physicians would be asked to see patients with 'transaminitis'; for most, the cause would not be evident, nor would a treatment be forthcoming; hence there would be no means available to allay the apprehensions of these rejected donors. When compared with the test of hepatitis B surface antigen to detect carriers of hepatitis B, the ALT test is non-specific and would eliminate 10 to 20 times more blood donors. The manifold effects of ALT testing must be thoroughly considered before there is wide-spread adoption of such an interim measure (to be used until specific tests for non-A, non-B viruses become available).<sup>27</sup>

**27.23** At that stage, Dr Alter's group had itself completed a small scale study at the NIH which supported the TTV study group's data (discussed below). It noted that screening blood donors for ALT appeared to be a promising way to decrease the risk of transmitting hepatitis but it did not support the immediate introduction of screening. In substance they advised caution and developed their concerns in the published study report.

**27.24** That NIH study into surrogate testing for NANB Hepatitis was reported on 7 August 1981.<sup>28</sup> In it, 283 transfused patients were prospectively followed up after open heart surgery. All donors in the study were volunteers. Hepatitis<sup>29</sup> developed in 9% of 231 patients who received blood from donors with normal ALT levels. In contrast, hepatitis developed in 29% of 52 patients who received blood from donors with elevated ALT levels. The NIH group stated:

<sup>26</sup> Holland et al, 'Post-Transfusion Viral Hepatitis and the TTVs', *New England Journal of Medicine* 1981, 304:1033-1034 [LIT.001.1630]

<sup>27</sup> Ibid [LIT.001.1630] at 1631

<sup>28</sup> Alter et al, 'Donor transaminase and recipient hepatitis', *Journal of the American Medical Association*, 1981; 246:630 [LIT.001.1817]

<sup>29</sup> As determined by clinical jaundice or elevated ALT in the absence of other likely causes.

The present study ... confirms the significant association of an elevated ALT level in donor blood and the development of recipient posttransfusion hepatitis; it suggests that pre-transfusion screening of donor blood for ALT level can identify some carriers of the NANB hepatitis virus and possibly prevent approximately 30% of transfusion-related hepatitis.<sup>30</sup>

**27.25** The paper went on:

It is important to emphasize the negative aspect of the donor ALT-recipient hepatitis relationship, namely, that 70% of PTH will not be prevented by screening donors for ALT. In addition, 40 (72%) of the 56 donors with elevated ALT levels were not associated with a case of PTH .... These imperfect correlations reflect the non-specific nature of the ALT test and emphasize that adoption of donor ALT screening will, at best, be an interim measure. Continued vigorous pursuit of a specific serological test for the agent or agents of NANB is mandatory.<sup>31</sup>

**27.26** The NIH group concluded:

For the blood recipient, the ALT test offers new hope for hepatitis prevention; for the donor, it offers new information, but perhaps information that is not really desired; for the blood supplier, it increases the complexity and cost of blood delivery and reduces the available amount of a product already in critically short supply. The ALT testing of donors is thus in a tenuous balance between risk and benefit. The balance shifts toward testing when one considers that approximately 30% of PTH might be prevented ... but this is tempered by the realisation that 70% will not be prevented and that even the prevention of 30% is in some doubt unless confirmed by a randomized clinical trial. The balance also shifts away from testing when one considers the estimated additional \$20 million in the annual cost of blood in the United States alone and the potential national loss of 45,000 donors and more than 90,000 blood units. It is a difficult equation, whose solution will require thought and planning.<sup>32</sup>

**27.27** In subsequent correspondence in the following issue of the *NEJM*, the leader of the TTV group, Dr Aach, responded as follows to the suggestion that the recommendation to introduce screening was premature:

The [TTVS] Group did not recommend that routine screening of blood-donor ALT be initiated immediately on the basis of their findings presented in this article. A number of questions that we believed should be answered first were listed in the Discussion section of the paper .... The TTVS paper stressed the non-specificity and relative insensitivity of ALT screening as compared with the potential of a specific serologic assay for a [NANB hepatitis] virus (or viruses). A serologic assay is clearly preferable if and when it becomes available. However, despite more than five years of intensive effort by many investigators a confirmed, reproducible serologic test is not available, and even if it were developed in a research laboratory in the very near future, three to five years would be needed to adapt the test to large-scale screening. Until that time,

---

<sup>30</sup> Alter et al, 'Donor transaminase and recipient hepatitis', *Journal of the American Medical Association*, 1981; 246:630 [LIT.001.1817]

<sup>31</sup> Ibid [LIT.001.1817] at 1821

<sup>32</sup> Ibid



screening of donor ALT might provide an interim means to reduce the incidence of [NANB] post-transfusion hepatitis in the United States ....<sup>33</sup>

**27.28** At this stage, then, two highly qualified research groups were converging on the view that ALT testing provided a promising possible approach to testing donor blood in the USA with the objective of limiting NANB Hepatitis virus transmission, pending the introduction of a specific serological test, but neither could mount an adequate argument on scientific grounds to justify immediate general implementation of ALT screening. Further, in its paper of 7 August 1981, the NIH group had developed the suggestion that, if populations with increased exposure to HBV also had increased exposure to the NANB Hepatitis virus, then the presence of antibodies to HBV might be used as an indirect measure of immunity to NANB Hepatitis.<sup>34</sup>

### *Reaction to the studies*

**27.29** Following the 1981 reports by the TTV and NIH groups of a correlation between elevated ALT levels in donors and the development of NANB Hepatitis in recipients, the American Association of Blood Banks (AABB) set up an ad-hoc committee to consider the question of ALT testing of donors.<sup>35</sup> The committee reported in 1982, concluding that the available evidence did not justify testing donors for ALT as a means of reducing the incidence of NANB Hepatitis. The committee listed its main concerns as follows:

1. The measurement of ALT, although a test for one aspect of liver function, is not a specific test for [NANB] hepatitis .... This lack of specificity will result in an intolerably high rate of unnecessary rejections ....
2. No study has shown that the actual elimination of donors with elevated levels of ALT will reduce the incidence of elevated levels of ALT posttransfusion, much less hepatitis ....
3. The significance of elevations of ALT after transfusion is unknown ....
4. There is insufficient information to establish a cut-off level that will separate acceptable from non-acceptable donors ....
5. The methods for ALT testing need to be evaluated ....
6. The effect on the donor base is unknown. The loss of an estimated three per cent of current blood donations may seriously stress the nation's already precarious donor supply. Studies on the effect of such reduction should be available to ensure that severe blood shortages do not cause more morbidity and mortality than might be prevented by universal testing .... More information is needed about the long- and short-term effects of an elevated ALT in otherwise healthy donors so that they and their physicians can be counseled appropriately.<sup>36</sup>

<sup>33</sup> Aach, 'Post-transfusion hepatitis and serum [ALT] in blood donors', *New England Journal of Medicine*, 1981; 305:403 [LIT.001.2156] at 2157

<sup>34</sup> This would be proved wrong: antibodies to NANB Hepatitis/HCV did not imply immunity, but it did anticipate an alternative surrogate test using anti-HBc.

<sup>35</sup> In his evidence to the Inquiry, Professor Leikola described the AABB as 'the leading organisation for transfusion matters in the United States': Day 71, page 14.

<sup>36</sup> 'Report of the AABB *ad hoc* committee on ALT testing', *Transfusion*, 1982; 22:4 [LIT.001.2217] at 2217-2218

**27.30** Alter and Aach's publications were noted in Finland;<sup>37</sup> Australia;<sup>38</sup> Canada;<sup>39</sup> the UK (see below) and elsewhere. In the USA, the results of a detailed economic analysis were published in November 1982.<sup>40</sup> It was concluded that current information about clinically apparent post-transfusion NANB Hepatitis was not sufficient to provide the precision required to estimate the benefits of ALT testing for the purpose of policy decisions. Since there was no randomised prospective study showing that exclusion of blood from donors with elevated ALT levels reduced the incidence of either symptomatic or asymptomatic post-transfusion NANB Hepatitis, there was no way of establishing the appropriateness of the clinical model used in the analysis. Further, these deliberations were taking place against a background in which the natural history of NANB Hepatitis was largely unknown but was generally thought to be not very serious. Five years later this view would be changing.

### The *Vox Sanguinis* forum and widening debate

**27.31** In 1983, *Vox Sanguinis*, the journal of the International Society of Blood Transfusion, asked a number of transfusion doctors for their opinions on the following question: 'Based on your analysis of the benefits and costs of routine donor screening for ALT-GPT<sup>41</sup> to reduce the incidence of post-transfusion non-A, non-B hepatitis in your blood services region, what action would you recommend on this matter?'<sup>42</sup>

**27.32** Dr Aach contributed to the forum.<sup>43</sup> He rehearsed the factors supporting the need for caution, already set out by his TTV group and the NIH group; acknowledged that the cost/benefit ratio could not be assessed; and emphasised the uncertainty around the prospects of developing a specific test. Nevertheless, he argued that a decision could not be postponed indefinitely and, in what became something of a fall-back argument that some action was better than none, proposed that steps should be taken to develop instrumentation and standardisation of procedures with a view to implementing ALT detection. In his view, if a decision could not be taken, then a properly designed randomised study should be initiated immediately and a target date set for testing those donor populations in which an association with post-transfusion NANB Hepatitis had been established. Dr Rainer Müller from Germany, where ALT testing had been routine for many years for identifying parenchymal liver damage,<sup>44</sup> thought that current practice there should not be abandoned.<sup>45</sup>

**27.33** In contrast to Drs Aach and Müller, most of the contributors did not support the introduction of ALT screening of donors without further research, in particular into the actual efficacy of ALT screening in reducing the incidence of post-transfusion hepatitis. In this group were William Bayer (Kansas, USA), Robert Gerety (Office of Biologics, USA

<sup>37</sup> Lagerstedt et al, 'Post transfusion non-A non-B hepatitis in Finland: a prospective study', *Scandinavian Journal of Clinical and Laboratory Investigation*, 1982; 42:567-570 [PEN.018.1141]

<sup>38</sup> Cossart et al, 'Post Transfusion Hepatitis in Australia', *The Lancet*, 1982; 208-211. [SNB.008.0578] Surrogate testing for anti-HBc was also mentioned as a possibility in this article.

<sup>39</sup> Steinbrecher et al 'Abnormal [ALT] Level in Blood Units from Donors in Montreal does not Indicate High Risk of Transmitting Hepatitis', *Clinical and Investigative Medicine*, 1983; 6:327-330 [LIT.001.2207]

<sup>40</sup> Hornbrook et al, 'Reducing the Incidence of Non-A, Non-B Post-Transfusion Hepatitis by Testing Donor Blood for [ALT]', *New England Journal of Medicine*, 1982; 1315-1321 [PEN.017.1950]

<sup>41</sup> Alanine transaminase (ALT), sometimes referred to as serum glutamic-pyruvic transaminase (SGPT), is a protein synthesised in liver cells. Normally present in low levels in the blood, it becomes elevated when the liver is disordered by virus infection or other hepatic disorders.

<sup>42</sup> Responses to ALT survey, *Vox Sanguinis*, 1983; 48 [LIT.001.1837]

<sup>43</sup> Ibid [LIT.001.1837]

<sup>44</sup> 'Parenchymal damage' is damage to the functional elements of an organ.

<sup>45</sup> Responses to ALT survey *Vox Sanguinis*, 1983; 48 [LIT.001.1837] at 1847-1848

FDA), Paul Holland (Clinical Centre Blood Bank, Bethesda, USA), Brian McClelland (SNBTS, Edinburgh), Ruthven Mitchell (SNBTS, Glasgow) and Henk Reesink and Eveline Reerink-Brongers (Amsterdam, Netherlands).<sup>46</sup>

**27.34** In a review article published in September 1983, Dr Jules Dienstag (Massachusetts General Hospital and Harvard Medical School) discussed the options for surrogate testing that had emerged by that date.<sup>47</sup> For present purposes it is sufficient to note his views on testing for the Hepatitis B surface antigen (anti-HBs), anti-HBc and ALT.<sup>48</sup> He was dismissive of anti-HBs testing, essentially on the grounds that there had been no confirmation of an association between anti-HBs in donor blood and enhanced risk of post-transfusion hepatitis in recipients. Relying on data from the TTV Study group, he commented that anti-HBc could theoretically serve as an indirect donor screening test: recipients of at least one unit of blood with anti-HBc were three times more likely to acquire NANB Hepatitis after transfusion than recipients of blood that was all negative for anti-HBc. The test would, however, involve the loss of twice the blood lost in ALT testing, without a corresponding advantage in recipient safety. His conclusions were:

If prospects for a specific test for NANB hepatitis were bright, this interim test might not be worth considering. On the other hand, an intensive search for serologic markers begun a decade ago has yet to bear fruit, and as many as 5–10 yr may pass before a specific, sensitive screening test is developed and introduced into practice. Therefore, despite the poor sensitivity and predictive value of the test, and despite the difficulties and questions generated by a policy of screening, ALT screening may be warranted until NANB-specific tests become available.<sup>49</sup>

**27.35** Dienstag noted that, although no policy to adopt ALT testing had been adopted officially, several large centres in the USA were screening and withholding blood with high ALT levels. Prospective studies were planned.

### *Continuing debate to 1986*

**27.36** The *Vox Sanguinis* forum was inconclusive but stimulated further debate. The data from the TTV Study that formed the basis of an association between raised ALT levels in donors and an increased risk of transfusion recipients developing NANB Hepatitis, were taken up and studied again in 1984 by Dr Cladd Stevens and others (New York and other US centres).<sup>50</sup> This group analysed the data to test the hypothesis that '[e]pidemiologic circumstances predisposing donor populations to infection with hepatitis B virus may also favour exposure to [NANB] agents'. The issue was whether patients who received blood from donors who tested positive for anti-HBs and anti-HBc were at increased risk of developing NANB Hepatitis.

<sup>46</sup> While expressed more equivocally, this also appears to have been the view of Chataing et al (Lyon and Toulouse, France). Responses to ALT survey *Vox Sanguinis*, 1983; 48 [LIT.001.1837] at 1851-3.

<sup>47</sup> Dienstag, '[NANB] Hepatitis. II. Experimental Transmission, Putative Virus Agents and Markers and Prevention', *Gastroenterology*, 1983; 85:743-68: [LIT.001.1213]

<sup>48</sup> Various tests for Hepatitis B had been developed or were under development at this time. See Chapter 25, *Screening of Donated Blood for Hepatitis B*, paragraphs 25.28–25.31.

<sup>49</sup> Dienstag, 'Non-A, Non-B Hepatitis. II. Experimental Transmission, Putative Virus Agents and Markers and Prevention', *Gastroenterology*, 1983; 85:743-68 [LIT.001.1213] at 1229

<sup>50</sup> Stevens et al, 'Hepatitis B virus antibody in blood donors and the occurrence of [NANB] hepatitis in transfusion recipients', *Annals of Internal Medicine*, 1984; 101:733 [LIT.001.3755]

**27.37** The authors reported an association between units of donor blood that were positive for anti-HBc and an increased risk of recipients developing NANB Hepatitis. Elevated ALT levels in donors had a similar association with NANB Hepatitis in recipients but would have resulted in fewer units of blood being discarded than would screening for anti-HBc (2.8% as against 5.1%). They did not find a statistically significant association between donors who were positive for anti-HBs and the development of NANB Hepatitis in recipients. The authors considered that 21.4% of cases of NANB Hepatitis might have been prevented by screening for anti-HBc, 29.9% of cases might have been prevented by screening for ALT and 39.2% of cases might have been prevented by screening for both anti-HBc and ALT. Adjusting these figures to take into account the incidence of NANB Hepatitis in non-transfused control patients resulted in figures of 33.3%, 47.4% and 61.2% respectively. Screening for both ALT and anti-HBc would have resulted in a loss of nearly 8% of donor units.

**27.38** The authors emphasised that their calculations were only rough estimates of the potential impact of donor screening based on their data. Other critically important factors affecting the risk to recipients – such as the prevalence of NANB Hepatitis among donors and the susceptibility to infection among recipients – remained unknown in the absence of specific serological tests and were presumed to vary among both donor and recipient populations.

**27.39** The paper noted that only eight per cent of anti-HBc positive donors had elevated ALT levels, with the result that ‘these two markers identified overlapping, but different, donor subsets’.<sup>51</sup> Having regard to the lesser quantity of blood that would be discarded by ALT screening when compared with anti-HBc screening, it was noted that ‘the consensus of the study group is that ALT screening of donors is favored over anti-HBc screening’.<sup>52</sup>

**27.40** The same edition of the *Annals of Internal Medicine* also contained the following commentary by Drs Alter and Holland on the TTV study group findings:

The possibility that a specific marker for anti-HBc might be useful in detecting carriers of the [NANB] virus was an unexpected and confounding outcome of the TTV study. Of the potential explanations for this observation, the one favored by the TTV group is that persons exposed to the hepatitis B virus are also more likely to have been exposed to the [NANB] virus and, hence, that a marker for one is indirectly a marker for the other. This assumption would be more tenable if the same association could be shown for antibody to hepatitis B surface antigen (anti-HBs) because anti-HBs is an equally good indicator of past exposure to hepatitis B virus. However, in the TTV study, recipients of only anti-HBs positive blood were not at higher risk for [NANB] hepatitis, and in three previous studies no significant association between donor anti-HBs and recipient hepatitis was demonstrable.

....

If both the tests for ALT and anti-HBc are indirect indicators of the [NANB] carrier state, one by detecting subclinical liver disease and the other by indicating the likelihood of virus exposure, then both tests should detect the same

---

<sup>51</sup> Ibid [LIT.001.3755] at 3757

<sup>52</sup> Ibid [LIT.001.3755] at 3759

[NANB] hepatitis carrier population. In fact, the tests do not .... These tests are identifying two different, seemingly high-risk populations. This dichotomy is disturbing, suggesting either that the tests are not really detecting carriers of [NANB] hepatitis and that their apparent association with [NANB] hepatitis is a statistical artifact, or that they are detecting two different carrier populations perhaps harbouring different agents for [NANB] hepatitis.<sup>53</sup>

**27.41** Alter and Holland commented as follows on the efficacy of surrogate testing:

The key question in this study is test efficacy: How effective would anti-HBc testing of donors be in preventing cases of transfusion-associated hepatitis? Unfortunately, true efficacy cannot be determined from this study or from the previous studies of ALT because none were randomized, controlled trials that compared tested blood with untested blood.<sup>54</sup>

**27.42** The reason for any association between anti-HBc in donors and an increased risk of NANB Hepatitis in recipients thus was, and in fact remains, something of a puzzle, as was the lack of overlap between the groups of subjects testing positive for elevated levels of ALT and anti-HBc. In his evidence to the Inquiry, Dr John Gillon, SNBTS, said:

[T]his has always been a huge puzzle to me and it's one of the things that instinctively did not make sense about this whole business. There should be a very considerable overlap, and there just isn't. And I think reading [what] Harvey Alter said then<sup>55</sup> is what I felt. And I do remember at the time ... I tried to stratify theoretical hundreds of donors into categories who got 1 unit of blood, 2 units, 10 units, 20 units and worked on different prevalences of the putative infection, the ALT, [anti-HBc] and stratified them. And I became convinced that a lot of the association was coincidental, that it was entirely – well, not entirely but at least substantially a function of having a large volume of transfusion, so that ... patients who got, say, 15/20 units of blood at given prevalences were much more likely to get one thing and the other thing, more or less by coincidence, compared with people who only got one unit of blood, when it was much more unlikely that there would be a coincidence.

....

So I still don't have a satisfactory explanation for that, but it was part of the instinctive feeling that there was something going on here which was not just about you use a test and you identify somebody who might transmit [NANB] Hepatitis. So it was not as simple as that. And I remain convinced there was a statistical artefact. That doesn't mean that identifying people with high ALT wouldn't have prevented Hepatitis C but it does call into question the exact relationship between the two and the exact outcome if you did it prospectively.<sup>56</sup>

---

<sup>53</sup> Alter and Holland, 'Indirect tests to detect the [NANB] hepatitis carrier state', *Annals of Internal Medicine*, 1984; 101:859 [PEN.018.1156] at 1156–1157

<sup>54</sup> *Ibid* [PEN.018.1156] at 1157

<sup>55</sup> *Ibid*

<sup>56</sup> Day 65, pages 94 – 96

**27.43** In due course, later studies were carried out to investigate whether there was an association between donors testing positive for anti-HBc and an increased risk of NANB Hepatitis in recipients. While some studies found such an association,<sup>57</sup> others did not.<sup>58</sup> Of these later studies, the NIH study<sup>59</sup> investigated whether the presence of antibodies to HBsAg in the donor correlated with the development of NANB Hepatitis in the recipient and, like the TTV study, found that it did not.

**27.44** Dr Alter's views on surrogate testing in 1985 were as follows:

The question of whether or not the ALT test should be routinely adopted for donor screening was widely debated and currently remains an essentially unresolved issue. Inherent in the debate were questions as to whether the predicted efficacy could actually be achieved in clinical practice, and questions relating to test standardization, non-specificity, responsibility to the donor and the ability to sustain the donor loss which would ensue. The major organizations of the national blood delivery complex, ARC,<sup>60</sup> AABB<sup>61</sup> and CCBC,<sup>62</sup> opted not to adopt routine donor ALT testing until additional data were available, whereas the New York Blood Center initiated such testing and subsequently proved its feasibility though they did not accumulate additional efficacy data.<sup>63</sup>

**27.45** Dr Alter referred to a small-scale prospective study carried out by the NIH into the impact of ALT testing on the incidence of post-transfusion hepatitis. In 1981 the NIH had introduced ALT testing and had excluded all blood donations with high ALT levels. Perhaps surprisingly, it was found that '[t]he incidence of NANB hepatitis in the 3 years post-ALT testing was virtually identical in both patients and non-transfused controls to that in the 2 years prior to ALT testing'. That is, there was no significant decline in the incidence of hepatitis after ALT testing was introduced. Alter observed that, therefore, '[e]fficacy cannot be reliably predicted; it must be randomly and prospectively demonstrated'.<sup>64</sup>

**27.46** Dr Alter set out three options in respect of ALT testing: (i) to decide that existing data were inconclusive and that, given the difficulties with ALT testing, it was best not to adopt such screening at that time; (ii) to decide that, although the data relating to ALT efficacy were not definitive, they were scientifically valid and, overall, were sufficiently compelling to warrant the introduction of donor testing and (iii) to decide that existing data were inconclusive but were sufficiently compelling that a definitive answer must be sought by means of a randomised, controlled study, to be instituted as rapidly as

<sup>57</sup> Studies which found such an association included: Koziol et al (Alter's NIH group), 'Antibody to hepatitis B core antigen as a paradoxical marker for [NANB] hepatitis agents in donated blood', *Annals of Internal Medicine*, 1986; 104:488 [LIT.001.1869]; Hyland et al (Australia), 'Predictive markers for hepatitis C antibody ELISA specificity in Australian blood donors', *Transfusion Medicine*, 1992; 2:207 [LIT.001.3794]; Sugg et al (Germany), 'Antibodies to hepatitis B core antigen in blood donors screened for [ALT] level and hepatitis [NANB] in recipients', *Transfusion*, 1988; 28:386 [LIT.001.3813].

<sup>58</sup> Studies which found no such association included: Aynard et al (France), 'Post-transfusion [NANB] Hepatitis after cardiac surgery: prospective analysis of donor blood anti-HBc antibody as a predictive indicator of the occurrence of [NANB] hepatitis in recipients', *Vox Sanguinis*, 1986; 51:236 [LIT.001.3810]; Van der Poel et al (the Netherlands), 'Infectivity of blood seropositive for hepatitis C virus antibodies', *The Lancet*, 1990; 335:558 [SNB.001.9850]; Esteban et al (Spain), 'Evaluation of antibodies to hepatitis C virus in a study of transfusion-associated hepatitis', *New England Journal of Medicine*, 1990; 323:1107 [LIT.001.3892]; Ebeling (Finland), 'Alanine Aminotransferase, Gamma-Glutamyltransferase, Antibodies to Hepatitis B Core Antigen and Antibodies to Hepatitis C virus in blood donor screening', *Vox Sanguinis*, 1991; 60:219 [PEN.017.1763].

<sup>59</sup> Koziol et al (Alter's NIH group), 'Antibody to hepatitis B core antigen as a paradoxical marker for [NANB] hepatitis agents in donated blood', *Annals of Internal Medicine*, 1986; 104:488 [LIT.001.1869].

<sup>60</sup> American Red Cross

<sup>61</sup> American Association of Blood Banks

<sup>62</sup> Council for Community Blood Centers

<sup>63</sup> Alter 'Post-transfusion hepatitis: clinical features, risk and donor testing', in Dodd et al (eds), *Infection, Immunity and Blood Transfusion*, 1985, Alan R. Liss, New York, pages 47-61 [LIT.001.0811] at 0818

<sup>64</sup> Ibid [LIT.001.0811] at 0819-20

possible. Dr Alter noted that implicit in the second option was the assumption that 'if an interpretive error is to be made, it is best to err on the side of recipient safety and that to withhold such testing is ethically unjustified'.<sup>65</sup>

**27.47** Dr Alter's preference was for the third option:

It is my opinion that option 3 is the most tenable alternative. Had this controlled study been performed three years ago when first proposed, a definitive answer would be at hand. Instead, the same uncertainties persist. A randomized, controlled trial could be completed in 1½ years, could address both the ALT and anti-core issues and could provide a definitive and rational basis for making these complex decisions. Even at this late date ... we find ourselves still far from the core (or the ALT) of this issue.<sup>66</sup>

**27.48** In the period 1984–85, therefore, scientific opinion in the United States remained divided on the usefulness of surrogate testing, whether for anti-HBc or for ALT. Neither could be fully justified on scientific criteria alone but practical steps were beginning to be taken by some blood transfusion organisations to implement ALT testing – an understandable approach in a litigation-driven society such as the USA. In the event, no definitive controlled study, as proposed by Alter, was ever carried out in the USA.

### **1986: A change of direction in the USA**

**27.49** On 21 February 1986, *Blood Bank Week*, the official publication of the AABB, reported that:

The Blood Products Advisory Committee of the Food and Drug Administration will recommend that both ALT and anti-core testing be performed on donated blood to reduce the incidence of transmission of [NANB] hepatitis through transfusion. In a February 13-14 meeting, the panel received reports on two studies showing that recipients of blood from donors with elevated ALT and anti-core had a higher incidence of NANB hepatitis.<sup>67</sup> While questions were raised about the data, it was noted that the carrier rate of NANB is higher than previously thought, that cases are underreported and that NANB is now considered to be a much more serious disease.<sup>68</sup>

**27.50** The views of Dr Alter on the introduction of surrogate testing appear to have changed around this time. While, as discussed above, Dr Alter had expressed the view in 1985 that a randomised prospective study into the efficacy of surrogate testing in reducing the incidence of post-transfusion hepatitis should first be carried out, in February 1986 he co-authored a paper with Dr Dienstag in which the opinion was expressed that, despite the negative features of ALT and anti-HBc screening already reported:

[T]he accumulating data that chronic NANB hepatitis leads to cirrhosis in 10 to 20% of cases has served as compelling evidence for the need to rely on indirect assays as an interim measure until such time as specific NANB hepatitis

---

<sup>65</sup> Ibid [LIT.001.0811] at 0821

<sup>66</sup> Ibid [LIT.001.0811] at 0822. In fact, these three options and the conclusion had first appeared in the December 1984 editorial by Alter and Holland noted above; Alter and Holland, 'Indirect tests to detect the [NANB] hepatitis carrier state', *Annals of Internal Medicine*, Dec 1984; 101:859 [PEN.018.1156]

<sup>67</sup> Presumably a reference to the TTV and NIH studies

<sup>68</sup> 'FDA advisory panel recommends surrogate testing for NANB', *Blood Bank Week*, February 21, 1986 [SGF.001.0783] at 0784

assays are developed .... [I]ncreasing documentation of the chronic sequelae of NANB hepatitis and the continued high incidence of this disease after transfusion have tipped the balance in favour of adopting indirect assays for NANB hepatitis carrier detection.

....

Specific therapy for either acute or chronic NANB hepatitis is not available .... In the absence of effective treatment, the need for prevention assumes even greater importance.<sup>69</sup>

**27.51** In this careful review no new scientific evidence was produced to support a change of opinion on the sensitivity or specificity of either surrogate test for NANB Hepatitis. The major participants in the 'blood delivery complex' were at the time considering the adoption of either the ALT test or the anti-HBc test or both. Dr Alter might be thought to have bowed to the inevitable consequences of pressure from the blood delivery complex, although increasing evidence of the potential seriousness of NANB Hepatitis infection emerging in the USA and Europe, compared to what had been perceived to be the position about four years earlier, was clearly influential and was taken into account in this landmark opinion. A similar view was expressed by Dr Alter's NIH group in April 1986 when the authors re-visited their earlier data to investigate further the association between anti-HBc in donor blood and the development of transfusion-associated hepatitis.<sup>70</sup>

**27.52** Two factors entered into the decision whether to adopt either test: the unlikelihood that a specific test would become available in the near future and the developing knowledge of the severity of NANB Hepatitis. It was now estimated that up to 7500 cases of cirrhosis might be induced annually in the USA by NANB Hepatitis. The high risk of developing progressive liver disease resulting in serious liver damage tipped the balance for Dr Alter's group:

If, as predicted, surrogate screening of blood donors could prevent approximately one third of these cases [of NANB Hepatitis], then this could represent an annual reduction of 50000 cases of hepatitis and 2500 cases of cirrhosis. The potential to achieve this degree of disease prevention now appears to outweigh the disadvantages inherent in the adoption of surrogate tests for the [NANB] virus carrier state.<sup>71</sup>

**27.53** In August 1986, the AABB recommended that all donor blood be tested for ALT and anti-HBc with effect from 30 November 1986 in an attempt to reduce NANB Hepatitis transmission.<sup>72</sup> Despite the difficulties with surrogate screening, the AABB believed that 'the importance of a potential increase in the safety of the blood supply outweighs the negative aspects of this testing'. As discussed so far, the scientific basis for this view remained questionable but the perceived interests of patient recipients had influenced the decision.

---

<sup>69</sup> Dienstag, and Alter, '[NANB] hepatitis: evolving epidemiologic and clinical perspective', *Seminars in Liver Disease*, 1986; 6:67 at 76 [LIT.001.1675] at 1684

<sup>70</sup> Koziol et al, 'Antibody to hepatitis B core antigen as a paradoxical marker for [NANB] hepatitis agents in donated blood', *Annals of Internal Medicine*, 1986; 104:488 [LIT.001.1869]

<sup>71</sup> Ibid [LIT.001.1869] at 1875

<sup>72</sup> AABB statement dated 15 August 1986 [PEN.016.0312]



**27.54** In his evidence to the Inquiry, Professor Juhani Leikola of the Finnish Red Cross Blood Transfusion Service accepted that patient safety was a factor behind the introduction of surrogate testing in the USA.<sup>73</sup> However, the impression of the experts attending the meeting of the Expert Committee of the Council of Europe in May 1987, discussed below, was that the decision in the USA to introduce surrogate testing had also been taken for non-scientific reasons, in particular because the transfusion community had been criticised for being slow to react to the AIDS crisis and because of the fear of litigation. He also stated that the information from the TTV and NIH studies had made it clear that NANB Hepatitis was a serious risk associated with transfusion.<sup>74</sup> He explained that important factors in the USA were ‘the higher incidence’ of NANB Hepatitis than seemed likely in northern Europe and also ‘public opinion and media coverage’.<sup>75</sup>

**27.55** Surrogate testing was introduced generally in the USA between 1986 and 1987. In an article published in *Nature* on 4 September 1986, the positions adopted by the major bodies were summarised.<sup>76</sup> The AABB, as noted above, expected its members to implement surrogate testing (apparently by raised ALT levels) of all donated blood, by 30 November 1986. The American Red Cross was also implementing ALT testing at its blood banks. Its programme had begun on 7 July and was expected to be completed by 1 October 1986. A third organisation, the Council for Community Blood Centers (CCBC), had not officially declared a position on ALT testing but its President was reported as saying that ‘most members [would] go ahead with ALT testing’. The article stated that the use of anti-HBc testing was far more contentious. A major concern for all blood centres was the loss of donors due to false positives in both surrogate tests and the cost of testing. Notwithstanding these concerns, the President of the AABB considered that the tests were ‘essential to increase the safety of the blood supply’.<sup>77</sup>

**27.56** Throughout the period of developing thought, from the paper by Aach and others in 1981 to the observation of the AABB last quoted, the emphasis was on reducing risk for transfusion recipients. There was relatively little discussion of the implications for *donors* found to have significantly elevated ALT levels or of the need for care and counselling of such donors.

**27.57** For the time being that concluded the issue in the USA. The history provides an appropriate point of reference for discussing events in Europe where, among other significant differences, there was considerably more concern about donors’ interests.

### The European response

**27.58** In his written evidence to the Inquiry, Professor Leikola set out the position in Europe in the early to mid-1980s, referring in the first place to the AABB view in 1982 that ALT screening of donors was not justified:

In the early 1980’s the conclusion by the AABB ad hoc committee was considered reasonable, and there was no move in Europe to introduce surrogate testing.

<sup>73</sup> Day 71, pages 25–26. Professor Leikola was a former Director of the Finnish Red Cross and spent a number of years as head of the Blood Programme of the League of Red Cross and Red Crescent Societies in Geneva.

<sup>74</sup> Day 71, pages 19–23

<sup>75</sup> *Ibid* page 24

<sup>76</sup> Palca, ‘Hepatitis screening extended’ *Nature*, 1986; 323:7 [SGF.001.2108]

<sup>77</sup> On the question of surrogate testing in the USA, see also the memorandum dated 27 June 1986 by Dr Sandler, Associate Vice President, Medical Operations of the American Red Cross, on the phase-in of ALT testing [SGF.001.2123]. See also the memorandum dated 4 September 1986 by Dr AuBuchon, Medical Officer, Medical Operations, American Red Cross, on ALT cut-off values [SGF.001.2113].

It was recognized that the incidence of NANBH varied from country to country and in different donor populations. In northern parts of Europe there were less cases of NANBH than in the south, and there were differences between urban and rural populations. Australia was considered to belong to the lowest prevalence countries, similar to Northern Europe and dissimilar to the United States.

There was a general feeling that more information was needed of the possible correlation between screening for surrogate markers and prevention of NANBH. The journal *Vox Sanguinis* published in 1983 nine short articles .... All contributors took a cautious view on ALT screening.

....

The American finding that anti-HBc correlated with NANBH was disturbing and could not be explained .... There were soon reports appearing, notably from France, the Netherlands and the United Kingdom, showing that in the European donor populations studied anti-HBc did not correlate with recipient NANBH. The pattern was clearly different from the American donors: Incidence of NANBH much less and anti-HBc meaningless as a surrogate marker. There was some association between elevated ALT and recipient NANBH, but its efficacy as a possible surrogate test was considered weak. This view was supported by the negative findings of the NANBH incidence after ... ALT screening in Germany on one hand and in the New York Blood Center and at the NIH on the other.<sup>78</sup>

**27.59** There was soon progress. Professor Leikola continued:

After the American organizations decided to recommend the introduction of routine ALT and anti-HBc testing it was necessary to decide also in European countries whether or not to follow ... suit. There was a consensus among the scientific and blood transfusion expert community that prospective studies were urgently needed before a decision could be taken.<sup>79</sup>

**27.60** The Council of Europe Committee of Experts on Blood Transfusion and Immunohaematology met in May 1987.<sup>80</sup> The general impression from the returns to questionnaires sent to Member states was that the incidence of NANB Hepatitis was rather low but varied widely among different regions. The value of surrogate tests such as ALT and anti-HBc had been studied by various groups but there was doubt about their cost and effectiveness. After discussion by the Committee, it was decided that a working group would prepare a report and, if possible, make recommendations. In due course the working group reported and, in summary, concluded:

(i) The use of a non-specific test for the purpose of reducing the incidence of transfusion-associated NANB Hepatitis and its possible value as a public health measure remained controversial issues.

---

<sup>78</sup> Professor Leikola's statement on surrogate testing [PEN.017.1837] at 1839

<sup>79</sup> Ibid [PEN.017.1837] at 1839-40

<sup>80</sup> Council of Europe: extract from the report of the Committee of Experts on Blood Transfusion and Immunohaematology, 19-20 May 1987 [SNB.001.9445]. The working group comprised Professor van Aken (Holland), Dr Gunson (UK), Dr Habibi (ISBT) and Dr Leikola (Finland).

(ii) If a stance was taken that blood should be as safe as possible, then tests would be introduced, but the benefits derived from this testing would not be uniform throughout every country. There was also no guarantee that, in a given country, there would be a significant reduction in the transmission of NANB Hepatitis.

(iii) The introduction of non-specific tests might compromise the blood supply and this was a factor which had to be taken into account.

(iv) When non-specific testing was introduced in a country, provision would have to be made for the interviewing, counselling and further medical examination and treatment which might be required for donors found to have raised ALT levels or who were anti-HBc positive.

(v) The Committee could not make a general recommendation on the routine introduction of non-specific tests for evidence of the NANB Hepatitis infectivity of blood donors. Individual countries would have to assess the situation locally and decide on the appropriate action to take.<sup>81</sup>

**27.61** In his written evidence to the Inquiry Professor Leikola stated:

Most countries that I know elected in 1987 not to blindly follow what the Americans did but to first find out the situation in their own donor population. Thus, the attitude towards surrogate testing was not negative per se, but before making a decision in Europe the expert community wanted to know whether the concept would really produce results.<sup>82</sup>

**27.62** Professor Leikola explained that, in Finland, the decision of the US blood banks in 1986 to commence surrogate testing prompted further consideration of the issue by the Finnish blood transfusion service which, in 1987, decided to undertake a new study 'to determine the current incidence and types of post-transfusion hepatitis among open-heart surgery patients from all parts of Finland.' A second objective was 'to obtain donor samples for future evaluation of possible preventive strategies'.<sup>83</sup> A doctoral student was engaged to organise the study and the service had the resources to collect and analyse the samples.<sup>84</sup> The study began in the beginning of December 1987 and lasted one year. It was carried out at all five of the Finnish university hospitals and included 685 patients and 8346 donors. Several candidate surrogate markers were investigated, as were (retrospectively) tests for antibodies to HCV once they became available.<sup>85</sup> A correlation between elevated ALT levels in donors and an increased incidence of post-transfusion NANB Hepatitis in recipients was established.<sup>86</sup> In his oral evidence Professor Leikola said that Finland did not introduce ALT testing before the study was done and that that reflected the general view in the mid-1980s of the European transfusion community, that surrogate testing was not something to be started without first performing such a study.<sup>87</sup>

---

<sup>81</sup> Ibid [SNB.001.9445] at 9450

<sup>82</sup> Professor Leikola's statement on surrogate testing [PEN.017.1837] at 1840

<sup>83</sup> Ibid [PEN.017.1837] at 1841

<sup>84</sup> Day 71, page 52

<sup>85</sup> The findings of the study are discussed above: Ebeling, 'Alanine Aminotransferase, Gamma-Glutamyltransferase, Antibodies to Hepatitis B Core Antigen and Antibodies to Hepatitis C virus in blood donor screening', *Vox Sanguinis*, 1991; 60:219 [PEN.017.1763]

<sup>86</sup> Day 71, page 56

<sup>87</sup> Ibid pages 61–62. The study also found that Ortho's HCV test appeared to detect post-transfusion NANB Hepatitis in recipients and in positive donors.

**27.63** The situation in Europe generally in 1989 was set out in a document compiled by Dr Harold Gunson<sup>88</sup> on behalf of the Council of Europe's Committee of Experts following their meeting in May 1989. Significantly, by this stage it was known that Chiron had discovered HCV (see paragraphs 27.238–27.241 below) and that an anti-HCV test had been developed (see Chapter 31, *The Introduction of Screening of Donated Blood for Hepatitis C*). The document stated:

1. Replies to the questionnaire were received from 10 countries.
2. Examination of the replies revealed that in 4 countries routine screening of donations with ALT is being performed. These countries are the Federal Republic of Germany, France, Malta and Switzerland. Anti-HBc is routinely performed in France.
3. There are several studies being undertaken in some countries to determine the policies which should be undertaken to protect the blood supply with respect to the transmission of [NANB] hepatitis. These countries are Denmark, Norway, United Kingdom and Finland.
4. There is clearly an interest in the Chiron anti-HCV test and several countries are planning to conduct trials with this test.
5. There is a potential difficulty with respect to the use of the surrogate ALT and anti-HBc testing of donations with particular reference to source plasma for fractionation. The practice of routine ALT testing by the Federal Republic of Germany for many years means that plasma or its fractions, cannot be imported into that country unless the starting plasma has been ALT tested. This could have considerable implications for the standardisation of the quality requirements for plasma in 1992.<sup>89</sup>

**27.64** In his evidence to the Inquiry Professor Leikola explained:

In Europe, France was one of the few countries which decided to go for surrogate testing any way. ALT testing became mandatory in April 1988. In the aftermath of the "tainted blood affair" (HIV contaminated blood) the decision is understandable. It was not motivated by ... scientific knowledge but by ... political necessity. Something had to be done, whether or not it truly reduced the risk of NANBH transmission by blood. Northern countries with low NANBH incidence such as the Netherlands, Denmark, Norway, Sweden and Finland decided not to introduce surrogate testing before more was known of the efficacy in the respective donor populations. There were many articles published by UK authors in the *Lancet* and *Vox Sanguinis* advising against a hasty introduction of surrogate testing.<sup>90</sup> These opinions in the prestigious medical journals were not without influence in the international community.<sup>91</sup>

<sup>88</sup> Chairman of the UK Advisory Committee on Transfusion Transmitted Diseases (ACTTD), discussed below, from October 1989. Dr Gunson became Chair in February 1989.

<sup>89</sup> Council of Europe – Dr Gunson's analysis of questionnaires [SNB.001.9534] at 9536

<sup>90</sup> Anderson et al 'Surrogate testing for [NANB] hepatitis', *The Lancet*, 1987:912 [LIT.001.1854]; Dow et al, '[NANB] hepatitis surrogate testing of blood donations', *The Lancet*, 13 June 1987 [LIT.001.0346]; Gillon et al, 'Post-transfusion [NANBH]: significance of raised ALT and anti-HBc in blood donors', *Vox Sanguinis*, 1988; 54:148–153 [SNB.008.3536]

<sup>91</sup> Professor Leikola's statement on surrogate testing [PEN.017.1837] at 1840

**27.65** Professor Leikola agreed with the suggestion that the introduction of surrogate testing was 'a sort of emotional reaction to the situation that says we really have to do something, rather than a scientific or logical answer to the situation'.<sup>92</sup>

**27.66** In a 2001 court case, *A v The National Blood Authority and others*,<sup>93</sup> it was noted that, '[n]ot many countries apart from the United States (both tests) and Germany (ALT only) introduced surrogate tests'.<sup>94</sup> The full picture was stated to be as follows:

**Table 27.1: Introduction of Surrogate Testing**

Germany	1965	ALT <sup>95</sup>
Italy	1970	ALT <sup>96</sup>
USA	Sep 1986 onwards	Both <sup>97</sup>
Luxembourg	1 Oct 1986 Mid 1987 onwards (for new donors)	ALT Anti-HBc
France	15 April 1988 3 Oct 1988	ALT Anti-HBc
Switzerland	1 June 1988	ALT
Malta	Early 1989	ALT

**27.67** It was also noted that:

There was some partial routine ALT testing in certain centres in Austria, Belgium and Spain, from about 1987, and Queensland (alone of the Australian states) introduced compulsory ALT testing in about April 1989. Dr Högman told the Council of Europe in 1987 that Sweden was to introduce anti-HBc testing for first time donors, but he explained in evidence that this was intended in fact as a supplementary Hepatitis B screening. No other countries, so far as is known, ever introduced either test.<sup>98</sup>

**27.68** From the above, it is apparent that most European countries did not introduce surrogate testing of blood donors on account of the association of ALT with NANB Hepatitis<sup>99</sup> and that, with the exception of France, those that did carried out their own preliminary evaluations before doing so.

<sup>92</sup> Day 71, page 33

<sup>93</sup> The claimants in *A v National Blood Authority* contracted Hepatitis C as a result of treatment with blood and blood products and sought damages in the English courts relying on the strict liability provisions of the Consumer Protection Act 1987 (the Act is discussed below). While the ultimate findings of the court are not directly relevant to the Inquiry (given that they are based on different evidence, for a different purpose, in a different forum), some of the evidence noted in the judgment of Mr Justice Burton is of assistance and, where relevant, has been noted in this Report. The full Judgment is reported at [2001] 3 All ER 289 [PEN.017.0302].

<sup>94</sup> *A v The National Blood Authority*, [2001] 3 All ER 289, paragraph 108(v) [PEN.017.0302] at 0369

<sup>95</sup> In his evidence to the Inquiry Professor Leikola stated his understanding that ALT was gradually introduced in every region in Germany. He also stated that German transfusion doctors remained sceptical about the efficacy of ALT screening: Day 71, pages 7 and 10

<sup>96</sup> Professor Leikola told the Inquiry that it was unclear whether every region in Italy had introduced ALT testing: Day 71, pages 8-9

<sup>97</sup> In his evidence to the Inquiry Dr Gillon stated: '[I]n the USA, in fact they didn't introduce [anti-HBc] testing in 1986 as planned because core testing was technically difficult and they were having problems with reproducibility. I'm not sure it was ever universally introduced but if it was, it was certainly not before the middle of 1987.' Day 65, page 80

<sup>98</sup> *A v The National Blood Authority*, [2001] 3 All ER 289, paragraph 108(v) [PEN.017.0302] at 0369

<sup>99</sup> As noted in paragraph 27.32, ALT testing in Germany had a particular long standing purpose unrelated to the postulated association with NANB Hepatitis.

**27.69** As reflected in Professor Leikola's evidence, there were particular concerns about the relevance of the anti-HBc test. There seemed to be no logical basis for a correlation between the presence of antibodies to one disease in donors (Hepatitis B) and the presence of a different disease in recipients (NANB Hepatitis). The most plausible theory appeared to be based on 'lifestyle' factors, in that a donor whose lifestyle (such as injecting drug use) exposed them to HBV infection might have been at a higher risk of being exposed to other blood borne diseases such as NANB Hepatitis. The difficulty with that hypothesis was that, if it were correct, one would also have expected there to be a correlation between the presence of HBsAg in donors (which was an indicator of Hepatitis B infection) and recipient incidence of NANB Hepatitis. The TTV and NIH studies did not find such a correlation. In addition, while some studies showed a correlation between donor anti-HBc and recipient NANB Hepatitis, other studies showed no such correlation.<sup>100</sup>

**27.70** As regards the possible correlation between anti-HBc and NANB Hepatitis, Professor Leikola observed:

[M]ost people thought that ... it really doesn't make any sense and therefore these European studies that showed that there was no correlation between [anti-HBc] and [NANB] Hepatitis was, for me at least, a relief, to see that ... it wasn't logical to include hepatitis core antibody in this whole exercise, and therefore I was quite happy to see that it was confirmed in our material and also in the other European [studies].<sup>101</sup>

**27.71** To this day it is quite unclear why some studies found this association.

### The position in the United Kingdom

**27.72** Having regard to the variety of positions adopted in Europe, it is clearly necessary to consider developments in the UK specifically. There are, however, some points that should be kept in mind. Until the developments in 1986 described above, there was no consensus in favour of the adoption of surrogate testing in the USA and still less in Europe. When the introduction of surrogate testing became a real issue for blood transfusion services, following the advice of the AABB in the USA, it was recognised that the decision for individual regions had to be taken in light of local factors that required specific investigation. There were also other developments that would inevitably have had a bearing on the course adopted. For example, in the UK progress with virus inactivation would inevitably have become a consideration in assessing the cost/benefit balance of implementation as far as blood products (particularly coagulation factor concentrates) were concerned.

#### 1970s to early 1980s

**27.73** In the late 1970s there were no reliable data on the prevalence of NANB Hepatitis in the UK. The Medical Research Council (MRC) report published in 1974 has already been mentioned.<sup>102</sup> In his evidence to the Inquiry, Dr McClelland stated that when he read the 1974 study in the early 1980s he realised that it did not really tell relevant practitioners what they needed to know.<sup>103</sup>

<sup>100</sup> Professor Leikola agreed with the suggestion that part of the reason for that may have been that the TTV and NIH studies were carried out before steps had been taken to try to exclude donors at risk of transmitting AIDS, whereas some later studies were carried out after donors had been excluded by these steps and that the lifestyles of these excluded donors may have meant that they were both more likely to be anti-HBc positive and were at a higher risk of transmitting NANB Hepatitis: Day 71, pages 35-36 Day 71, page 35

<sup>102</sup> Medical Research Council, 'Post-transfusion hepatitis in a London hospital', *Journal of Hygiene*, 1974; 73:173-188 [LIT.001.0116] The report is discussed more extensively in Chapter 14, *Knowledge of Viral Hepatitis 1*, Paragraphs 14.19-14.22.

<sup>103</sup> Day 63, page 71. Comments on the study were made in the Preliminary Report at paragraphs 6.23 and 6.24.

**27.74** As discussed more fully in Chapter 15, *Knowledge of Viral Hepatitis 2 – 1975-1985*, the discussions in the Advisory Group on Testing for the Presence of Hepatitis B Surface Antigen and its Antibody led to an ad hoc meeting at the MRC on 12 February 1979 to consider the question of NANB Hepatitis.<sup>104</sup> The meeting concluded that a survey of post-transfusion hepatitis was not warranted.<sup>105</sup> Professor Cash commented that the decision was a serious blow to those BTS colleagues who believed that surrogate testing of blood donations in the UK should only be considered when appropriate prospective studies had been carried out. In Scotland, research showing that there was NANB Hepatitis infection in the blood donor population began to produce results only in the second half of 1979.<sup>106</sup>

**27.75** Following the meeting at the MRC in February 1979 a Working Party on Post-Transfusion Hepatitis was set up and met for the first time on 14 February 1980.<sup>107</sup> The Working Group was chaired by Dr Gunson.<sup>108</sup> Its functions included examining the position of research to characterise the agent(s) associated with NANB Hepatitis and to derive diagnostic tests.

**27.76** At that meeting, Dr McClelland advised that work was progressing at the South East Scotland Regional Transfusion Centre (RTC) into the problem of NANB Hepatitis associated with blood transfusion and suggested that a multi-centre study might be sponsored by the MRC into the problem of transfusion-associated NANB Hepatitis transmission. The minutes state: 'It was agreed, however, that this matter should be deferred until candidate laboratory tests were available'.<sup>109</sup>

**27.77** It was noted at the meeting that the following problems required investigation: (i) the identification of donors and units of blood associated with possible cases of NANB Hepatitis; (ii) research into methods of identifying the viruses associated with NANB Hepatitis and (iii) epidemiological surveys to assess the size of the problem in relation to blood transfusions. The minutes record that, following the ad hoc meeting at the MRC in February 1979, three special project grants had been supported for research into the incidence, epidemiology and clinical features of NANB Hepatitis and a fourth would probably soon be approved. It was noted that it was 'open to the Working Party to initiate fresh projects in this field'.<sup>110</sup>

**27.78** The second and, as it turned out, last, meeting of the MRC Working Party was on 25 June 1981.<sup>111</sup> At that meeting Dr McClelland tabled a protocol for a prospective study of post-transfusion hepatitis in the UK (to be carried out at Edinburgh and Manchester) based on the protocol used in the TTV study.<sup>112</sup>

**27.79** Dr McClelland had reported to a meeting of SNBTS Directors on 23 June 1981 that he had prepared the protocol for presentation to the MRC on 25 June for a two-centre study. The directors agreed that similar studies might be made in Scotland generally. Discussion noted at the meeting recorded that:

<sup>104</sup> Meeting minutes [PEN.017.1737]

<sup>105</sup> The proceedings are discussed in Chapter 15, *Knowledge of Viral Hepatitis 2 – 1975-1985*, paragraph 15.69.

<sup>106</sup> Chapter 15, *Knowledge of Viral Hepatitis 2 – 1975-1985*, paragraphs 15.61–15.62.

<sup>107</sup> Meeting minutes [PEN.017.1710]

<sup>108</sup> Then Director of the Oxford Regional Transfusion Centre (RTC) and who would later become Director of the Manchester RTC and Chairman of the Regional Directors of the National Blood Transfusion Service for England and Wales.

<sup>109</sup> Meeting minutes [PEN.017.1710] at 1711

<sup>110</sup> Ibid [PEN.017.1710] at 1711

<sup>111</sup> Meeting minutes [PEN.017.1478]

<sup>112</sup> Day 63, pages 71–72: Dr McClelland's proposed protocol is [PEN.017.1486]. In fact, Dr McClelland had corresponded with the TTV study group and obtained a copy of its protocol.

Dr McClelland offered to circulate to the Directors the text of a leading article in the *New England Journal of Medicine* of 23 April 1981 and (if the MRC permitted) the document which he had prepared for the MRC. Scottish Directors would not proceed with liver function tests on existing donations for the time being.<sup>113</sup>

**27.80** The objectives of Dr McClelland's proposed study included: (i) to establish the incidence and causes of transfusion-related hepatitis; (ii) to establish the incidence of elevated ALT in donors to evaluate the effectiveness of methods of donor screening; (iii) to establish a library of samples for future serological studies; (iv) to provide data for assessing the effectiveness of any new methods of donor screening and (v) to establish the long-term outcome of post-transfusion NANB Hepatitis by prolonged follow-up of all cases identified. Dr McClelland emphasised the desirability of obtaining accurate data concerning the incidence of transfusion-transmitted NANB Hepatitis in the UK.

**27.81** The minutes of the June 1981 meeting of the MRC Working Party note Dr McClelland's position when tabling his protocol:

Apart from the desirability of obtaining accurated [sic] data concerning the incidence of [NANB] transfusion hepatitis in the UK, it was also important to obtain information as to whether the screening of blood donors by the [ALT test] might be of value in the UK. It was also essential to obtain well documented specimens of serum from known cases of [NANB Hepatitis] for evaluation of any tests which might be of value for the diagnosis of this disease, and the screening of blood donors.<sup>114</sup>

**27.82** In oral evidence, Dr McClelland repeated his belief that it was essential to assess the importance of the NANB Hepatitis problem as a basis for the planning and evaluation of future donor screening strategies.<sup>115</sup>

**27.83** Dr McClelland's proposal had noted that there had been no prospective study in the UK of the incidence of sub-clinical hepatitis following transfusion of blood or single-donor blood products. That provoked a reaction from Professor Arie Zuckerman of the London School of Hygiene and Tropical Medicine.<sup>116</sup> The minutes note that Professor Zuckerman pointed out that a study had already been undertaken in the 1970s and that the sera from that study were available for the evaluation of any candidate tests for NANB Hepatitis.<sup>117</sup> A fresh study could cost from £50,000 to £100,000 to undertake. In Professor Zuckerman's view, a 'careful evaluation' of the need for such a project should be carried out before the Working Party could recommend to the MRC that a fresh study should be sponsored as 'the administrative difficulties encountered in the last project had been very hard to solve'. It was also noted that an evaluation of ALT screening of blood donors had been carried out at North West Thames RTC, Edgware, and that problems had been encountered as it had proved difficult to trace the fate of donors found to have raised ALT values.<sup>118</sup>

---

<sup>113</sup> Minutes of SNBTS Directors' Meeting, 23 June 1981 [SGF.001.0211] at 0215

<sup>114</sup> Minutes of MRC Working Party, 25 June 1981 [PEN.017.1478] at 1480. Professor Cash, who was a member of the MRC Blood Transfusion Research Committee, supported the proposed study. In his evidence to the Inquiry he stated: 'I believe we couldn't even think seriously about surrogate testing until we had done some important research, and much of that needed to be a replication in the UK context of the TTV study in the States. So I was very supportive': Day 64, pages 147–148. He also stated: 'I see no reason why a properly resourced and supported UK group could not have achieved parity of performance with the US TTV study group': Day 72, page 45

<sup>115</sup> Day 63, page 70; Dr McClelland's proposal for a prospective study of post transfusion hepatitis [PEN.017.1486]

<sup>116</sup> Day 63, page 70

<sup>117</sup> This is a reference to the MRC study which reported in 1974.

<sup>118</sup> Minutes of MRC Working Party 25 June 1981 [PEN.017.1478] at 1480



**27.84** In his evidence to the Inquiry, Dr McClelland explained that he had felt encouraged by the discussion at the meeting in February 1980 and particularly the reference to establishing fresh projects to produce proposals. Professor Zuckerman was very eminent, however, and his view, which carried particular weight, was that a study into post-transfusion hepatitis had already been carried out (the MRC study reported in 1974) and ‘it didn’t need to be done again’.<sup>119</sup> The Minutes record that Professor Zuckerman left the meeting before discussion of this topic was concluded. Dealing with the period after his departure, the minutes note that the Chairman, Dr Gunson, would write to Professor Zuckerman and to Professor Sheila Sherlock of the Royal Free Hospital, London, to see if the patient records and serum samples from the previous MRC study were still available and that ‘Dr McClelland’s project could then be reconsidered in the light of the specimens and clinical data available from the earlier study’.<sup>120</sup>

**27.85** In the event, the MRC Working Party did not meet again. The Working Party’s parent committee, the MRC Blood Transfusion Research Committee, was disbanded in July 1982, the MRC Board having concluded, in the light of activities of outside bodies and the proposal to set up a British Society of Blood Transfusion, that the committee’s work was being duplicated elsewhere.<sup>121</sup> This view was not shared by Professor John Cash, Medical Director of the SNBTS, who tried unsuccessfully to form a joint UK transfusion services’ research committee to fill what he saw as a gap.<sup>122</sup> He was concerned in particular because he knew as a council member of the recently formed British Blood Transfusion Society that the Society could not fund the studies advocated by the sub-committees of the MRC Blood Transfusion Research Committee.

**27.86** In addition, the sera from the earlier MRC study would turn out to have been destroyed. Dr McClelland, who was perplexed by the decision of the MRC Board,<sup>123</sup> persisted in his efforts to persuade colleagues of the need for a study. That position would be vindicated in 1987 by the Council of Europe’s Committee of Experts on Blood Transfusion and Immunohaematology, as described by Professor Leikola and discussed above, although Dr McClelland considered, and continues to believe, that it was by that time too late. It will be necessary to return to a discussion of that matter later. In the meantime, further research was ongoing.

**27.87** An editorial in *The Lancet* in July 1981 gave the flavour of the thinking at that time.

Despite 40 years’ efforts to find ways of preventing it, hepatitis still arises after transfusion of blood and blood products. The discovery of the hepatitis B virus and the development of increasingly sensitive tests for markers of hepatitis B infection was a major step forward, but a bigger contribution came from the recognition that paid blood donors, probably because of their lower socioeconomic status, were much more likely to transmit hepatitis than unpaid donors. In the United Kingdom, since the introduction of hepatitis B screening, transfusionists seem to have been mesmerised by this one virus and the thrust of hepatitis prevention has been towards introducing ever more sensitive tests for it, even though the evidence is that little additional protection is gained

---

<sup>119</sup> Day 63, pages 66–67

<sup>120</sup> Minutes of MRC Working Party, 25 June 1981 [PEN.017.1478] at 1481

<sup>121</sup> Letter dated 19 July 1982 [SNB.002.5864]

<sup>122</sup> Letter from MRC to Dr Cash dated 19 July 1982 [SNB.002.5864]; Letter from Dr Cash to the SNBTS Directors dated 23 July 1982 [SGH.001.0087]; Report from Dr Cash to Blood Transfusion Service Sub-Committee dated 24 November 1982 [SNB.003.3603]

<sup>123</sup> Dr McClelland – Day 63, page 73

from tests more sensitive than the widely used haemagglutination assay. When non-A non-B hepatitis was first recognised, many British workers seemed to regard it as a purely American problem. Lately, non-A non-B hepatitis has been accepted in the U.K. as a serious hazard of treatment with factor VIII and factor IX concentrates, which are prepared from very large pools of donor plasma, but no-one has paid much attention to this type of hepatitis in the patient who receives a few units of blood or platelets. In a UK prospective study of post-transfusion hepatitis,<sup>124</sup> frank hepatitis developed in 1%, there were sustained increases of alanine aminotransaminase (ALT) in 4.5%, and the ALT was raised at some time after transfusion in 20%. Although only a small proportion of these cases of hepatitis and “transaminitis” seemed to be due to hepatitis B virus, nothing has been done to assess the value of preventive methods other than hepatitis B screening.

American workers have been less complacent.<sup>125</sup>

**27.88** The editorial traced some of the developments in the USA suggesting a need for careful examination and proceeded:

There are some other questions. How important in clinical terms is silent transaminitis after transfusion? Although regular users of blood products do get chronic liver disease which is probably due to non-A non-B agents, there is not much information about the long-term consequences of subclinical hepatitis after a single transfusion episode. In the U.K. there is no report about long-term follow-up of transaminitis patients from the earlier study. Furthermore, the value of ALT or other non-specific tests would have to be tested prospectively in various circumstances; after all, there are many reasons why the ALT may be raised, and in some communities a high proportion of blood donors might have to be rejected when the real reason for the abnormal result was alcohol.

If a new donor screening programme was set up, the high cost might be the least of the problems. Today, all transfusion services are aware of the plight of would-be donors who prove to be symptomless carriers of hepatitis B virus. Once these people are labelled as carriers, they may face difficulties in securing medical or dental care. We should be very much aware of the risks of creating a new and much larger group of donors who are rejected because of a new “hepatitis” test which does not necessarily signify infectivity, and which may be detecting a form of infection whose natural history we know very little about.<sup>126</sup>

**27.89** Indirectly, this provided eloquent support for Dr McClelland’s proposals.

**27.90** In July 1981 the need for research into post-transfusion NANB Hepatitis in the UK was raised by the Advisory Group on Testing for the Presence of HBsAg and its Antibody (also known as ‘the Maycock Group’ as it was chaired by Dr William Maycock) in its 3rd report.<sup>127</sup> While the Group’s remit dealt with testing for Hepatitis B, its report also

<sup>124</sup> Medical Research Council Working Party on Post-transfusion Hepatitis: Report to MRC Blood Transfusion Research Committee, *Journal of Hygiene*, 1974; 73:173-88 [LIT.001.0116]

<sup>125</sup> ‘Screening of blood donors for [NANB] hepatitis’, *The Lancet*, 11 July 1981:73 [LIT.001.0438]

<sup>126</sup> *Ibid* [LIT.001.0438]

<sup>127</sup> The third report of the Advisory Group, published in July 1981 [DHF.003.0037]

covered NANB Hepatitis. HBsAg screening of donations destined for fractionation was recommended, implying that all donations collected for transfusion purposes at RTCs would be tested for HBsAg.<sup>128</sup> Anti-HBs tests were recommended for as many new donors as possible to identify high titre donors to meet demand for the production of hepatitis B immunoglobulin. In relation to Anti-HBc, the report stated:

19. Blood donations which are negative for HBsAg by RIA and negative for anti-HBs, but positive for core antibody (anti-HBc) may occasionally transmit hepatitis B. Some of these donations are from donors recovering from unrecognised hepatitis B infections who still have minute but undetectable amounts of virus in their blood. At the present time there is no evidence that this type of donation causes more than a few cases of post-transfusion hepatitis (PTH) in the UK.

20. Screening all donations for anti-HBc would be costly and result in discarding many harmless donations from immune donors unless tests for anti-HBs were also carried out.

21. We recommend that there should be no general screening of donations for anti-HBc, but that all donors implicated in cases of PTH should be tested at reference centres for anti-HBc as well as for other hepatitis markers so that more information can be obtained on the dangers of HBsAg negative, anti-HBsAg negative, anti-HBc positive donors.<sup>129</sup>

**27.91** At this stage, the difficulty in assessing the frequency of post-transfusion NANB Hepatitis was, firstly, that there was no marker to show who had contracted it and, secondly, that most cases were asymptomatic. The Maycock Group's report noted further:

22. [NANB] hepatitis viruses are a common cause of PTH in the United States and are thought to have been responsible for cases of PTH in the UK.<sup>130</sup> Hepatitis due to these viruses is common among haemophiliacs and follows the administration of imported, and occasionally of British Factor VIII and Factor IX. There is evidence for the occurrence of sporadic cases of [NANB] hepatitis in the general adult population and in association with cryoprecipitate therapy in the UK.

23. There are at the present time no screening tests for detecting [NANB] hepatitis viruses in blood donations.

24. We recommend that research is undertaken in the UK to determine the extent and severity of PTH due to [NANB] hepatitis viruses. Unless this is done we will not have the knowledge on which to base any possible future recommendations about screening blood donations for these viruses. Regional Transfusion Directors should encourage hospital haematologists to report all cases of post-transfusion jaundice and where these could be due to [NANB] hepatitis, the facts should be reported to the appropriate Adviser in Blood Transfusion at the Department of Health and Social Security (DHSS) or Scottish Home and Health Department (SHHD).<sup>131</sup>

<sup>128</sup> Ibid [DHF.003.0037] at 0045

<sup>129</sup> Ibid [DHF.003.0037]

<sup>130</sup> NANB Hepatitis infection had been identified by Dr Follett in Glasgow by this stage.

<sup>131</sup> The third report of the Advisory Group, published in July 1981 [DHF.003.0037] at 0045-0046

**27.92** The same report dealt with 'Liver Function Tests':

25. Several categories of people are found to have raised blood transaminase levels which are not associated with viral hepatitis. Some 3% of new donors may be excluded if the criteria of one raised transaminase level is applied. In addition to the need for confirmatory transaminase testing the worry and inconvenience caused to donors would be unlikely to be compensated for by any clinical benefit. Therefore, we advise against these tests in screening blood donors at the present time but the subject should be kept under review.

26. Sporadic cases of apparent post-transfusion hepatitis due to the hepatitis B virus will continue to occur despite the most rigorous screening of donor blood samples because there are routes of infection other than transfusion; by coincidence, a transfusion may appear to have been responsible. Very few cases of PTH will continue to occur from donations with antigen below the present possible detection level. The donors involved may be in the early stage of incubating Hepatitis B.<sup>132</sup>

**27.93** Professor Cash was a member of the Maycock Group at this stage and the Group's third report was discussed at a meeting of the SNBTS Directors on 22 September 1981.<sup>133</sup> It was noted at the meeting that the transfusion services had various groups examining different topics but that hepatitis testing was not one of them. It was agreed that Professor Cash should write to Dr William Wagstaff<sup>134</sup> to propose that the UK transfusion services establish a post-transfusion hepatitis working group.

**27.94** Dr McClelland was by no means an isolated voice calling for research at this time, though it was to emerge that colleagues on relevant working parties, which may have held the key to organising and funding such studies, may not have shared his enthusiasm – as was to appear from the transactions of the next working party to be set up by the transfusion services: the Working Party on Transfusion Associated Hepatitis.

**27.95** The Working Party on Transfusion Associated Hepatitis met for the first time on 27 September 1982.<sup>135</sup> The Working Party comprised senior officials representing a range of transfusion interests in the UK. It was chaired by Dr Gunson, Regional Transfusion Director, Manchester, and its members were Dr John Barbara, North London, Dr Brian McClelland, Edinburgh, and Dr Mitchell, Glasgow, all RTDs, as well as Dr John Craske of the Public Health Laboratory, Dr Richard Lane of the Blood Products Laboratory, Dr Bruce Cuthbertson of the Protein Fractionation Centre (PFC),<sup>136</sup> Edinburgh, and Dr Howard Thomas of the Royal Free Hospital, London. The agreed Terms of Reference were:

To promote the investigations of the epidemiology of transfusion-associated hepatitis, to promote research into the methods of prevention, and to make recommendations to the Directors of the UK transfusion service regarding procedures and screening tests necessary for its prevention.<sup>137</sup>

---

<sup>132</sup> Ibid [DHF.003.0037] at 0046

<sup>133</sup> Minutes of Meeting [SGF.001.0316] at 0320

<sup>134</sup> Dr Wagstaff was Regional Transfusion Director at Sheffield and at this time was the representative of the RTDs of England and Wales

<sup>135</sup> Minutes of Meeting [PEN.017.1716]. The members of the Working Party are listed at 1719

<sup>136</sup> The manufacturer of NHS blood products in Scotland

<sup>137</sup> Minutes of Meeting [PEN.017.1716]

**27.96** At the first meeting of the Working Party, the minutes record that Dr Gunson felt that existing reports provided an inadequate estimate of the true incidence of transfusion-associated hepatitis. It was agreed that a library of existing information on post-transfusion hepatitis would be collected for consideration at the next meeting, that Dr McClelland would produce an outline protocol for a prospective study of either the incidence of transaminitis (elevated liver enzymes such as ALT) in recipients or for determining the incidence of post-transfusion hepatitis in recipients of blood positive for existing putative markers of NANB Hepatitis, and that an attempt would be made to see if samples from the 1974 MRC study were still available.<sup>138</sup>

**27.97** In *A v The National Blood Authority* it was said that in 1982 Dr Gunson, in the name of the National Blood Transfusion Service (NBTS), applied for a grant to carry out a study in the UK into surrogate testing for NANB Hepatitis and that the application was refused. Documentary evidence of the grant application, or to whom the application may have been made, or its refusal, has not been found.<sup>139</sup>

**27.98** The Working Party met for the second time on 18 January 1983<sup>140</sup> and preparations for a study were discussed. The minutes note that '[i]t was agreed that some form of study was needed so that the UK is equipped to answer queries about any specific or non-specific tests for [NANB Hepatitis] offered from abroad'.<sup>141</sup> Dr McClelland circulated an outline proposal for a prospective study of NANB Hepatitis.<sup>142</sup> The outline proposal stated that a large scale prospective study of transfusion recipients and their respective donors, along the lines of the US TTV study, was not considered further because a similar study had previously been done in Britain<sup>143</sup> and samples were said to be available for reanalysis. It was further noted that a preliminary look at the financial implications indicated that a large scale multi-centre study would cost £250,000 to £500,000 and that, without further resources, Dr McClelland was not in a position to prepare even an initial outline of a study on that scale. Dr McClelland on this occasion appears instead to have suggested a more modest study 'to investigate the possible value of one or more putative markers of [NANB Hepatitis] in predicting the ability of a given blood donor to transmit the disease to a transfused recipient.'<sup>144</sup> Although the proposed study appears to have been smaller than the study Dr McClelland had proposed at the meeting of the MRC Working Party on Post-Transfusion Hepatitis on 25 June 1981, the study proposed on 18 January 1983 continued to include the follow-up of recipients. It was estimated that this proposed study would cost £63,000 and members of the Working Party were asked to provide Dr McClelland with their comments.

**27.99** The minutes of the meeting record that Dr Gunson would make a further attempt to ascertain from the MRC whether the samples from the MRC study reported in 1974 were still available and whether the recipients had been followed up to look for long-term effects. The minutes of the meeting noted that, '[i]f MRC samples are not available the working party will put forward proposals for some form of study to the MRC and DHSS'.<sup>145</sup>

<sup>138</sup> Ibid [PEN.017.1716] at 1717–1718.

<sup>139</sup> *A v The National Blood Authority* [2001] 3 All ER 289, paragraph 126 [PEN.017.0302] at 0378–0379

<sup>140</sup> Minutes of Meeting [PEN.017.1507]

<sup>141</sup> Ibid [PEN.017.1507] at 1511–1512

<sup>142</sup> Dr McClelland's outline proposal [PEN.017.1514]

<sup>143</sup> A reference to the MRC study, reported in 1974

<sup>144</sup> Dr McClelland's outline proposal [PEN.017.1514] at paragraph 1.2. Notwithstanding some uncertainty on the part of Dr McClelland (Day 63, pages 80–83) the study proposed appears to have been more modest in cost and scale than a large scale study, along the lines of the TTV study.

<sup>145</sup> Minutes of Working Party meeting, 18 January 1983 [PEN.017.1507] at 1512

**27.100** The Working Party met for the third time on 20 April 1983.<sup>146</sup> It was by then known that the samples from the 1974 MRC study had been destroyed.<sup>147</sup> Dr McClelland had been sent the results of a prospective study at Newcastle involving the follow-up of 248 patients.<sup>148</sup> As regards Dr McClelland's outline proposal for a prospective study of NANB Hepatitis, it was noted that '[s]o far a source of funding has not been found.'<sup>149</sup> It was thought that there would be a low incidence of post-transfusion NANB Hepatitis at Edinburgh. It was suggested that the North London RTC, Edgware, might provide a higher incidence area for the study. Dr John Barbara agreed to discuss matters with his Director at the Edgware centre and plans for a joint study with Edinburgh might then be submitted to the MRC by the Working Party.

**27.101** In his evidence to the Inquiry Dr McClelland commented on the attitude of the Working Party to a study into post-transfusion NANB Hepatitis in the UK involving the follow up of transfusion recipients:

Q: And what was the view of this working party of the need for a study of the type you proposed?

A: Well ... there was really very little enthusiasm. There was polite interest. But when it says ... [in] the minutes, "No source of funding has been found", no source of funding had been seriously sought. Nobody had gone back to the MRC, and I wasn't going to go back to the MRC at that stage myself as an individual because I knew I wouldn't get anywhere .... [I]t was perfectly clear there was going to have to be a major effort made to obtain major funding for this study.

....

Q: Obviously, you were of the view that there should be such a study?

A: I was strongly of the view but I was beginning to get a little bit worn down by that time actually because, you know, there is only a certain amount one can do as an individual and it wasn't lighting fires for anyone else.

Q: By anybody else, do you mean the other members of this working party or do you mean more widely?

A: Well, I mean other members of this working party because this was the first jumping-off point to get something done. If the working party had – looking at the membership of the working party, if those people had all put their shoulders behind this, something probably would have happened but that didn't happen.

Q: So you were largely driving forward this proposal by yourself?

A: I was endeavouring to, yes.<sup>150</sup>

---

<sup>146</sup> Minutes of Working Party meeting, 20 April 1983 [PEN.017.1522]

<sup>147</sup> Letter from the MRC to Dr Gunson [PEN.017.1507]

<sup>148</sup> As discussed below, the results of the Newcastle study were published later in 1983.

<sup>149</sup> Meeting minutes [PEN.017.1522] at 1523

<sup>150</sup> Day 63, pages 87–88

**27.102** Dr Ruthven Mitchell, Director of the Glasgow and West of Scotland RTC, was also a member of the Working Party. In his evidence to the Inquiry he explained his view of the difficulties in undertaking a large scale study of the type proposed by Dr McClelland. A large number of patients would require to be enrolled in the study to make it statistically valid, patients would require to be followed over a number of years and many patients who received transfusion would have died of their underlying condition (necessitating blood transfusion) before meaningful data on post-transfusion NANB Hepatitis might come to light.<sup>151</sup> Dr Mitchell's view was that a prospective study into post-transfusion hepatitis involving the follow-up of patients was '[a] very good idea in theory but not practical – very difficult to do practically'.<sup>152</sup>

**27.103** The Working Party met for the fourth time on 27 September 1983. While the subject of transfusion-associated hepatitis, including the question of carrying out prospective studies into the disease, appeared on the agenda for the meeting,<sup>153</sup> the minutes of the meeting contain no reference to any discussion of transfusion-associated hepatitis; instead, the discussion was dominated by AIDS.<sup>154</sup> In his evidence to the Inquiry Dr Mitchell was asked why there does not appear to have been a discussion of hepatitis at the meeting and stated, 'I think it was a preoccupation with another, much more lethal problem that we had [that is, HIV/AIDS]'.<sup>155</sup>

**27.104** As it turned out, the transfusion services' Working Party on Transfusion Associated Hepatitis did not meet again until it was reconvened in late 1986. The reasons for that are discussed below. Dr McClelland's view that there was very little enthusiasm in the Working Party for his proposals clearly understates what was at least tacit opposition from senior members of the group.

**27.105** As noted above, a team at Newcastle carried out a prospective study of post-transfusion hepatitis in cardiac surgery patients and reported in November 1983.<sup>156</sup> The study involved 248 patients who received a total of 1796 units of blood or blood components. All surviving patients were seen six months after surgery and were tested for ALT.<sup>157</sup>

**27.106** Six patients were found to have an increase in ALT levels which was unexplained and reached over 100 IU/L (normal < 40 IU/L). The authors considered that the incidence of 'acute short term incubation' post-transfusion NANB Hepatitis was therefore 2.4% (6/248). While these six patients had normal liver function six months after transfusion, a further two of the surviving 228 patients had raised ALT levels at six months. In one of these, liver biopsy disclosed chronic persistent hepatitis;<sup>158</sup> in the other, alcoholic liver disease was suspected. Overall, the authors considered that the incidence of 'significant chronic liver disease' after blood transfusion possibly attributable to an NANB Hepatitis agent was only 0.4% (ie 1/248). The paper concluded that '[NANB] hepatitis after blood

---

<sup>151</sup> Day 65, pages 3–8

<sup>152</sup> *Ibid* page 24

<sup>153</sup> Agenda for Working Party meeting on 27 September 1983 [SNB.014.3029]

<sup>154</sup> Minutes of Working Party meeting on 27 September 1983 [SNB.014.3030]

<sup>155</sup> Day 65, page 12

<sup>156</sup> Collins et al, 'Prospective study of post-transfusion hepatitis after cardiac surgery in a British centre', *British Medical Journal*, 1983; 287:1422 [LIT.001.0212]

<sup>157</sup> In addition, 44 patients who lived within a 10 mile radius of the hospital were tested every two weeks for two months and thereafter at monthly intervals for six months.

<sup>158</sup> Chronic persistent hepatitis was considered a generally mild, benign condition – see Chapter 14, *Knowledge of Viral Hepatitis 1*, paragraph 14.37.

transfusion from a largely British blood donor group probably leads to clinically significant chronic liver disease very rarely indeed'.<sup>159</sup>

**27.107** In oral evidence Dr McClelland said that the interpretation placed upon their data by the Newcastle group was consistent with the understanding of post-transfusion NANB Hepatitis at the time.<sup>160</sup>

**27.108** As noted already, *Vox Sanguinis* conducted a survey in 1983 of the opinions of various experts relating to the costs and benefits of routine donor screening for ALT. Dr McClelland expressed the following view in his contribution to the forum:

The only action which I would recommend at present is that there should be a thorough prospective study to determine the frequency with which post-transfusion hepatitis occurs in the regions served by this centre, or in a closely comparable population.

If the results of such a study indicate that post-transfusion hepatitis due to [NANB] viruses (PTH) occurs sufficiently frequently to cause concern, I would recommend further study be carried out to determine whether the introduction of a donor ALT screening programme does in fact reduce the attack rate for PTH. As an alternative it may well be possible to study simultaneously the attack rate for PTH in the recipients of ALT screened or nonscreened blood.

I consider that without undertaking thorough studies along these lines, the potential and actual scale of the 'benefit' side of the cost benefit calculation is unknown and therefore no rational decisions can be taken ....

I would therefore recommend that we are careful to establish the benefits *before* we become committed to the costs. We must know what improvement in the quality of our blood and blood products we are asking the community to pay for.<sup>161</sup>

**27.109** Dr Mitchell expressed the following view in the publication:

As ... ALT testing has obviously high false-positive and also high false-negative rates, we have no intention of suspending 3% of our volunteer blood donors on the basis of an ... ALT test when they may have only transient elevations. Furthermore, such a policy would discourage donor recruitment among the few willing to donate for the good of the community and would cause some anxiety in donors and their families when we cannot offer anything more than the argument that [NANB] hepatitis may exist. We have been most disturbed by the treatment or lack of treatment for unrelated diseases available to HBsAg positive blood donors and fear that donors with elevated ... ALT levels may suffer the same problems.

We await the development of a specific serological test for [NANB] hepatitis. The use of nonspecific tests such as ... ALT can have deep sociological and psychological effects on established blood donors and would necessitate the recruitment of voluntary nonremunerated replacements.<sup>162</sup>

---

<sup>159</sup> Collins et al, 'Prospective study of post-transfusion hepatitis after cardiac surgery in a British centre', *British Medical Journal*, 1983; 287:1422 [LIT.001.0212] at 0214

<sup>160</sup> Day 63, pages 14–15

<sup>161</sup> Responses to ALT survey *Vox Sanguinis*, 1983; 48 [LIT.001.1837] at 1846

<sup>162</sup> *Ibid* [LIT.001.1837] at 1846–1847



**27.110** It is significant that within the Scottish service such strongly differing views should have been expressed by the Directors of the two major Regional Transfusion Centres. Faced with such a powerful statement by Dr Mitchell, Dr McClelland was most unlikely to make progress with his proposal.

### **1984–1985**

**27.111** The Inquiry has found little evidence to show that the issue of surrogate testing was considered in the UK in 1984 and 1985 or that consideration was given in these years to carrying out a UK study into the prevalence of post-transfusion NANB Hepatitis and its association with surrogate markers in donors. As noted above, for example, the transfusion services' Working Party on Transfusion Associated Hepatitis last met on 27 September 1983 (when discussion was dominated by AIDS) and did not meet again until, as discussed below, it was re-convened in late 1986.

**27.112** At a meeting called by the National Institute for Biological Standards Control (NIBSC), on 9 February 1984, Dr Terry Snape (BPL, Elstree, the manufacturer of NHS blood products for England and Wales) commented that screening for serum ALT had been considered in the USA but not used in the UK; this appears simply to have been a factual comment.<sup>163</sup> In the discussion that followed, there was no reference to its possible use in the UK. In the context of AIDS, testing for anti-HBc was discussed but there was no general agreement that the test should be part of the routine screening carried out on donors: its possible relevance to hepatitis was not mentioned.

**27.113** Dr Edward Follett and Dr Brian Dow,<sup>164</sup> reporting on a study of NANB Hepatitis in the West of Scotland in 1984, wrote:

Evidence from USA would suggest that if ALT/SGPT testing is performed on all blood donations and those with high levels excluded, around 29–40% of non-A, non-B PTH cases could be prevented with the loss of around 3% of blood donations.

A total of 10,655 West of Scotland blood donors have been tested for elevated SGPT(ALT) levels.<sup>165</sup>

**27.114** The table of results showed the concentration of ALT (measured in U/ml) in blood samples. Levels exceeding 35 U/ml were found in 367 individuals (3.4%), levels exceeding 92 U/ml in 55 individuals (0.51%) and those exceeding 125 U/ml in 41 individuals (0.38%). Prison session donors showed ten times more donations with grossly elevated ALT levels than others.<sup>166</sup>

**27.115** Drs Follett and Dow had shown that 'around 3% of blood donations' in the West of Scotland had elevated ALT values. Recipients of the donations were not followed up and no data were gathered on the use of the 10,655 donations or their destination within the blood services. Data were available of clinically likely cases of post-transfusion NANB Hepatitis reported to the Glasgow and West of Scotland BTS: there had been reports of nine cases only. The notification requirements related to 'infective jaundice'.<sup>167</sup> They

---

<sup>163</sup> Draft minutes of meeting [SNB.004.8628] at 8636

<sup>164</sup> Dr Follett worked at the Regional Virus Laboratory, Ruchill Hospital, Glasgow. Dr Dow worked in the Glasgow and West of Scotland BTS.

<sup>165</sup> Final Report to Scottish Hospital Endowments Research Trust [SGH.002.8040] at 8044–8045

<sup>166</sup> Ibid [SGH.002.8040] at 8045

<sup>167</sup> See Chapter 14, *Knowledge of Viral Hepatitis 1*, paragraph 14.12.

were not well adapted to generate reports of NANB Hepatitis which was, in fact, seldom associated with clinical jaundice. In addition, reports of notifications of an infectious disease whose characteristics were poorly understood by clinicians generally were most unlikely to provide sound evidence of prevalence of the condition. Without follow-up of the donations tested, the study did not provide a basis on which the prevalence of post-transfusion NANB Hepatitis could, or should, have been drawn. Unfortunately, it was concluded on the basis of the reported cases that post-transfusion NANB Hepatitis was 'not a major problem' in the region. That conclusion was not based on sound evidence. Nor did it indicate the potential value of ALT surrogate testing, or a basis for assessing that value.

**27.116** Even more unfortunately, as will be seen below, the conclusions from the report were for several years used to support the contention that post-transfusion NANB Hepatitis was not a significant problem.

**27.117** After an outbreak of post-transfusion NANB Hepatitis following the use of certain BPL immunoglobulin concentrates,<sup>168</sup> Professor Andrew Lever, Professor Howard Thomas<sup>169</sup> and others contrasted the lack of tests for the NANB Hepatitis virus(es) with tests for other viruses, at the end of 1984:

Sensitive radioimmunoassays for hepatitis B surface antigen and IgM anti-HB-core allow identification of cases of post-transfusion hepatitis caused by the hepatitis B virus, and similar assays exist for the diagnosis of hepatitis A, cytomegalovirus, and Epstein-Barr virus infections which are rarer causes. Most post-transfusion hepatitis, however, is caused by a group of unidentified viruses designated non-A, non-B.<sup>170</sup>

**27.118** As others had, they commented that a screening test was needed to identify NANB Hepatitis. However, by this time there had been no progress on that front and, in general terms, the 1984–85 period saw a low level of activity in post-transfusion hepatitis research.

**27.119** One significant reason for the relative lack of consideration given to post-transfusion NANB Hepatitis in this period was the priority given to tackling AIDS. In Dr McClelland's written evidence to the Inquiry, for example, he stated that, '[l]ooking back, I think it is the case that the work related to AIDS, firstly developing donor information and selection procedures and later evaluating and introducing the test for HIV antibody, distracted the attention of both the SNBTS and the [NBTS] from [NANB] hepatitis for about 3 years'.<sup>171</sup> A further reason for the apparent lack of consideration given to post-transfusion NANB Hepatitis in the UK at this time is likely to have been, as discussed above and below, that post-transfusion NANB Hepatitis was regarded as having a low prevalence in the UK (at least when compared with the USA) and that it was considered to be a relatively mild disease.

<sup>168</sup> It had been thought that Cohn fractionation either excluded or inactivated viruses from such preparations. That had not occurred in the instant cases.

<sup>169</sup> At that time, Professor Lever was an MRC Research Fellow in Immunological Medicine at the Clinical Research Centre, Harrow and Professor Thomas was Professor of Medicine at The Royal Free Hospital, London.

<sup>170</sup> Lever et al, 'Non-A, Non-B Hepatitis Occurring in Agammaglobulinaemic Patients after Intravenous Immunoglobulin', *The Lancet*, 10 November 1984 [LIT.001.0449]

<sup>171</sup> Dr McClelland's statement on surrogate testing [PEN.017.0754] at 0763. As he put it in his oral evidence, '[b]asically we were overtaken by HIV': Day 63, page 89

1986

**27.120** The SNBTS Directors continued to follow developments in the USA and so became aware of the FDA's 1986 recommendation on surrogate testing. A copy of the February 1986 edition of *Blood Bank Week* was circulated for the 25 March 1986 meeting of the SNBTS Directors.<sup>172</sup> Dr John Forrester, Senior Medical Officer, SHHD, attended the meeting and was noted in the minutes as stating that it was highly unlikely that the UK Departments of Health would fund testing based on data from the USA. Dr Forrester said that he would be glad to hear of research proposals but could not guarantee funding. The minutes record that, after a full discussion, the Directors agreed to give consideration to funding someone to undertake research. Professor Cash was to think about the possibilities in association with Dr Ian Fraser, Director, Bristol RTC,<sup>173</sup> and make proposals to the Directors.

**27.121** In the meantime, Professor Cash had made direct contact with the American Red Cross. He wrote to Dr Gerry Sandler of the American Red Cross Blood Services on 17 February 1986 to ask what had transpired at the meeting of the FDA Blood Products Advisory Committee with regard to surrogate testing for NANB Hepatitis and what the American Red Cross had decided.<sup>174</sup> Dr Sandler replied on 4 March advising on the position at that stage: there was a divergence of view and the Red Cross was not proceeding to test but would review the position.<sup>175</sup>

**27.122** Dr Forrester produced a note of the SNBTS Directors meeting for his SHHD medical colleagues, Dr Archibald McIntyre, Principal Medical Officer (PMO) and Dr Graham Scott, Deputy Chief Medical Officer (DCMO).<sup>176</sup> As regards testing of blood donations for NANB Hepatitis, Dr Forrester noted that in America it was proposed to reduce the transmission of 'this medley of conditions' by testing all blood donations for evidence of faulty liver function. Dr Forrester's note went on:

Since any additional test of this kind must necessarily be non-specific and could well prove expensive, I have as you know immediately made further enquiries, and have discovered that the number of cases in Scotland due to blood transfusion is probably exceedingly low, there is a solid body of work (a Ph.D. thesis)<sup>177</sup> exploring the matter, and I am securing Dr Dan Reid's opinion in writing in the near future. It was argued at the meeting that urgent action was called for rather than a search for reliable information, and that the case was comparable with that of AIDS. I pointed out however that the steps taken to deal with AIDS were taken in face of a rapidly rising incidence, while in the present case the incidence so far as I know is small and steady. There is thus no justification for panic measures. I also indicated that the Department was perfectly open to proposals for funding research in this field, if research is required to determine the true size of the problem and the likely effect of any proposed remedy.<sup>178</sup>

---

<sup>172</sup> Minutes of SNBTS Directors' Meeting [SNF.001.0135] at 0142

<sup>173</sup> And Chairman of the Regional Directors of the National Blood Transfusion for England and Wales

<sup>174</sup> Professor Cash's letter to Dr Sandler [SGF.001.2149]

<sup>175</sup> Dr Sandler's letter to Professor Cash [SGH.002.8189]; American Red Cross circular to regional blood services [SGH.002.8190]

<sup>176</sup> Note by Dr Forrester dated 26 March 1986, [SGH.002.7496]

<sup>177</sup> This is a reference to Dr Dow's 1985 PhD thesis, '[NANB] Hepatitis in West Scotland', discussed below.

<sup>178</sup> Note by Dr Forrester dated 26 March 1986 [SGH.002.7496] at 7497

**27.123** Dr Forrester wrote to Dr Reid on 26 March 1986 seeking information on the likely incidence of NANB Hepatitis in Scotland, the proportion attributable to blood transfusion and how far any proposed test could reduce this proportion.<sup>179</sup>

**27.124** Despite the views of the SNBTS Directors on the need for research into transfusion-associated hepatitis, there seems to have been little appetite among the Transfusion Directors in England and Wales for such research. At the meeting of the English and Welsh Directors on 24 and 25 April 1986 the question of whether a study into NANB Hepatitis should be carried out was raised. The minutes state:

The Chairman reported that this had been discussed by the Scottish Directors and that he had agreed to raise it with RTDs. [Name redacted] reminded Directors of two previous attempts, one by the MRC and one by the Transfusion Associated Hepatitis Working Party, to study this problem. After discussion it was agreed that this should not be pursued because of lack of time and resources.<sup>180</sup>

**27.125** Around May 1986, the SNBTS prepared its submission for the 1986 Public Expenditure Survey (PES).<sup>181</sup> This was an annual bidding process in which public bodies submitted applications for funding to the government. The Common Services Agency (CSA)<sup>182</sup> submitted the application for funding for all of the activities within its remit, including the SNBTS, to the SHHD. The administrative officials in the SHHD critically examined the funding application, taking advice from their medical colleagues on medical matters, before deciding on the items which should be forwarded to the SHHD's Finance Division. The Finance Division would then further examine funding applications before they were put to the relevant minister for approval, before ultimately being voted upon by Parliament.<sup>183</sup>

**27.126** In its 1986 bid, the SNBTS included a sum of £810,000 to commence new mass donation screening programmes in 1987–88, with a forward projection of £836,000 for 1988/89.<sup>184</sup> The fate of the funding request is discussed below. The reason for the funding request was set out in the 1986 PES, which was drafted by Professor Cash, as follows:

Despite the absence of specific tests to detect donations which transmit [NANB] hepatitis there is increasing evidence that both in Europe and North America formal moves will be made, within the next 12-18 months, to introduce surrogate testing of all donations (liver function and [anti-HBc] tests).<sup>185</sup>

---

<sup>179</sup> Letter [SGH.002.8187]. Dr Reid was Director of the Communicable Diseases Surveillance Unit, Ruchill Hospital, Glasgow. The Inquiry has, unfortunately, been unable to obtain a copy of Dr Reid's response to Dr Forrester which appears to have been dated 4 June 1986.

<sup>180</sup> Minutes of Meeting [DHF.002.1290] at 1296 (Item 16)

<sup>181</sup> SNBTS 1986 PES Programme Narrative [SNB.011.2637]

<sup>182</sup> Section 19 of the National Health Service (Scotland) Act 1972 provided for the constitution of the Common Services Agency for the Scottish Health Service with effect from 1 April 1974. Amongst its several responsibilities was the operational management of the blood services. See Chapter 17, *Blood and Blood Products Management*, paragraphs 17.23–17.25.

<sup>183</sup> Mr Macniven – Day 65, pages 148–159, 168–172; Mr Murray's statement [PEN.017.1755]. The PES set out the sums granted for the then current financial year (1 April to 31 March), the sums sought in the next financial year and, more speculatively, the sums sought for the following two years: Day 65, pages 164–165

<sup>184</sup> SNBTS 1986 PES Programme Narrative [SNB.011.2637] at 2640

<sup>185</sup> *Ibid* [SNB.011.2637] at 2649. Indeed, in a 'long-range' budget expenditure forecast prepared in 1982, Professor Cash had predicted that '[i]t is anticipated that technical developments will have reached a point within the next 5 years that the introduction of the testing of all donations for [NANB] hepatitis markers or associated markers will be mandatory.' SNBTS Forecast Development Estimates 1984–1986 – Introductory Comments by National Medical Director [SGH.001.8873] at 8878.

**27.127** In May 1986, Dr Dow, then a Senior Grade Scientific Officer in the Glasgow and West of Scotland RTC, produced a special report for the SNBTS Directors on 'Surrogate tests for non-A, non-B Hepatitis'.<sup>186</sup> Drawing on the work undertaken as part of his 1985 PhD thesis<sup>187</sup> and, in particular, looking at the extent to which reported cases of post-transfusion NANB Hepatitis in the West of Scotland were associated with surrogate markers in donor blood, Dr Dow was of the view that '[e]ven if the combination of anti-HBc and ALT tests were shown to be 100% effective the economics involved in conducting these tests would greatly outweigh the costs of hospitalization of the few reported NANB PTH cases'.<sup>188</sup> He concluded that:

The present UK policy of accepting donors with raised ALT levels (i.e. not routinely ALT testing), anti-HBc or histories of jaundice would appear to be correct. It would appear from the study that the introduction of such surrogate screening procedures would have little impact on reducing the already low level of NANB PTH cases at present reported within the West of Scotland region.<sup>189</sup>

**27.128** Dr Reid replied on 4 June 1986 to Dr Forrester's letter of 26 March.<sup>190</sup> He sent a copy of Dr Dow's thesis and, from Dr Forrester's note next referred to, appears not to have recommended surrogate testing. Dr Dow's thesis was then the only piece of work which related specifically to Scotland.

**27.129** On 12 June 1986 Dr Forrester produced a note, 'Transmission of [NANB] hepatitis by blood and blood products: is it practicable to reduce or prevent it by introducing ALT testing of donations?' Dr Forrester set out the outcome of his enquiries as follows:

1. The information in this note is mostly derived from the PhD thesis entitled "Non-A, Non-B Hepatitis in West Scotland", completed in 1985 by Dr BC Dow under the supervision of Dr Follett and others.
2. Hepatitis can be transmitted by blood and blood products, and is in Scotland an occasional but serious consequence of blood transfusion. In contrast, in USA as many as 10% of recipients may develop it. Established causes include Hepatitis B virus, Hepatitis A virus, Epstein-Barr virus and cytomegalovirus. Hepatitis B virus is now successfully excluded by testing of donations. Hepatitis A has caused little trouble because virus is only found in blood over a brief period.
3. [NANB] hepatitis is not a specific disease, but a heterogeneous collection of diseases. The hepatitis conditions due to the Epstein-Barr virus and cytomegalovirus are a substantial part of it, but there is general belief that some as yet unidentified virus infection is also part of it. Thus there can be no accepted test capable of detecting the virus in blood; detection is by exclusion of other conditions such as those mentioned.
4. [NANB] hepatitis, thus defined, is not uncommon in the population; Dr Dan Reid reckons an incidence for Scotland of 154 cases per year, but has little confidence in this estimate because it can only be derived by starting from

---

<sup>186</sup> Dr Dow's report [SNF.001.1109]

<sup>187</sup> Dr Dow's PhD thesis [LIT.001.3300]

<sup>188</sup> Dr Dow's report [SNF.001.1109] at 1110

<sup>189</sup> Ibid [SNF.001.1109] at 1111

<sup>190</sup> Preliminary Report, para 9.28. The Inquiry has, unfortunately, been unable to obtain a copy of Dr Reid's response to Dr Forrester.

the total of all hepatitis cases reported (probably under-reported) by clinicians, and deducting the cases of hepatitis B detected in laboratories (probably fully reported). It is common among drug-abusers. But in association with blood transfusion [NANB Hepatitis] is very uncommon in the west of Scotland. Over the last 8 years, 1-5 cases are found each year there, and there is no upward trend. There are peculiar difficulties in identifying its presence in haemophiliacs, since their blood exhibits diverse reactions because of repeated administration of blood products, but Dr Dow found no evidence of any substantial problem. Dr Dow reckons that the proportion of donations infected with [NANB] hepatitis may be 18 per hundred thousand [0.018%].

5. The condition is not as a rule serious, and most of the cases detected have not even been jaundiced. There may however be a tendency for it to become chronic, and the long-term outlook is inevitably not yet known. The case fatality rate is estimated in a textbook consulted by Dr Dan Reid at less than 0.1%, except in pregnant women, who are at much greater risk...

6. In the absence of a specific test, for some years the suggestion has been made that an enzyme test ("ALT") which detects faulty liver function should be applied to every donation. The advantage is that some donations might thus be excluded which would transmit [NANB] hepatitis. The drawbacks are that some infective donations might still be missed ("false negatives") and some harmless donations might be excluded ("false positives"). The American evidence is that both drawbacks are serious: only perhaps 38% of the genuinely infective donations are detected, and some 70% of the apparently infective donations are harmless. Rejection of donations might reach 3% – a grave loss.

7. ... Dr Dow concludes that in Scotland "cost would be extremely high and benefit minimal, especially when only a few cases of [NANB] post-transfusion hepatitis are reported each year."

8. Dr Dan Reid and Dr Follett do not recommend the introduction of ALT testing of Scottish blood donations, for the above reasons.<sup>191</sup>

**27.130** The issue of surrogate testing was considered by the SNBTS Directors at their meeting on 25 June 1986.<sup>192</sup> The minutes note that there was increasing evidence that the USA and several European countries were introducing surrogate testing of blood donors in an effort to minimise the risks of NANB Hepatitis transmission through blood and blood products. Professor Cash was noted as believing that the SNBTS would soon come under pressure from clinicians to introduce testing. A limited study involving the follow-up of donors (but not recipients) with abnormal liver function tests was about to take place in Edinburgh. Dr Fraser (Bristol) and Dr Contreras (Edgware) were keen to set up a small group to explore the feasibility and practicability of this development and hoped that a Scottish RTC would contribute. The Scottish Directors agreed to await the outcome of joint deliberations by Dr Fraser and Dr Contreras and to discuss the matter again at that time.

---

<sup>191</sup> Dr Forrester's note [SGH.002.8142]

<sup>192</sup> Minutes of SNBTS Directors' Meeting [SGH.001.6286] at 6290

**27.131** Further pressure was placed on the UK transfusion services by the recommendation in August 1986, noted above, from the AABB that all donor blood be tested for ALT and anti-HBc with effect from 30 November 1986, in an attempt to reduce NANB Hepatitis.<sup>193</sup> The positive response of the major blood delivery institutions in the USA, including the Red Cross, added to the pressure.

**27.132** Again, the SNBTS Directors were aware of developments in the USA. In a letter to Dr Fraser on 28 August 1986 on the question of surrogate testing, Professor Cash stated, 'I have a feeling that as the drums are beating louder and louder in other parts of the world on this topic the Brits remain fast asleep'.<sup>194</sup> While he noted that the suggestion of a UK prospective trial had been raised at the recent NBTs meeting and 'went down like the proverbial lead balloon', Professor Cash considered that the matter could not be left as it was. He proposed a meeting to look at the issues associated with donation testing, with a view 'to see whether we can reach conclusions which would enable us to make some clear operational decision[s] and that these would be transmitted to the various Departments of Health'.

**27.133** In his evidence to the Inquiry, Professor Cash stated that he did not support the introduction of surrogate testing at that stage but, instead, wanted more information upon which to base a decision. He explained that the benefit surrogate testing would bring to patients in the UK was unknown, the financial cost of testing would probably be taken from elsewhere in the NHS budget, the use of surrogate markers would cause uncertainty and concern among individual donors and blood collection would go down. He stated, '[t]his was making a major tactical moral position and we needed the data. So I supported ... getting the data very strongly'.<sup>195</sup>

**27.134** Dr Fraser replied to Professor Cash's letter and expressed the hope that if he, Professor Cash and Dr Contreras 'rowed hard enough' they could 'get our colleagues to move in the same direction'.<sup>196</sup>

**27.135** On 8 October 1986 the English and Welsh Transfusion Directors met.<sup>197</sup> In a discussion of surrogate testing the minutes noted:

The Chairman [Dr Fraser] reminded Directors that the possibility of screening for anti-HBc had been discussed previously .... Developments in America meant that this topic must be considered again as anti-HBc/ALT screening were soon to be essential for the accreditation of Blood Banks in the USA. The Chairman proposed that RTDs should approach the DHSS to fund a prospective study of 10,000 donations to see if the incidence of anti-HBc had changed since this was last examined. He added that Haemophilia Directors were pressing for plasma for fractionation to be tested both for anti-HBc and for abnormal ALT levels. It was agreed that a further trial should be undertaken at Edgware, Bristol and, possibly, Manchester and that an approach be made to Dr Smithies and Dr Moore<sup>198</sup> for assistance with this. It was recognised however that even if the incidence had reduced significantly since the last trial, because of self

---

<sup>193</sup> AABB guidelines [PEN.016.0312]

<sup>194</sup> Letter dated 28 August from Dr Cash to Dr Fraser [SGH.001.6269]

<sup>195</sup> Day 64, page 169

<sup>196</sup> Letter dated 4 September 1986 from Dr Fraser to Dr Cash [SNB.002.4227]

<sup>197</sup> Minutes of Regional Transfusion Directors' Meeting, 8 October 1986 [SNB.011.3106]

<sup>198</sup> Both of the DHSS

exclusion or for other reasons, the introduction of anti-HBc/ALT screening seemed very likely.<sup>199</sup>

**27.136** It is interesting to contrast the position of the English and Welsh Transfusion Directors in April 1986, when there appeared to be little interest in undertaking a study into NANB Hepatitis,<sup>200</sup> with their position in October of the same year when, following the introduction of surrogate testing in the USA, they considered that the introduction of surrogate testing in the UK now seemed ‘very likely’. Dr Fraser was, in his own terms, ‘rowing hard’, having aligned himself with Professor Cash’s position.

**27.137** The SNBTS Directors met on 9 October 1986.<sup>201</sup> Dr Gunson was present and, in a discussion on surrogate testing, advised that three English centres (Edgware, Bristol and Manchester) were to study the incidence of raised ALT levels and anti-HBc in their donor populations. It was agreed by the Scottish Directors that the UK Working Party on Transfusion Associated Hepatitis<sup>202</sup> was the most appropriate body to pursue the issue of implementing surrogate testing in RTCs and that Professor Cash would write to Dr Gunson on behalf of the SNBTS Directors, formally requesting that this Working Party be reconvened with a view to making proposals to the Department of Health.<sup>203</sup>

**27.138** On 16 October 1986 Dr Scott, DCMO, sent a minute to Dr Forrester and Mr Alexander Murray, a Senior Executive Officer in the SHHD, on the question of NANB Hepatitis screening. Dr Scott’s minute stated:

I should like to know where this stands. CMO DHSS is worried that if we go ahead England and Wales will have to follow suit.

I think there must be consultation with DHSS before we agree to provide funds for this screening.<sup>204</sup>

**27.139** Dr Forrester replied on 17 October:

The recent situation is described in paragraph 5 of my note of the SNBTS Directors’ meeting of 9 October, which runs:

“Dr Cash is pressing the English BTS to seek a start of this, apparently on the grounds that UK are lagging behind “other parts of the world”. The initial – and very prudent – response is likely to be a call for research. Some has already been done last year in Scotland,<sup>205</sup> but turned out discouraging to Dr Cash’s purposes; certainly he never mentions it. Dr Gunson of English BTS believes that “external pressures” will compel a start of Surrogate testing. One may guess that this testing would cost the UK about £8m.”

....

---

<sup>199</sup> Minutes of Regional Transfusion Directors’ Meeting, 8 October 1986 [SNB.011.3106] at 3112–13 (Item 14)

<sup>200</sup> Minutes of Regional Transfusion Directors’ Meeting, 24 and 25 April 1986 [DHF.002.1290] at 1296 (item 16). See paragraph 27.124

<sup>201</sup> Minutes of SNBTS Directors’ Meeting, 9 October 1986 [SGF.001.0268]

<sup>202</sup> Which, as discussed above, paragraph 27.104, had last met on 27 September 1983

<sup>203</sup> Minutes of SNBTS Directors’ Meeting, 9 October 1986 [SGF.001.0268] at 0272

<sup>204</sup> Letter dated 16 October 1986 from Dr Scott to Dr Forrester and Mr Murray [SGH.002.8146]. In his evidence to the Inquiry, Dr Iain Macdonald, Chief Medical Officer, stated that, for his part, he would have had in mind ‘agreement’ with the DHSS rather than ‘consultation’: Dr Macdonald – Day 66, pages 105–106. The relationship between the DHSS and the SHHD is discussed more fully below.

<sup>205</sup> A reference to the Dow/Follett research project in the West of Scotland



There seems no justification for introducing this screening without gathering further British evidence, because the American experience of frequent post-transfusion hepatitis does not seem to be duplicated here.<sup>206</sup>

**27.140** Also on 17 October 1986 Dr Forrester wrote to Dr Alison Smithies, DHSS,<sup>207</sup> enclosing a copy of his note of 12 June 1986,<sup>208</sup> a letter dated 4 June 1986 from Dr Reid of the Communicable Diseases Centre,<sup>209</sup> the special report on surrogate testing compiled by Dr Dow for the SNBTS Directors in May 1986<sup>210</sup> and the 1983 discussion in *Vox Sanguinis*.<sup>211</sup> Dr Forrester ended his letter:

I have no reason to think that Scotland is imminently about to adopt Surrogate testing. I hope that the message south and north of the Tweed will be “research first, action later.”<sup>212</sup>

**27.141** On 21 October 1986 Mr Murray responded to Dr Scott’s minute of 16 October.<sup>213</sup> In his response Mr Murray stated that ‘the bid we are making to our Finance colleagues for money for the SNBTS in 1987/88 makes no provision for [NANB] Hepatitis screening’.<sup>214</sup>

**27.142** In his written evidence to the Inquiry, Mr Murray stated that ‘[i]t was technically my call not to include funding for screening in the overall bid as I was the person responsible for drafting and submitting the bid to Finance Division, but I made my call based on advice from my medical colleagues’.<sup>215</sup> It is apparent that the decision was, in substance, treated as a matter for the medical officers of the SHHD. The timing of the decision reflected in Mr Murray’s minute is significant. In particular, it was before the sequence of events described in the following paragraphs.

**27.143** As a result of the suggestion by the SNBTS Directors at their meeting in October 1986 that the issue of surrogate testing should be pursued by the UK transfusion services’ Working Party on Transfusion Associated Hepatitis, that Working Party was re-convened with a view, amongst other matters, to making proposals to the DoH (see paragraph 27.137 above).<sup>216</sup>

**27.144** In advance of the meeting of the re-convened Working Party, Dr Gunson circulated a report dated October 1986 on ALT and anti-HBc screening of blood donations.<sup>217</sup> In his report, Dr Gunson stated that the best estimate of the incidence of transfusion-associated NANB Hepatitis in the UK was 3%. If it was assumed that the 2.3 million donations in the UK were transfused to 750,000 recipients annually then one would expect 22,000 icteric or anicteric cases of NANB Hepatitis (cases, that is, with or without clinical jaundice) in each year. If the morbidity pattern of the disease was similar to that in the USA then one

<sup>206</sup> Letter dated 17 October 1986 from Dr Forrester to Dr Scott [SGH.002.8141]

<sup>207</sup> Letter to Dr Smithies dated 17 October 1986 [SGH.002.8145]

<sup>208</sup> Dr Forrester’s note of 12 June 1986 on ALT testing [SGH.002.8142]

<sup>209</sup> As noted above, the Inquiry has, unfortunately, been unable to recover this letter

<sup>210</sup> Dr Dow’s special report [SNF.001.1109]

<sup>211</sup> ‘International Forum’, *Vox Sanguinis*, 1983; 48 [LIT.001.1837]

<sup>212</sup> Letter to Dr Smithies dated 17 October 1986 [SGH.002.8145]

<sup>213</sup> Minute dated 21 October 1986 from Mr Murray to Dr Scott [SGH.002.8140]

<sup>214</sup> A reference to the SNBTS 1986 PES, discussed above, in which the sum of £810,000 had been sought with a view to surrogate testing being introduced in 1987/88

<sup>215</sup> Mr Murray’s written statement, [PEN.017.1755] at 1758. Mr Macniven accepted, however, that, as Mr Murray’s superior, he would require to have approved the bid to the Finance Division: Mr Macniven – Day 65, pages 157–158

<sup>216</sup> The Working Party had last met on 27 September 1983

<sup>217</sup> Report by Dr Gunson dated October 1986 [PEN.017.0806]

might expect half of these patients to have chronic ALT elevation and 10% (that is, 2250) to develop cirrhosis. As regards the projected value of ALT and anti-HBc screening in preventing transfusion-related NANB Hepatitis, the report stated that if 30–40% of NANB Hepatitis could be prevented by the use of these tests then the reduction in the number of cases would be 6750–9000 a year and, by extrapolation, 675–900 cases of cirrhosis. The argument followed the approach of Dr Alter's group in February 1986 when it changed direction and supported surrogate screening.<sup>218</sup>

**27.145** The report went on to say, however, that qualifications required to be made to these estimates. In summary, these were:

(i) The course of the chronic disease in NANB hepatitis was thought to be mild and it was therefore thought that many cases probably remained undiagnosed, even when cirrhotic changes occurred. Dr Gunson felt certain that was why they had not been aware of what appeared to be quite serious statistics. It was also necessary to bear in mind that approximately 50% of patients died of their primary disease within one year of transfusion.

(ii) The incidence of NANB Hepatitis had been determined in the USA, often with multiply-transfused patients and in the TTV study there was clearly a dose relationship. Even in the second of the two UK studies the patients (6) received an average of 6.28 units each.

(iii) The data from the USA was from transfusions administered in the 1970s and early 1980s and even the more recent studies in the UK were undertaken before attempts to encourage the self-selection of donors.

(iv) It had to be questioned, therefore, whether the incidence of transfusion-associated NANB Hepatitis was as high as the estimates suggested.<sup>219</sup>

**27.146** As regards the likely effect of surrogate screening on blood collection, Dr Gunson's report estimated that ALT screening might cause the loss of 0.7–0.9% of donations, anti-HBc might cause the loss of 1% of donations and, assuming some overlap between these two groups, one might expect a loss of donations of approximately 1.5–1.75%. Since the data were largely from the time period before self-exclusion of donors for HIV infection, it was considered 'important to determine in a new study, preferably carried out in three Centres in England ... how many donations are rejected. Preferably, also one Centre in Scotland should join the study .... [A]nalysis of the results should yield information from which a prediction of loss of donations throughout at least England and Wales, can be estimated'.<sup>220</sup> Other topics for discussion mentioned in the report were the costs of implementing ALT and anti-HBc screening, the effect of screened donations in lessening the occurrence of NANB Hepatitis from fractionated products derived from pooled plasma and how donors would be managed if routine screening was introduced.

**27.147** Dr Gunson's report was considered on 24 November 1986 at the meeting of the re-convened UK Working Party on Transfusion Associated Hepatitis. The Inquiry has not been able to recover the minutes of the meeting. The Inquiry does, however, have a copy of Dr McClelland's handwritten notes of the meeting<sup>221</sup> and a note of the meeting prepared

<sup>218</sup> See paragraphs 27.49–27.50

<sup>219</sup> Report by Dr Gunson dated October 1986 [PEN.017.0806] at 0809

<sup>220</sup> Ibid [PEN.017.0806] at 0810

<sup>221</sup> Or, at least, part of the meeting as Dr McClelland was late in attending the meeting as a result of transport delays: Dr McClelland's note [PEN.017.1540]

by Dr Forrester on 1 December 1986.<sup>222</sup> Dr Forrester's note, expressing his personal view and intended for his SHHD colleagues, states:

1. Is the American experience of frequent [NANB] hepatitis in recipients of blood and blood products reproduced here? If so, a 40% reduction in it would follow screening. The answer is No. Such evidence as exists does not bear out the American experience, but to examine the question properly would be a long and expensive business ....

2. ... Dr McClelland put the proportion of local donations showing an ALT test in excess of 45 i.u. (a credible place for the line) at ... 3.4%. The proportion excluded by [anti-HBc] screening is put at 1 to 1.8% .... It is clear that much "innocent" blood would be excluded.

....

4. Is research indicated? The meeting felt that a prospective study to discover the present burden of transfusion-associated [NANB] hepatitis was impracticable on grounds of cost and huge sample size. They propose instead a study to identify in three centres (1 Scottish) donors positive for ALT or core antibodies, and search for other risk factors in them ....

5. There was some discussion of the cost of screening all donations (perhaps £8m). I asked the Chairman [Dr Gunson] whether he would advise screening if it were free of cost. He said No.<sup>223</sup>

The position explicitly reached at the meeting is to recommend research of no great significance or scientific interest because the prospect of research would serve to counter pressure from for example haemophiliacs and Haemophilia Directors to embark on an indirect and largely ineffective form of screening, which would also lose us a certain amount of perfectly harmless blood. Figures were produced at the meeting for the total number of [NANB] hepatitis cases encountered annually among haemophiliacs (A and B) and patients with von Willebrand's disease. The average UK total per year is 35 over the past 6 years, but 1985 saw a sharp decline to 11 in all. A proportion of these cases among haemophiliacs and similar patients are asymptomatic.<sup>224</sup>

**27.148** It is difficult to reconcile Dr Forrester's note of the total number of NANB Hepatitis cases encountered annually among patients with haemophilia, with UK reports from the early 1980s showing that most haemophilia patients who received Factor VIII and Factor IX blood products for the first time, whether manufactured by the NHS or by commercial companies, were likely to develop NANB Hepatitis.<sup>225</sup> In his evidence to the Inquiry Dr McClelland thought that what was reported by Dr Forrester in this regard must have

---

<sup>222</sup> Dr Forrester's note [PEN.017.1554]

<sup>223</sup> In closing submissions to the Inquiry it was suggested that this must be an inaccurate reporting of Dr Gunson's position [PEN.019.0605] at 0620. That does not, however, appear to be the case. As noted below, Professor Cash's view at the time was that given the difficulties with surrogate testing and the uncertainties about the benefits it would bring, his position in late 1986 would also have been that he would not have recommended the introduction of surrogate screening even if it were free of cost.

<sup>224</sup> Dr Forrester's note [PEN.017.1554]

<sup>225</sup> Fletcher et al, '[NANB] hepatitis after transfusion of factor VIII in infrequently treated patients', *British Medical Journal*, 1983; 287:1754 [LIT.001.0239]; Kernoff et al, 'High risk of [NANB] hepatitis after a first exposure to volunteer or commercial clotting factor concentrates: effects of prophylactic immune serum globulin', *British Journal of Haematology*, 1985; 60:469 [LIT.001.0800]. This is discussed further in Chapter 15, *Knowledge of Hepatitis 1975 to 1985*, paragraph 15.95

been a misunderstanding of what was said at the meeting.<sup>226</sup> Whether or not that is the case, Dr Forrester's note contains the information circulated to SHHD colleagues, including the inaccurate assessment of the prevalence of NANB Hepatitis infection among haemophilia patients before effective viral inactivation was introduced. Dr McClelland also cast doubt on the accuracy of Dr Forrester's description of the meeting, indicating that the suggestion that they would 'do some research to shut people up', would be untypical and uncharacteristic of the sort of discussion that took place at such meetings. Dr Alison Smithies, a member of the Secretariat to the Working Party, also expressed surprise at the suggestion that the position explicitly reached at the meeting was to recommend research which was of 'no great significance or scientific interest' in order to 'counter pressure' for the introduction of surrogate screening. She, too, considered that such a position would have been uncharacteristic of the discussions of the Working Party and refuted the suggestion that the study was put forward for any reason other than to clarify the likely consequences of introducing surrogate screening and to provide information which would allow the number of lost donations to be estimated.

**27.149** As indicated above (paragraph 27.141), a decision had already been taken before this meeting that provision would not be made in the PES bid for funding the SNBTS for screening in 1987/88. It appears that opposition to screening within the SHHD, at least on the part of Dr Forrester, became more deeply entrenched at the meeting.

**1987**

### Product liability

**27.150** In 1985, a European Directive was adopted which provided for strict liability for harm caused by defective products.<sup>227</sup> Member states were required to implement the Directive in their national legal systems by July 1988. In the UK, the Department of Trade and Industry (DTI) was the lead department responsible for implementing the Directive. The Consumer Protection Bill was drafted to give effect to the Directive and, in due course, the Bill became the Consumer Protection Act 1987. The part of the Act providing for strict civil liability for harm caused by defective products came into force on 1 March 1988.<sup>228</sup>

**27.151** During 1986 Professor Cash had expressed concerns about the implications of the proposed legislation<sup>229</sup> and had made representations for blood and blood products to be removed from the ambit of the legislation with a view to preventing the transfusion services and, possibly, blood donors being held strictly liable for harm caused to patients by treatment with blood and blood products.

**27.152** Dr Graham Calder, Chief Pharmaceutical Officer, SHHD, raised Professor Cash's concerns with the DTI who, by letter dated 9 February 1987, advised that they were not persuaded that there was any justification for removing blood and blood products from the provisions of the legislation.<sup>230</sup>

<sup>226</sup> Day 63, page 120

<sup>227</sup> Council Directive 85/374/EEC of 25 July 1985 on the approximation of the laws, regulations and administrative provisions of the Member States concerning liability for defective products

<sup>228</sup> Section 2 of the Act provides that, subject to certain defences, the producer of a product was liable, without evidence of fault, for damage caused wholly or partly by a defect in the product. Part I of the Act came into force on 1 March 1988 by virtue of The Consumer Protection Act 1987 (Commencement No.1) Order 1987, No. 1680: [PEN.017.2557]

<sup>229</sup> See, for example, the note dated 30 June 1986 by Dr Forrester of the meeting of the SNBTS Directors on 25 June 1986 at which Professor Cash had continued to express 'grave anxiety' in respect of product liability. [SGH.001.6295] at 6296

<sup>230</sup> Letter [SGH.005.0155]

**27.153** By a minute dated 13 February 1987, Mr Calder advised Dr Scott, DCMO, and the SHHD administrative officials of the DTI's response.<sup>231</sup> By letter dated 13 March 1987, Mr Hugh Morison, Under Secretary, SHHD, wrote to Mr Jim Donald, General Manager, CSA, advising him of the decision by the DTI that blood and blood products would remain within the provisions of the Act.<sup>232</sup> Mr Morison sent a copy of that letter to Professor Cash.<sup>233</sup>

**27.154** The risk of product liability became a new and material factor influencing policy.

### Surrogate screening

**27.155** The reconvened UK BTS Working Party on Transfusion Associated Hepatitis met for the second time on 22 January 1987. Dr Forrester was present and wrote a note of the meeting.<sup>234</sup> Those present were still not happy about proceeding with ALT screening and anti-HBc tests without further research to ascertain the infectivity of the donations and the meaning of the presence of anti HBc. There was discussion on the proposal for research into ALT and anti-HBc screening. It was hoped that the research might start on 1 April, subject to funding.

**27.156** On 26 January 1987, Dr Forrester produced a note, 'Material for PMO Report'. He made the following comments on blood transfusion and NANB Hepatitis:

This "hepatitis" is a residual rag-bag when Hepatitis B and Hepatitis A are excluded, and consequently no specific test can detect it. It is relatively benign. But U.S. blood banks have noted that the combination of a liver function test and a test for the core (not the surface) antigen of Hepatitis B distinguishes perhaps a third of blood donations which would convey [NANB Hepatitis] and allows them to be excluded. Exclusion is far from complete, and besides, some 2% of "innocent" donations may also be excluded.

....

Here, it is intended instead to enquire into the number of relevant donations and the characteristics of the donors, before taking any further step.<sup>235</sup>

**27.157** Dr Forrester's unqualified statement that NANB Hepatitis was 'relatively benign' would have been difficult to sustain in the light of research published by the end of January 1987. (See Chapter 16, *Knowledge of Hepatitis 3 – 1986 Onwards*, paragraphs 16.5 and 16.6.)

**27.158** The SNBTS and Haemophilia Centre Directors met on 9 February 1987.<sup>236</sup> Dr Forrester reported on the recent meeting of the Working Party on Transfusion Associated Hepatitis and the proposal to set up a UK study based on four centres, one of which would be in Scotland. The purpose of the study would be to discover the number of donations affected, what a positive test result meant about the donor, the effect of giving

<sup>231</sup> Minute [SGH.005.0149]

<sup>232</sup> Letter [SGH.005.0140]

<sup>233</sup> At a meeting on 31 March 1987 between Mr Macniven, Dr McIntyre, Dr Forrester, Mr Donald and Professor Cash, at which various blood transfusion issues were discussed, Professor Cash once again made representations, unsuccessfully, that product liability should not extend to blood products – Note of meeting [SNB.009.0041] at 0043 (item 11). Detailed guidance was not issued on how the Act impacted on blood transfusion practice. See letter dated 5 April 1988 [SGH.005.0054] and reply dated 25 April 1988 [SGH.005.0049]

<sup>234</sup> Note of meeting [SGF.001.2102]

<sup>235</sup> Dr Forrester's note [SGH.003.1657]

<sup>236</sup> Minutes of SNBTS and Haemophilia Directors' meeting, 9 February 1987 [SGF.001.2261]

blood positive on this screening and the cost of screening. Professor Cash noted that commercial products, if derived from screened plasma, might enjoy an advantage over products derived from unscreened plasma. The Haemophilia Directors indicated that they would not elect for commercial products on that basis. Their preference was to be supplied with heat-treated products. The cost of screening in Scotland was estimated to be approximately £750,000 per annum.<sup>237</sup>

**27.159** On 10 February 1987, having received a letter from Dr Susan Lader (Medical Officer, DHSS) on the proposal for a multi-centre study of ALT and anti-HBc in blood donations,<sup>238</sup> Dr Forrester wrote a memorandum to Dr Boyd Moir, Director of the SHHD's Chief Scientist Office on Scottish participation in the research project.<sup>239</sup> The SNBTS had sought approximately £600,000 to institute screening and conduct it for a year. That request was declined. Dr Forrester noted that joint consideration by the SNBTS, SHHD, DHSS and the English transfusion service indicated that 'instead of blindly adopting American practice, research should be conducted' and that 'a project involving 3 English and 1 Scottish transfusion centres' was being planned. Funding for the Scottish component of the research was sought from the CSO, to be determined in cooperation with the Research Management Division, DHSS. Dr Moir replied in a memorandum dated 17 February 1987.<sup>240</sup> He had very strong reservations about funding a research project including a Scottish transfusion centre, stating that the proposal would appear to 'merely repeat a study we have already carried out' over a three year period by Drs Follett and Dow, reported two years earlier and funded by the CSO. If the SNBTS wished to formulate a research proposal for funding from the CSO it should be submitted as an application for formal review by the Biomedical Research Committee.

### **SNBTS Directors meeting on 3 March 1987**

**27.160** The SNBTS Directors met on 3 March 1987.<sup>241</sup> The minutes of the meeting record the discussion of surrogate testing. It was reported that the UK Working Party on Transfusion Associated Hepatitis had been reconvened to pursue the issue of implementing surrogate testing for NANB Hepatitis. The proposal for a study which would include the Glasgow or Edinburgh Transfusion Centres had been modified and no Scottish Centre was now being asked to participate. It was noted that the Haemophilia Society might adopt a position which put pressure on BPL to ensure surrogate testing was introduced. The Directors discussed the options open to Scotland and agreed to recommend to the SHHD that surrogate testing for NANB Hepatitis should be implemented with effect from 1 April 1988 as a national development requiring strictly new funding. The individual Directors were to let Professor Cash know what funds would be required in each region, assuming that both anti-HBc and ALT testing would be undertaken in the regional transfusion centres.

**27.161** In oral evidence Professor Cash explained that by early 1987 surrogate testing had commenced in the USA and he was aware that his colleagues in Europe were considering the issue. He said:

I began to get the jitters that once again in the UK we had gone to sleep, we were off the ball, and I felt that I had a duty as national director to advise my colleagues that we should get in an application for money in the event –

---

<sup>237</sup> Ibid [SGF.001.2261] at 2263–2264

<sup>238</sup> The Inquiry does not have this letter

<sup>239</sup> Minute from Dr Forrester to Dr Moir, dated 10 February 1987 [SGF.001.2100]

<sup>240</sup> Minute [SGH.002.8123]

<sup>241</sup> Minutes of SNBTS Directors' meeting [SGH.001.6653] at 6657–6658

knowing that in the event of the Department of Health saying, “Yes, okay, go,” at least the budget was there to get down to the detailed difficulties of doing it.<sup>242</sup>

**27.162** He was asked what the reasons were for the Directors’ recommendation that surrogate testing should be introduced and replied that ‘[t]he reasons were that the rest of the world seemed to be walking in that direction ... and associated ... the product liability and the whole question of patient safety’.<sup>243</sup> Professor Cash was asked how it was envisaged that the recommendation would be taken forward and replied that the attendance of an SHHD official (in this case, Dr Forrester) at the Directors meeting was one means. He went on:

The other method, which was in parallel, was going through our PES submissions ... that would go into the department and we thought that would generate discussion and debate and so on and so forth, and we would get the thing going.

What we were concerned about is that we didn’t seem to be able to get it going in the ... post-transfusion hepatitis working parties<sup>244</sup> ... Harold [Gunson] was alerting to us in interactions with the DHSS. What we were doing was saying, “We have a responsibility here. Let’s lead off and get the debate going,” and the way we can get this going that we felt most comfortable with was a suggestion that we need some money to do that and that would, we felt, trigger off debate.<sup>245</sup>

**27.163** It was put to Professor Cash that if the SNBTS was serious about the recommendation to introduce surrogate testing then the SNBTS should have formally made the case by some form of detailed, reasoned, submission to the SHHD. Professor Cash said that the case he and his colleagues were trying to make was weak because of the lack of data on patients.<sup>246</sup> Consequently, they required to rely on the fact that other countries appeared to be moving towards such testing and that the UK licensing authority now recognised that ALT testing improved product safety. He was, simply, trying to draw their attention towards testing that he perceived as existing elsewhere.

**27.164** In his oral evidence Dr McClelland stated that he had no recollection of the meeting of the Directors on 3 March 1987 but was surprised on recently reading the minutes to see the clarity of the recommendation that surrogate screening should be implemented. He considered that it must have been primarily motivated by the awareness of what was going on in the USA. His recollection was that there wasn’t much enthusiasm among the other Scottish Directors for the introduction of surrogate testing.<sup>247</sup> In a memorandum dated 18 May 1987, Dr Forrester recorded his astonishment that Dr McClelland had agreed to the proposal, although he had heard Dr McClelland say on other occasions that he viewed the institution of screening as inevitable.<sup>248</sup>

---

<sup>242</sup> Day 70, page 175

<sup>243</sup> Ibid

<sup>244</sup> Professor Cash also stated: ‘we reached a point where it was evident to me, and I think Brian McClelland, that that working party yet again – it was nobody’s fault, was not going to go anywhere.’ Day 70, page 179

<sup>245</sup> Day 70, page 176

<sup>246</sup> Ibid pages 177–178

<sup>247</sup> Day 63, pages 122–124.

<sup>248</sup> Dr Forrester’s memorandum [SGH.002.8117]

**27.165** In his oral evidence, Dr Mitchell stated that if American blood banks and fractionators introduced surrogate testing then the UK might have been 'forced' to do the same thing. Impending product liability legislation was also a factor. He was very doubtful, however, whether surrogate testing would have materially increased patient safety, in particular against the background of very few reports in his region of patients developing post-transfusion hepatitis.<sup>249</sup>

**27.166** In his written evidence to the Inquiry Dr Macdonald, CMO, referred to:

[T]he increasing pressure perceived by SNBTS from about mid-1986 to introduce surrogate testing. A major source of this pressure was that moves were afoot elsewhere in the world, including particularly among commercial producers in USA, to introduce surrogate testing. The existence of these commercial producers cast a long shadow over fractionation activities within the NHS.<sup>250</sup>

**27.167** During his oral evidence Dr Macdonald was asked what he meant by the reference to commercial producers casting 'a long shadow' over fractionation activities within the NHS and explained:

I think this was a very peculiar situation, in which the NHS was itself a producer and in that sense it was in competition with commercial producers, in a way that I don't think was replicated anywhere else in the service. I think what struck me at the time, when I wrote that ... [was] that commercial producers, particularly in the United States, were beginning to introduce surrogate testing. In the way in which commercial operators work, they would be presenting this in the publicity in their advertising as an advantage. My stuff is better than your stuff. I wouldn't be sure that that was altogether fair but we, really, I don't think I felt that we could quite adopt these standards.

So there was a lack of balance.<sup>251</sup>

**27.168** Professor Cash stated that the SNBTS was concerned that the UK Medicines Licensing Authority was being persuaded that the introduction of surrogate testing of the plasma feed-stock of commercial fractionators would further enhance the safety of their products and that this unproven claim could be included in package inserts and marketing materials. He noted that the SNBTS view was that it had a moral obligation to patients in Scotland, Scottish based Haemophilia Directors and tax payers who had invested in the PFC, to seek funding to enable the SNBTS to follow this lead. Consequently, the PES proposal that they put to the SHHD was not 'directed to routine blood transfusions but to large pooled high risk PFC products'.

**27.169** Dr Macdonald agreed with the suggestion that the Directors' recommendation to introduce surrogate testing came as something of a surprise and, in particular, that it was such a firm recommendation, although there was an awareness that it was coming. He would have expected the interests of donors to have been given more attention.<sup>252</sup>

---

<sup>249</sup> Day 65, pages 18–24, 32 and 59–63

<sup>250</sup> Dr Macdonald's supplementary statement on surrogate testing [PEN.017.2048] at 2051

<sup>251</sup> Day 66, pages 90–91

<sup>252</sup> Ibid pages 128 and 143



**27.170** Dr Macdonald was also asked about the working relationship between the SNBTS and the SHHD at the time and replied that it was 'a little difficult'.<sup>253</sup> He stated:

What I learned, I suppose mostly from casual conversations with colleagues like Dr Scott and Dr McIntyre – I think they had some difficulty in understanding, at times, just where the regional directors stood and would be a little uncertain if the position that they seemed to be taking was the position they were going to hold. I'm not referring specifically to this surrogate testing issue, but I think there was an uneasy relationship.<sup>254</sup>

**27.171** As noted below, there were different views in the SNBTS on whether surrogate testing should be introduced. In his evidence to the Inquiry Dr McClelland said that that did not worry him very much because 'I felt it was a matter that was highly controversial and there was nothing particularly wrong with having a lively debate in the organisation. Not everybody felt that way about it'.<sup>255</sup> In a subsequent letter to Professor Cash, responding to a draft paper by Dr Gillon in which Dr Gillon had expressed the view that surrogate testing should not be introduced without further research, Dr McClelland acknowledged that there was undoubtedly a problem in facing in both directions. The obvious difficulty was that, on commercial competitive grounds,<sup>256</sup> the SNBTS needed to introduce screening, but on scientific and value for money for the health service grounds they should be opposing it. He did not know if there was any way out of this dilemma.<sup>257</sup>

**27.172** In due course Dr Gunson was sent a copy of the minutes of the meeting of the SNBTS Directors of 3 March 1987. By letter dated 21 April he advised Professor Cash that he was 'dismayed' that the SNBTS Directors were putting forward proposals for the funding of surrogate tests for NANB Hepatitis in Scotland from 1 April 1988.<sup>258</sup> Dr Gunson enclosed a copy of the proposals for research submitted by the UK Working Party on Transfusion Associated Hepatitis. Edinburgh was included as a participating RTC (contrary to what was stated in the minutes of the meeting of 3 March that there were no participating Scottish RTCs). The cost of participation by the Edinburgh Centre was not to be met from non-recurring funds; a bid would probably be made to the Chief Scientist for a research grant. He stated:

This decision seems to go against the proposal ... to which I thought that the SNBTS was a party.<sup>259</sup> Of course, I accept that it might be prudent to have funds ear-marked should the recommendation of the study be that such testing should be introduced, but the tenor of this minute does not suggest that consideration of the results of the multi-centre [study] would be a factor before introducing surrogate testing. Also, I recall your telling me that Scotland would not take unilateral action in this matter without consultation with RTDs in England and Wales.<sup>260</sup>

---

<sup>253</sup> Ibid pages 143–144

<sup>254</sup> Ibid page 144

<sup>255</sup> Day 63, page 127

<sup>256</sup> Presumably a reference to the competitive advantage of American screened products as against blood products from the PFC and Scottish blood. That, and the BPL's interest in exporting excess blood products, emerged explicitly about a year later as factors supporting ALT testing. See paragraph 27.231

<sup>257</sup> Memorandum from Dr McClelland to Professor Cash, dated 15 April 1987 [SNB.006.0715]

<sup>258</sup> Letter [SGH.001.6628]

<sup>259</sup> The proposal to undertake a multi-centre study into surrogate markers in donors, as agreed at the meeting of the re-convened Working Party on Transfusion-Associated Hepatitis on 24 November 1986.

<sup>260</sup> Letter from Dr Gunson to Professor Cash, dated 21 April 1987 [SGH.001.6628] at 6628–6629

**27.173** Professor Cash replied on 27 April. He stated:

I don't think you should take the content of minute 3(f), with regard to the introduction of surrogate testing for NANB, too seriously at this stage. I think it would be appropriate to say that it was a decision made with our PESC submission in mind and, I suspect, a view that we have often expressed – that the results of the UK study are unlikely to have a material affect on future operational practice.<sup>261</sup>

**27.174** In oral evidence Professor Cash explained that in that letter:

I think I was conveying something that Harold [Gunson] actually knew from our conversations, that whatever submission we made, and however we thought we may go off on our own, we couldn't and wouldn't, simply because we would need significant funding and this would have to be approved by the [SHHD].

So any panic that he had in seeing these things, he could relax because this would all be part of the UK exercise, hence reference to the PESC submission.

I think I was also explaining to him, which he knew very well, that we didn't really think the currently floated new study of the transfusion hepatitis working party would materially affect any of the ultimate outcomes in terms of practice, if we in fact implemented it all.<sup>262</sup>

**27.175** Professor Cash was asked at the Inquiry how serious the Directors' recommendation to introduce surrogate testing was and he replied:

[I]t was serious in the sense we were trying to alert the people, the minister, ultimately, that things were happening outside the UK that we believed – we were not certain – could have an influence upon us; and that concept was very serious indeed.<sup>263</sup>

**27.176** He continued:

What I'm meaning for him [Dr Gunson]: do not take it seriously in [the] sense you are going to wake up tomorrow morning and the Scots are testing and you are caught. That is what I was signalling to Harold.<sup>264</sup>

**27.177** Professor Cash was asked whether the position of the SNBTS was that it was alerting the SHHD to something which might be on the horizon and which might be unstoppable and that there might be a need to make provision for funding it. He replied: 'Absolutely. We were later to discover that Brian McClelland's opinion was doing a big study – we were too late. The whole world was moving on and we accepted that, perhaps too easily, but we accepted that.'<sup>265</sup> Professor Cash stated that the position of the Directors, ultimately, was that they did not wish to introduce surrogate testing because they did not have clear evidence of its value (because a large scale prospective study had not been carried out in the UK) but they thought they might have to introduce such testing because

---

<sup>261</sup> Letter from Professor Cash to Dr Gunson, dated 27 April 1987 [SGH.001.6627]

<sup>262</sup> Day 70, page 185

<sup>263</sup> Ibid page 188

<sup>264</sup> Ibid page 189

<sup>265</sup> Ibid

other countries either had done so or were moving in that direction. He said, 'we felt we were drifting, and the effort we made was one last effort to stop the drift and get people to sit down and seriously talk about it'.<sup>266</sup> He went on: 'I think what we want and what we are being forced into by dint of other people's practice doesn't, sometimes, match.'<sup>267</sup>

**27.178** On 14 May 1987 Dr Forrester sent a memorandum to Dr McIntyre, Dr Scott and Mr Macniven.<sup>268</sup> He reported that the outcome of Dr Gillon's discussions with Dr Forbes was that the Scottish component of the UK NANB Hepatitis research project was being abandoned. He said that Dr Gillon's Director, Dr McClelland, was unlikely to press it as his current view was that the SHHD had better simply institute screening.

**27.179** On 19 June 1987 Dr Archibald McIntyre, SHHD, wrote to Professor Cash about Scottish participation in the proposed UK research project on transfusion-associated NANB Hepatitis.<sup>269</sup> Dr McIntyre noted that there appeared to have been some confusion on the subject. He observed that on 22 April application forms for funding had been sent to the Edinburgh and South East Scotland RTC. For reasons Dr McIntyre had not fully understood, it was decided by the RTC not to proceed with the application. Following a telephone conversation on 15 June between Dr McIntyre and Professor Cash, Dr McIntyre understood that the SNBTS did now wish to proceed with the research project and would submit an application to the CSO for funding. The application would be considered at the meeting of the Biomedical Research Committee on 25 September. The outcome of the research would have considerable implications as it was unlikely that funds would be made available for the routine screening of blood donations for NANB Hepatitis unless it could be clearly shown that such screening was practicable and worthwhile.

**27.180** In due course, the SNBTS PES bid submitted in 1987 made provision for the introduction of surrogate testing, for expenditure in 1988–89 and 1989–90, on the basis that it was likely that a new mass screening programme would commence in the foreseeable future.<sup>270</sup> It was suggested that surrogate screening might be made a special project with separate funding. The accompanying narrative stated:

The SNBTS Directors have now decided that in the light of the advent of new Product Liability laws in 1988 and an emerging unchecked private sector blood collection services<sup>271</sup> it would be prudent to plan to commence this programme in the financial year 1988/89. The costing are estimates only and it is proposed that we plan to ensure the financial burden covers two financial years but begin in July 1988 (the date new Product Liability legislation will be introduced).<sup>272</sup>

**27.181** The initial provisions were for £300,000 for 1988–89 and £105,000 for the following year. At that stage there was no provision for 1990–91.

**27.182** At their meeting on 10 June 1987 the SNBTS Directors noted Dr Gunson's letter of 27 April to Professor Cash and Professor Cash's reply.<sup>273</sup> It was noted that Dr McClelland

---

<sup>266</sup> Ibid page 190

<sup>267</sup> Ibid page 191

<sup>268</sup> Mr Macniven was an Under Secretary in the SHHD between May 1986 and July 1989 with responsibility, among other things, for the SNBTS Minute [SGH.002.8119]

<sup>269</sup> Letter from Dr McIntyre to Professor Cash, dated 19 June 1987 [SGH.002.8107]

<sup>270</sup> SNBTS PES 1987, prepared in June 1987, [SNB.011.3743] at 3750

<sup>271</sup> In his evidence to the Inquiry Professor Cash explained that around that time there was discussion of private hospitals in the UK setting up their own blood transfusion service and introducing ALT testing of the blood they collected: Day 72, pages 26–28

<sup>272</sup> SNBTS PES 1987, prepared in June 1987 [SNB.011.3743] at 3755

<sup>273</sup> Minutes [SGF.001.0127] at 0132

would probably apply to the next meeting of the Chief Scientist's Office<sup>274</sup> for a research grant in respect of the cost of participation by the Edinburgh centre in the proposed UK research into surrogate testing. The need for synchrony with England and Wales was noted.

### The Scottish Home and Health Department

**27.183** The evolving position of the Transfusion Directors from the early summer of 1986 to the spring of 1987 reflects a degree of inconsistency of approach among them on the question as to whether surrogate testing should be introduced. On the other hand, the SHHD had consistently resisted the introduction of surrogate testing: as already noted, Dr Forrester indicated at the SNBTS Directors' meeting on 25 March 1986 that it was unlikely that the UK Departments of Health would fund testing on the basis of data from the USA (paragraph 27.120 above); Dr Forrester's advice to colleagues on 12 June 1986 summarised his reasons against introduction of surrogate testing at that time (paragraph 27.129 above); and the SNBTS bid for funding in the PES programme for 1987-88 was rejected prior to 2 October 1986 (paragraph 27.141 above).

**27.184** While Dr Forrester was present at the meeting of the SNBTS Directors on 3 March 1987 at which the recommendation to introduce surrogate testing was made, the Inquiry has been unable to recover a copy of any note he sent his medical or administrative colleagues reporting on the meeting or the recommendation that surrogate testing should be introduced. In his evidence to the Inquiry, Dr Forrester had no recollection of the meeting or recommendation but did not think that he would have been the messenger for transmitting the recommendation to the SHHD and thought, instead, that it would have been transmitted formally, in writing, through a different channel, perhaps via the PES funding bid.<sup>275</sup>

**27.185** Regardless of the means by which the Directors' recommendation was supposed to reach the SHHD, it is clear that the SHHD was aware of the Directors' recommendation that surrogate testing should be introduced, as Dr McIntyre's minutes to Drs Scott, Forrester and Moir and Messrs Morison and Macniven dated 6 April 1987 show.

**27.186** Dr McIntyre's minute to Dr Moir dated 6 April 1987, explained that the bid by the SNBTS of £810,000 to introduce surrogate screening of all donations in 1987-88 was not advanced because:

[T]he research already conducted in the West of Scotland with CSO<sup>276</sup> funding indicated that the impact there of transfusion-associated '[NANB] Hepatitis' was not great; also that the indirect screening proposed would be expensive, could not in any event abolish the transmission of this 'Hepatitis' by blood and blood products, and would lead to a loss of a perceptible amount of 'innocent' blood which nevertheless failed to pass the screen. We also wished to await DHSS thinking on this subject.<sup>277</sup>

**27.187** He reported that the DHSS had now invited the UK Transfusion Associated Hepatitis Working Party to consider the issue.

---

<sup>274</sup> The minute refers to 'the Chief Scientist's Organisation' but it is assumed this is a typographical error.

<sup>275</sup> Day 66, pages 32-34 and 55

<sup>276</sup> Chief Scientist Office

<sup>277</sup> Minute [SGH.002.8127]

**27.188** On the question of Scottish participation in the proposed UK multi-centre study into surrogate markers in donors, the minute stated:

The Directors of SNBTS are unanimous, and are now pressing fairly strongly, that this screening should be instituted; though perfectly aware that it would be costly and could not abolish transmission [of NANB Hepatitis] completely, they could then claim to have taken all steps open to them to reduce transmission. Before embarking on such an expensive programme it would seem logical to participate in the proposed research<sup>278</sup> and to delay any further action until the results of this were known.

If recipients of this minute are agreeable that this is the correct line to adopt then the Edinburgh SNBTS will be asked to prepare a detailed proposal along similar lines to that of their English counterparts.<sup>279</sup>

**27.189** The minute contained a handwritten note by Mr Hugh Morison<sup>280</sup> as follows:

Mr Macniven,

Advise please. My initial reaction is -

- (a) it would not make sense to screen all blood for [NANB Hepatitis] as benefits appear out of all proportion to the risks,
- (b) we should therefore participate in the research,
- (c) CSO should be encouraged to fund it.<sup>281</sup>

**27.190** In a minute dated 7 April 1987 Dr Scott, DCMO, agreed with Dr McIntyre that further research should be carried out into surrogate testing, stating:

We must do whatever we can to prevent the BTS going ahead with a full scale introduction of this testing – or at least trying to blackmail us into the provision of funds.

The research proposal from Edinburgh will of course have to be subject to the scrutiny of the appropriate CSO group and the availability of finance. I would not like to see it fail on the grounds of finance because the stakes are high.<sup>282</sup>

**27.191** Mr Macniven responded on behalf of himself and Mr Morison. They agreed with the comments in Dr Scott's minute and expressed the view that:

It is important that the decision on whether or not to screen all blood for [NANB] Hepatitis, which will not be cheap and may not be certain, should be taken on the basis of the sort of UK research you suggest.<sup>283</sup>

**27.192** The strong support of the SHHD for the multi-centre study proposed by the Working Party on Transfusion Associated Hepatitis seems, on the face of it, surprising given Dr Forrester's note following the meeting of the Working Party on 24 November 1986 that the proposed research was 'of no great significance or scientific interest'.<sup>284</sup>

---

<sup>278</sup> The multi-centre study into surrogate markers in donors proposed by the Working Party on Transfusion Associated Hepatitis

<sup>279</sup> Minute [SGH.002.8127] at 8128

<sup>280</sup> Mr Macniven identified the handwritten note as having been written by Mr Morison: Day 65, page 175

<sup>281</sup> Minute [SGH.002.8127]

<sup>282</sup> Minute [SGH.002.8127] at 8128

<sup>283</sup> Minute by Mr Macniven dated 9 April 1987 [SGH.002.8125]

<sup>284</sup> Dr Forrester's note [PEN.017.1554] at 1555

Similarly, it is not entirely clear what Dr Scott meant in his minute of 7 April 1987, above, that he would not like the research proposal to fail on the grounds of finance 'because the stakes are high'.

**27.193** In his evidence to the Inquiry Dr Macdonald stated:

I think one must be truthful and say that – and I think this applied at that stage [late 1986] to – certainly to the directors in England and perhaps a bit later for the ones in Scotland. But we were really trying to, I think, give ourselves a bit more time and not be rushed by the pressure coming from the commercial producers.<sup>285</sup>

**27.194** Dr Macdonald was later examined as follows:

Q: [One] might think ... that there was a preoccupation within SHHD with undertaking research, whatever its purpose, at all costs, as a means of putting off making a decision about surrogate testing ....

A: I think it was reasonable to argue that we didn't have sufficient information to know exactly how it would work out in our population and therefore we should look to the possibility of research. At the same time, I think it has to be admitted that that would postpone a final decision inevitably.

Q: But was it the postponement of the final decision that was really the priority at this time?

A: It certainly – it is certainly fairly clear that neither DHSS nor SHHD were persuaded that we should go ahead with surrogate testing.<sup>286</sup>

**27.195** The reasonableness of the SHHD position is discussed further below.

### Correspondence in *The Lancet*

**27.196** The picture in the second half of 1987 is confused, with different groups of Scottish experts expressing apparently conflicting views. Debate on the introduction of surrogate testing became focused in a chain of correspondence in *The Lancet* beginning in June, to which SNBTS specialists contributed. It is necessary to note the positions that had been reached in research by Scottish scientists by June. The work of Dr Dow and Dr Follett has been discussed above. As noted in paragraph 27.127 above, Dr Dow's view was that there was a low level of post-transfusion NANB Hepatitis in the West of Scotland region (with 23 possible cases reported in eight years) and that the introduction of screening would have little impact. In Edinburgh and the East of Scotland, Dr Gillon and colleagues had carried out research between April and November 1986 into ALT activity in a cohort of regular blood donors.<sup>287</sup> They had concluded that the introduction of ALT/anti-HBc screening tests as an indicator of NANB Hepatitis carrier status in blood donors could not be justified at that stage.

---

<sup>285</sup> Day 66, page 141

<sup>286</sup> Ibid pages 162–163. See also, the views expressed in the DHSS minute of 29 January 1988 discussed below [PEN.016.0216]

<sup>287</sup> The results of which were first reported on 13 June 1987 in the course of the debate in *The Lancet*: Gillon et al, 'Non A, Non B Hepatitis Surrogate Testing of Blood Donations', *The Lancet*, 1987; 1366-67 [LIT.001.0346]. They were more fully reported in 1988: Gillon et al, 'Post-transfusion [NANBH]: significance of raised ALT and anti-HBc in blood donors', *Vox Sanguinis*, 1985; 54:148–153 [SNB.008.3536].

**27.197** The chain of correspondence in *The Lancet* began with a letter from Dr Catherine Anderson and colleagues at the North London BTC, Edgware, in April 1987, arguing against the introduction of surrogate testing without further research.<sup>288</sup> The authors argued that a national study was required to assess the incidence of raised ALT levels and anti-HBc in donors in different parts of the country; the incidence of acute post-transfusion NANB Hepatitis; and how many of those affected developed evidence of chronicity and serious clinical sequelae. The authors concluded:

Before we are forced to accept two screening tests of unproven benefit, which have high revenue implications, we need a national study to assess the incidence of raised ALT and anti-HBc in donors in different parts of the country. Also, and perhaps more importantly, a study is needed to assess the incidence of acute post-transfusion NANB hepatitis and to assess how many of those affected develop evidence of chronicity and serious clinical sequelae.

If the true incidence of post-transfusion NANB hepatitis and its serious clinical sequelae are at a much lower level than reported from the USA, then screening of donations to reduce the incidence of NANB hepatitis may not be cost effective in the UK.<sup>289</sup>

**27.198** In effect, the Edgware RTC group was repeating the call for a large, prospective, well organised and resourced study of post-transfusion NANB Hepatitis originally put forward by Dr McClelland in 1980–81.

**27.199** A similar view was expressed on 2 June 1987 in a paper by Dr Valerie Mijovic and colleagues (also at the North London BTC) reporting on a study of ALT testing in 2000 North London blood donors.<sup>290</sup> The percentage of the total donor population with raised ALT levels (4.6%) was greater than that found in earlier studies at the same centre in 1973 (2.8%) and 1982 (3.1%). The increase in donors with raised ALT values had occurred despite the intensification of donor education and the subsequent self-exclusion of donors in groups at high risk of HIV. The authors considered that as confirmation that many other factors, apart from NANB Hepatitis, affected ALT activity. Those other factors included high alcohol consumption, obesity, medication, strenuous activity and inhalation of solvents. The authors stated:

Before we even consider testing blood donors for ALT, a well designed prospective trial is needed to compare the incidence of hepatitis associated with transfusion in patients who have received blood only from donors with normal ALT activities with those receiving untested blood .... [E]ven in the United States the predictive value of ALT testing of blood donations for NANB hepatitis is very poor. The costs of testing and discarding donor blood would need to be examined as well as the costs of informing and counselling donors found to have ALT values repeatedly above the normal, or donors with excessively high values at any one time. Extrapolating data from the United States to this country without knowing the magnitude of the problem or its preventability would be ill advised.<sup>291</sup>

---

<sup>288</sup> Anderson et al, 'Surrogate testing for [NANB] hepatitis', *The Lancet*, 1987:912 [LIT.001.1854]

<sup>289</sup> Ibid [LIT.001.1854]

<sup>290</sup> Mijovic et al, 'Serum [ALT] and  $\gamma$ -glutamyltransferase activities in north London blood donors', *Journal of Clinical Pathology*, 1987; 40:1340-1344 [LIT.001.3907]

<sup>291</sup> Ibid [LIT.001.3907] at 3911

**27.200** In his evidence to the Inquiry Dr McClelland stated that he could not remember his reaction at the time to the suggestion by Anderson and colleagues that a prospective study should be carried out before surrogate testing was introduced but said:

I think I was in one sense probably glad that somebody was saying what I had been trying to say for quite a long time but at the same time ... I was aware that the study would take several years and I think I would probably have felt it was a bit late....

I felt that we had been prevaricating about this for a long time, and to sort of prevaricate for another three years, which was the minimum time it would have taken to do a decent prospective study, we were too late.<sup>292</sup>

**27.201** The suggestion had a greater impact on Dr Dow and Dr Gillon, and their respective research colleagues.

**27.202** In a letter in *The Lancet* on 13 June 1987 Drs Dow, Mitchell and Follett of Glasgow reported on Dr Dow's study of post-transfusion hepatitis in the west of Scotland. Their findings were analysed briefly and said to indicate that if ALT and anti-HBc tests had been carried out routinely over the eight-year period of their study, at an estimated cost of more than £1 million, with a loss of about 4% of the blood supply, only five of the reported cases of infection might have been prevented. They expressed the view that:

It would be prudent to do a UK study to assess the real incidence of acute post-transfusion NANB hepatitis and to assess the proportion of those chronically affected, before considering following the American surrogate testing policy.<sup>293</sup>

**27.203** In the same edition of *The Lancet*, Dr Gillon and his colleagues at Edinburgh reported the findings of their 1986 study into surrogate markers in blood donors attending their centre.<sup>294</sup> It stated:

Our findings confirm the doubts expressed by Dr Contreras and her colleagues [at Edgware] on the wisdom of introducing surrogate testing for NANB hepatitis into blood transfusion practice in the UK. We found a strong association between a raised ALT and both obesity and alcohol ingestion, and these two factors alone might account for 82% of the abnormal ALT values found .... Those who support ALT testing should recognise the tendency ... of ALT levels to fluctuate: the loss of donated blood would be far in excess of that suggested by published studies, and most of the excluded donors would not be NANB hepatitis carriers.

If the degree of benefit claimed from the retrospective American studies were to hold for the UK, the blood transfusion services would have to spend well over £5 million more every year (2½ million donations at £2-3 per donation). Account must also be taken of the consequences of identifying up to 5% of the donor population as being potential carriers – not just the costs of further laboratory tests, clinical assessments, and counselling but also the anxiety raised in the donors themselves.

---

<sup>292</sup> Day 63, pages 130–1

<sup>293</sup> Dow et al, 'NANB hepatitis surrogate testing of blood donations', *The Lancet*, 13 June 1987 [LIT.001.0346]

<sup>294</sup> Gillon et al, 'Non A, Non B Hepatitis Surrogate Testing of Blood Donations', *The Lancet*, 13 June 1987; 1366-67 [LIT.001.0346]



The Americans have concluded that a large, prospective, randomised trial to test the hypothesis that surrogate testing carries clinical benefit will never be done. Of the four small prospective studies, two using ALT screening and two using anti-HBc, three failed to demonstrate any reduction in post-transfusion NANB hepatitis as a result of donor screening and one found an apparent association between anti-HBc in donor units and recipient hepatitis.<sup>295</sup>

We conclude that the introduction of ALT/anti-HBc screening tests as an indicator of NANB hepatitis carrier status in blood donors cannot at present be justified.<sup>296</sup>

**27.204** In his evidence to the Inquiry, Dr Gillon said:

I think nobody would have denied that introducing surrogate testing would have identified some donors who were carriers of [NANB] Hepatitis. We knew that. We just didn't know how many. We didn't know enough about whether this test would perform as it was being predicted in the American literature.<sup>297</sup>

**27.205** Dr Gillon also advised that he had visited the USA in early 1985 and was aware of work being done there, and elsewhere, to try to identify the agent or agents responsible for NANB Hepatitis. While he had no particular knowledge in 1987 that a breakthrough was imminent, he said:

[T]he other thing I had in my mind was that there was the likelihood that there would be a scientific solution to this problem, we would hope in a very short time ....

....

[T]o say that ALT was the only show in town was perhaps true, but it's not that we didn't have other avenues that were opening up in a much more rigorously scientific way of dealing with this problem.<sup>298</sup>

**27.206** On 16 June 1987, three days after these letters had been published in *The Lancet*, the SNBTS Co-ordinating Group held an extra meeting.<sup>299</sup> All of the Scottish Transfusion Directors were present, along with Professor Cash and Mr John Francis of the SNBTS Finance Department. The SNBTS scientists contributing to *The Lancet* correspondence were not represented. Their view that surrogate testing was not justified on scientific grounds was noted, however, and acknowledged by the Directors. Dr McClelland tabled a draft letter to *The Lancet* 'in expansion of the SNBTS view of the need to commence surrogate marker screening of blood donations for NANB in the context of product liability and of competition from commercial producers who would be introducing it'.<sup>300</sup> After a few editing points were made the Directors agreed the terms of the letter.

---

<sup>295</sup> These studies are discussed later in this chapter

<sup>296</sup> Gillon et al, '[NANB] hepatitis surrogate testing of blood donations', *The Lancet*, 13 June 1987 [LIT.001.0346] at 0346-7. Dr Gillon's full paper was published in *Vox Sanguinis* in 1988 [SNB.008.3536]

<sup>297</sup> Day 65, page 76

<sup>298</sup> Ibid pages 87-88

<sup>299</sup> Minute of Meeting [SNB.004.0672]

<sup>300</sup> Ibid [SNB.004.0672] at 0674

**27.207** The letter from the SNBTS Directors was published in *The Lancet* on 4 July 1987 under the title, 'Testing blood donors for [NANB] hepatitis: irrational, perhaps, but inescapable'.<sup>301</sup> In the letter the Directors noted the recent correspondence by Drs Anderson, Dow and Gillon and colleagues to the effect that the UK transfusion services should not start donor screening until prospective controlled studies had been carried out in the UK to find out how many cases of post-transfusion hepatitis would be prevented. While the SNBTS Directors agreed that the size of the benefit to be gained from surrogate testing could not be accurately established without such a study, they considered that the time for such a study had already passed: 'Starting now will give us an answer in 3-4 years – and that is probably 3 to 4 years too late'. That conclusion clearly reflected Dr McClelland's considered position at this stage and his oral evidence was consistent with it.

**27.208** The letter stated that the introduction of surrogate testing was 'virtually inescapable' for a number of reasons. In summary, these were:

- Legislation would soon come into force providing for strict liability for harm caused by products unless all known methods had been taken to avoid the risk.
- Surrogate testing might modestly reduce the level of infectivity of pooled plasma products, in particular, pending the validation of methods of viral inactivation in large-scale trials and many would argue that some improvement was better than none.
- The UK transfusion services could not ignore the wishes of consumers to be supplied with 'NANB tested' products, when such testing had been introduced by commercial manufacturers who would market their products as being safer.
- Having regard to the number of cases of post-transfusion hepatitis that may be prevented, the cost of preventing morbidity by surrogate marker testing for NANBH might be no greater, and could be less, than that accepted for existing screening tests for Hepatitis B and HIV.

**27.209** In their letter the Directors concluded that 'the decision which has to be made is when rather than whether the UK transfusion services follow the lead of the United States and other European countries in donor screening'.<sup>302</sup>

**27.210** Dr McClelland was asked how strongly the various SNBTS Directors felt at the time about the issue of surrogate testing and replied that most of them were still 'pretty lukewarm' and that he didn't think they were 'enthusiastic'.<sup>303</sup> He explained that part of the reason he had drafted the letter was that:

[H]aving repeatedly failed to get anywhere ... on grounds of patient safety ... I thought it might be worth deploying some other arguments, because people were worried about ... the European directive on strict product liability which was about to be translated into the Consumer Protection Act, and that was quite exercising people in the transfusion service at this sort of time.<sup>304</sup>

<sup>301</sup> McClelland et al, 'Testing Blood Donors for Non-A, Non-B Hepatitis-Irrational perhaps but inescapable,' *The Lancet*, 1987:36 [LIT.001.0328]. The reference to surrogate testing being 'irrational' was a reference to a lack of scientific data, in particular, in the UK, that proved the efficacy of such testing in reducing the incidence of post-transfusion hepatitis: Professor Cash – Day 70, pages 194–195

<sup>302</sup> McClelland et al, 'Testing Blood Donors for Non-A, Non-B Hepatitis – Irrational perhaps but inescapable', *The Lancet* 1987, ii:36 [LIT.001.0328] at 0329

<sup>303</sup> Day 63, page 137

<sup>304</sup> Ibid pages 137–138

**27.211** Professor Cash was asked whether, although the ultimate decision was unanimous, some Directors had been uneasy about the idea of surrogate testing. He replied:

I think that all of us, certainly including myself, but all of us were very uncomfortable with finding our position – and we were not in that letter recommending the introduction; we were saying, “It’s too late. We are going to be forced into doing it.” But none of us wanted to go down that track and I think it is quite important that I make that very plain ....<sup>305</sup>

**27.212** He continued:

[A]ll of you keep saying we recommended it. We just simply said, “It’s inevitable. It’s going to happen. We are going to be caught here and we need to plan for that eventuality.”

....

[W]e were all very unhappy about this. We were not saying, “This is excellent, let’s go for it”. We were saying, “We are caught”... [P]lease, we did not recommend that we started it. We simply said, “The writing is on the wall, we think, as best we can judge”.<sup>306</sup>

**27.213** In his evidence to the Inquiry, Dr McClelland confirmed that he was of the view at that stage that surrogate testing, using both ALT and anti-HBc, should be introduced. He was asked for the main or the determining factor or factors that led him to recommend that surrogate testing should be introduced and replied:

I felt there was – even in the absence of a proper ... a definitive prospect of [a] randomised controlled study to provide a real answer, that there was sufficient evidence – the evidence which had convinced the Blood Products Advisory Committee of the FDA that surrogate testing needed to be introduced and led to the decision in the United States was, while not complete and not definitive, very, very difficult to ignore and I had no conviction that the epidemiological situation, the sort of prevalence, the amount of ... [NANB] Hepatitis infection in the UK was really that much less than it was in America, in 1986, because, you know, commercial paid donors had stopped. They had introduced similar changes in donor selection in relation to AIDS that we had, and I felt if, in the light of ... those two major changes, the United States felt it had to introduce this testing, we were in a very, very poor position to not follow suit in the UK, unless we had convincing evidence that it really genuinely wasn’t a problem .... And we didn’t have that.<sup>307</sup>

**27.214** As indicated in paragraph 27.208, Dr McClelland was deploying different arguments. It was, as he said, his ‘sort of last throw on this topic’. When asked to what extent patient safety was a factor in his consideration he replied it was ‘the’ factor in his consideration.<sup>308</sup> He went on to explain that his view was essentially an application of the precautionary principle: he was concerned that ‘despite the persisting uncertainties about the real safety gains that might be achieved, failure to introduce testing could constitute

---

<sup>305</sup> Day 72, pages 78–79

<sup>306</sup> Ibid pages 81–82

<sup>307</sup> Day 63, pages 141–142

<sup>308</sup> Ibid pages 143–144

a failure to protect patients from some degree of avoidable risk'.<sup>309</sup> There was evidence which, while imperfect, suggested that surrogate testing might increase the safety of blood, and:

[I]f something might make a patient safer, then you have to do it. That is in a very crude way, as I understand [it] ... the precautionary principle. And depending on whether you are a health economist or concerned primarily with the nation's economics or whether you're concerned with the public health or you are concerned with the health of an individual, you will view those things in different ways. There ain't no right answer.<sup>310</sup>

**27.215** Whether or not justified on the precautionary principle, the letter exposed the conflicting opinions within the SNBTS at this stage, in mid-1987. The letter also attracted considerable criticism and a degree of confusion about its purpose and the intentions of the SNBTS. The SNBTS Directors later acknowledged, at their meeting on 18 August 1987, that the rapid succession of the publications by the scientists and by the Directors 'had caused readers of *The Lancet* to be puzzled'.<sup>311</sup> Dr Mitchell, for example, had been a co-author of the letter published in *The Lancet* on 13 June 1987 which argued against the introduction of surrogate testing until further studies had been carried out, but was also a signatory to the letter of 4 July 1987 in which the SNBTS Directors argued that the time for further studies had passed and that the introduction of surrogate testing was virtually inescapable.

**27.216** Professor Cash had sent a pre-publication copy of the Directors' *Lancet* letter to Dr Fraser (Bristol) who replied on 2 July 1987, advising that:

I think you will find that the Transfusion Directors in England and Wales will not be very pleased at reading this letter.

....

We all managed to work together to introduce HIV antibody testing on the same date. I think it is only a shame that we have not been able to have the same type of discussion to agree whether or not to implement ALT and/or core antibody testing in the UK.<sup>312</sup>

**27.217** Professor Cash replied to Dr Fraser on 8 July 1987. He stated:

1. The SNBTS Directors do not wish, and currently have no intention, of introducing NANB surrogate testing unilaterally.
2. Current views, which as you know were crystallised last March, are being expressed to support our Public Expenditure Survey (PES) submissions to SHHD for the next 5 years.
3. We have no doubt that an important forum for the continued debate is indeed the BTS/NIBSC group(s) and the current NANB debate (which began some 2 years ago here) and the confused central management attitudes to the

<sup>309</sup> Dr McClelland's statement [PEN.017.0754] at 0769

<sup>310</sup> Day 63, pages 147–8. Dr McClelland accepted that there was a limit on the proposition that blood should have 'maximum safety' in that a proposal which offered minimal additional safety at enormous cost may not be worthwhile: Day 63, page 153

<sup>311</sup> Minute of Meeting [SNB.004.0728] at 0733

<sup>312</sup> Letter [SNB.008.3507]. On 1 August 1987 *The Lancet* published a letter by Drs Contreras and Barbara of the North London BTC, Edgware, taking issue with the views of the SNBTS Directors: see paragraph 27.218 below

Medicines Act and Product Liability had much to do with driving me to seek the establishment of this joint enterprise.

4. I really don't believe you should view The Lancet letter as any more than part of a debate which was initiated in this journal's columns by our friends and colleagues at Edgware. It can also be viewed as yet another attempt to persuade central management (DHSS) to give renewed thought to the way the transfusion services interface with the Medicines Act and forthcoming legislation on product liability and perhaps even to ways for improving the co-ordinated management of the transfusion services on a UK basis.<sup>313</sup>

**27.218** In a minute dated 21 July 1987, Dr McIntyre brought the SNBTS Directors' *Lancet* letter to the attention of Mr Macniven and others. In the minute Dr McIntyre stated:

The purpose of this minute is not to discuss all the relevant issues, but to point out that SNBTS may institute testing without further discussion as a fait accompli.

....

Professor Cash has assured Dr Fraser of Bristol NBTS, in a letter dated 8 July, that he will not institute testing 'unilaterally'. We have however no assurance that he will not do so in the near future without specific funding and without necessarily reporting what he has done to CSA or SHHD.

DHSS have expressed their concern and dismay at the letter by Professor Cash and colleagues and have interpreted this as being SHHD policy; we have attempted to reassure them that it is not so. Their concern is that if we should commence testing unilaterally they will feel obliged to follow.<sup>314</sup>

**27.219** It was noted that the SNBTS had been given the opportunity to engage in a research programme to evaluate the need for testing but had declined as they felt that the time for this study had already passed.<sup>315</sup> The background to that comment was confused. As indicated in paragraph 27.159 above, the proposal for Scottish participation in the UK programme envisaged in early 1987 was directed into the CSO funding process by Dr Moir, SHHD. The project seems to have made little progress for some time after that point, but was revived ('after much manoeuvring' by the SHHD)<sup>316</sup> in June 1987 when it was decided that an application would be made to the CSO. It was made in the names of Dr McClelland and Dr Gillon on 6 August but was later rejected.<sup>317</sup>

**27.220** The debate in *The Lancet* continued. Two English Directors, Drs Contreras and Barbara, responded to the Scottish Directors' letter to *The Lancet* in the edition published on 1 August. They argued that the transfusion service must not bow to irrational pressure to introduce surrogate screening, described as 'measures whose efficacy is unproven'.<sup>318</sup>

---

<sup>313</sup> Letter [SNB.011.3846]

<sup>314</sup> Minute [SGF.001.2085]

<sup>315</sup> In the event, an application for funding for the research project was made by Drs Gillon and McClelland and was refused on 25 September 1987.

<sup>316</sup> Memorandum by Dr Forrester to Mr Macniven dated 1 October 1987 [SGH.002.8077]

<sup>317</sup> Paragraph 27.229 below

<sup>318</sup> Contreras and Barbara, 'Testing of Blood Donations for Non-A, Non-B Hepatitis', *The Lancet*, 1 August 1987 [LIT.001.0326]

**27.221** At their meeting on 18 August 1987 the SNBTS Directors noted reactions to the Scottish Directors' letter to *The Lancet*.<sup>319</sup> Dr McClelland's application to the Chief Scientist Office for funding to enable him to participate in the UK study was reported. The Directors agreed that to be consistent with their policy decision (on the introduction of screening) it would be prudent to proceed to a Scottish national study to evaluate ALT and anti-HBc testing. Dr Cuthbertson and the SNBTS Microbiological Validation Group would consider how the SNBTS should examine the available technology for these tests.<sup>320</sup> At this stage, therefore, there were two lines of research for which funding would be required: Dr McClelland's UK project and a national Scottish project that had been remitted to the SNBTS Microbiological Validation Group.

**27.222** Preparatory work was started to cover the possibility that surrogate screening might be introduced. On 6 October 1987 the SNBTS Directors were told that Dr Cuthbertson's SNBTS/NBTS Microbiological Validation Group was due to make a proposal to the Directors concerning ALT and anti-HBc testing methodology.<sup>321</sup> The SNBTS Directors met on 8 December 1987.<sup>322</sup> It was reported that the Microbiological Validation Group was to reconsider to what extent it was necessary for every centre to be involved in evaluating the technology for ALT testing and would report on the matter by 31 March 1988. It was agreed not to consider anti-HBc testing until the report on ALT testing had been received and discussed by the Scottish Directors.<sup>323</sup> That work did not proceed quickly, however; when the SNBTS Directors met on 13 December 1988, it was reported that the Validation Group had not done any significant work since the last meeting. The Directors agreed that the group 'had more important matters to fulfil'.<sup>324</sup> The proposal for a national Scottish evaluation of surrogate screening appears to have proceeded no further after that point.

**27.223** Meanwhile, the commercial pressure anticipated by the Scottish Transfusion Directors in 1987 was indeed to become a reality and was noted within the SHHD. On 17 December 1987 Dr Forrester sent an internal SHHD memorandum to Mr Tom Macdonald and others.<sup>325</sup> He noted that commercial producers of blood products were being allowed by the DHSS to include in their product inserts a statement that the product was derived from donations which had been ALT tested and that that was likely to stimulate pressure for the introduction of surrogate testing in Scotland.

### Funding for Edinburgh RTC to join the multi-centre study

**27.224** As noted in paragraph 27.219, Drs Gillon and McClelland submitted an application to the Chief Scientist Office (CSO), SHHD, on 6 August 1987 for a research grant to enable the Edinburgh RTC to participate in the proposed UK multi-centre study into surrogate markers in donors.<sup>326</sup>

<sup>319</sup> Minutes of SNBTS Co-ordinating Group meeting, 18 August 1987. [SNB.004.0728] at 0732–0733

<sup>320</sup> The Microbiological Validation Group subsequently investigated the technology for carrying out ALT testing. A final report of the evaluation of the Eppendorff Epos system was produced on 25 August 1988 and concluded that the system was clearly suitable and that a cut-off of 2.5 Standard Deviations above the mean would lead to the exclusion of approximately 1.5% of donations whereas a cut-off of 2 Standard Deviations above the mean would lead to the exclusion of approximately 5% of donations [SNB.002.4423]. Similar work to evaluate anti-HBc testing technology appears to have been started but not concluded. See extract from minutes of SNBTS Directors' Meeting, 27 September 1988 [SGH.002.8027] and minutes of the SNBTS Directors' meeting, 13 December 1988 [SNB.002.7350] at 7353.

<sup>321</sup> Minutes of SNBTS Directors' Meeting, 6 October 1987 [SGF.001.0249] at 0253

<sup>322</sup> Minutes of SNBTS Directors' Meeting, 8 December 1987 [SNB.002.7234]

<sup>323</sup> Ibid [SNB.002.7234] at 7240

<sup>324</sup> Minutes of SNBTS Directors Meeting, 13 December 1988 [SNB.002.7350] at 7353

<sup>325</sup> Minute from Dr Forrester to Mr Macdonald, dated 17 December 1987 [SGH.002.8062]

<sup>326</sup> Grant application by Drs Gillon and McClelland dated 6 August 1987 [SNB.006.0791]

**27.225** On 20 August 1987 Dr Forrester (SHHD) sent a memorandum to Dr William Forbes (CSO) and others.<sup>327</sup> Dr Forrester wrote that the Department was required to make a well-informed decision on whether or not to support surrogate testing of blood donations for NANB Hepatitis. The benefits of such testing were not clearly established and there were drawbacks. The memorandum suggested a lack of significant support for the project at this stage. It stated:

The Department are well aware of the work by Dr Dow supported by CSO, and indeed so are the organisers of the current application .... The Department however do not believe that his work alone is a sufficient guide at present, because:

- It did not study [anti-HBc] ....
- More searching investigation is now possible into the significance of these antibodies ....
- It took place before the advent of screening for HIV antibodies, which may exclude some donations conveying in addition some non-A, non-B hepatitis agent; and
- It is not necessarily typical of the UK as a whole ....<sup>328</sup>

**27.226** In view of the interest of the SHHD, it was said that Dr Forrester or Dr McIntyre would welcome the opportunity to be present at the meeting of the CSO Biomedical Research Committee on 25 September. A manuscript note on the memorandum informed Mr Tom Macdonald, the branch head, that Dr Forrester was pressing forward with getting CSO money for the proposal, with the support of colleagues.

**27.227** In a minute to Mr Macniven dated 1 October 1987, Dr Forrester stated that the Gillon/McClelland grant application had been considered, and rejected, at a meeting of the CSO Biomedical Research Committee (BRC).<sup>329</sup> Dr Forrester was present at the meeting and noted on 25 September 1987 that the Committee had rejected the application on scientific grounds, which he agreed were 'substantial'. While the Inquiry has been unable to recover a minute of the BRC meeting of 25 September 1987, the surrounding documentation makes it reasonably clear that the BRC was of the view that restricting the proposed study into surrogate markers to donors and not including the follow-up of recipients, was of little or no scientific merit: it would not provide information on the prevalence of post-transfusion NANB Hepatitis, nor would it provide information on whether the presence of surrogate markers in donors was associated with the development of post-transfusion NANB Hepatitis in recipients.<sup>330</sup> These are substantially the reasons for the view that the Follett and Dow study of September 1984 provided no basis for arriving at conclusions on the prevalence of transfusion-transmitted NANB Hepatitis or on the likely efficacy of surrogate testing in reducing the incidence of transmission of the disease.

<sup>327</sup> Minute by Dr Forrester dated 20 August 1987 [SGH.002.8079]

<sup>328</sup> Ibid [SGH.002.8079]

<sup>329</sup> Dr Forrester's minute of 1 October 1987 to Mr Macniven [SGH.002.8077]

<sup>330</sup> See, for example, the following letters to Dr W Forbes, CSO, namely, (1) letter dated 4 September 1987 by Professor C. du V Florey, Head of the Department of Community Medicine, University of Dundee [PEN.016.0167], (2) letter dated 27 October by a redacted author [PEN.016.0210], (3) letter dated 2 November 1987 by Professor Hedley, Chair of Public Health and Head of the Department of Community Medicine, University of Glasgow [PEN.016.0156]. See also, letter dated 13 November 1987 from Dr W Forbes to Dr M Smith, DHSS [PEN.016.0152]

**27.228** In his minute to Mr Macniven of 1 October 1987, Dr Forrester indicated a major interest in the formulation of the BRC's reasons for rejection of the grant application. He had asked Dr Forbes, CSO, to ensure that the minutes of the BRC decision would confirm that the reason for rejection was not that research was 'superfluous', which he noted was the SNBTS position. He also asked that announcement of the decision should be withheld until 'CSO have put their act together with DHSS Research Management Division'. He had also asked for a statement in writing of the reasons for rejection, which he anticipated would take some time to prepare. In a summary he noted that, while agreeing that the scientific evidence was incomplete, the SNBTS nonetheless maintained that their general obligation to the recipients of blood and blood products required screening to start immediately, despite its recognised drawbacks and cost; that the Health Departments, along with the NBTS, were pressing for more scientific evidence before making any decision to screen; and that the gathering of the evidence, at least in Scotland, was obstructed by the limitations of the research proposal. These limitations meant that the results of the proposed research could prove inconclusive, which was a serious objection to undertaking it. In respect of the outstanding application by the SNBTS for funds to introduce surrogate testing he stated:

[I]f there is no hurry to reach a decision ... [I] would prefer to do so when the written statement of reasons for rejection [of the Edinburgh grant application] has arrived, and when our CSO and the DHSS have reached a common stance.<sup>331</sup>

**27.229** Mr Macniven replied to Dr Forrester on 2 October 1987. He noted that the PES timetable required a decision to be reached very soon on whether to earmark funds for the SNBTS for surrogate screening to commence in the second half of 1988. He had, however, taken steps to get round the problem by registering with Finance Division that a need for NANB Hepatitis testing may emerge but that it would be premature to allocate money to the SNBTS for that purpose at that time. Mr Macniven stated in his minute:

But I am a little anxious about the timescale implied by your minute. I am very anxious indeed [that] our decision (on whether or not to put resources into NANB testing) should be properly informed by research evidence. If that evidence justifies testing, then it is very important that we should be able to find the money to start it quickly. If it does not justify testing, it is equally important that we should not have allocated money to the SNBTS for the purpose, thereby sterilising it for other uses. But I think the worst of all possible worlds is that research cannot get off the ground: I fear that, in those circumstances, we would be subjected to increasingly irresistible pressure to spend the money in any case, for the sake of improving (at any price) the safety of blood and blood products.

... [I] can well understand the general CSO disinclination to "repair" research proposals: but I hope that too much stress does not need to be placed on that principle in this case, because of the substantial patient safety/expenditure issues which are stake.<sup>332</sup>

---

<sup>331</sup> Dr Forrester's minute of 1 October 1987 to Mr Macniven [SGH.002.8077] at 8078

<sup>332</sup> Mr Macniven's minute of 2 October 1987 to Dr Forrester [SGH.002.8076]



**27.230** In his evidence to the Inquiry, Mr Macniven agreed with the suggestion that the memorandum was consistent with him keeping an open mind on the subject of surrogate testing and that, if he had been persuaded on the evidence, he would have sought to ensure that funding was available. As he put it, ‘funding should not be the obstacle’<sup>333</sup> and ‘I was very keen to make sure that funding should not be the limiting factor if the scientific/technical light turned to green.’<sup>334</sup> He explained that it would be ‘the worst of all possible worlds’ if research could not get off the ground because ‘we would be taking the decision on information which was not properly informed by research evidence’.<sup>335</sup>

**27.231** Drs Gillon and McClelland were written to on 19 November 1987 advising that their grant application had been declined.<sup>336</sup>

**1988**

### Funding for the multi-centre study in England

**27.232** On 20 January 1988 a paper was produced for the Central Blood Laboratories Authority. ‘Screening of NBTS blood donors’<sup>337</sup> proposed that the BPL should come into line with all other major fractionators of human plasma by including ALT testing in the specification of source plasma collected by blood donor centres. The drive for ALT testing was said to have been strongly augmented by manufacturers’ liability and the demands of patients to eliminate NANB Hepatitis as a sequel to treatment, with the development of severe liver disease in up to 60% of sufferers.<sup>338</sup> The paper noted that the scientific basis for introducing ALT screening of donors was far from satisfactory and that, as regards Factor VIII, the BPL was distinguished from competitors by the use of dry heat virus inactivation and the use of plasma unscreened for ALT and so outside the ‘state of the art’ practised in the USA and Europe. The BPL had a clear commercial motivation for screening which was independent of safety issues. It would be necessary if surplus products were to be sold in Europe.

**27.233** The risk that the pressure on the BPL would result in the introduction of testing prompted a reaction in the DHSS. A DHSS minute in January 1988 reveals that an application for funding for the English part of the multi-centre study into surrogate markers in donors had been refused by the DHSS Research Management Division.<sup>339</sup> The minute argued that the study should nonetheless be funded for policy reasons and noted, particularly, that all major producers of blood products now used plasma from ALT-tested blood, which put pressure on the BPL to do likewise. In addition, if the BPL was forced to introduce ALT testing of the plasma used in its products, that would involve ‘writing off’ its stockpile of plasma, worth around £40 million, and importing commercial products at a further cost of around £10 million. The author of the minute, Mr Harris, noted that embarking on the proposed multi-centre study would reduce the likelihood of pressure from haemophilia centre Directors and the Haemophilia Society to introduce surrogate screening, in that

<sup>333</sup> Day 65, page 185

<sup>334</sup> Day 78, page 33

<sup>335</sup> Ibid pages 34–35

<sup>336</sup> The Inquiry does not have a copy of the letter to Drs Gillon and McClelland advising them that their application had been refused but notes the reference to this communication in a minute dated 15 April 1988 from Dr Moir, Director, CSO [SGF.001.2059]

<sup>337</sup> Screening of NBTS Blood Donors [DHF.003.0500]

<sup>338</sup> The meaning of, and basis for, this assertion is unclear. It is a much higher figure than was otherwise reported at the time for the percentage of NANB Hepatitis patients with chronically elevated ALT levels who developed cirrhosis (ie between 10 and 20%) and may have been intended to be a reference to the percentage of patients with NANB Hepatitis who developed chronically elevated ALT levels.

<sup>339</sup> Minute dated 29 January 1988 from Mr M Harris, DHSS [PEN.016.0216]

the study might demonstrate (i) the low incidence of NANB Hepatitis carriers in the NBTS donor pool and (ii) the low utility of the ALT test. The minute concluded:

Such a study could (against all expectations) prove the need for the ALT test, even so it would then have provided scientific justification for the resulting expenditure. Even having a study in train, would give Ministers a valid reason for not being “bounced” into accepting ALT testing.

The R&D programme cannot find room for this study – cost £72,000. In view of the serious financial consequences for the HCHS [Hospital and Community Health Services] can it be exceptionally found from the HCHS central fund?

I feel that Ministers would not thank us for failing to head off this folly.

**27.234** The arguments in the minute in favour of the study were, presumably, persuasive in that funding for the English part of the multi-centre study was duly found from the relevant DHSS policy division.<sup>340</sup>

**27.235** In a minute of 14 April 1988 Dr Forrester noted that the English part of the multi-centre had received funding and commented:

From now on the tables are turned. We will have to watch what England do, because they will be first to get the relevant research data; and they are, even now, under more external pressure to institute testing for ALT. The pressure here is still evidently internal: SNBTS striving to keep up with any competition.

... [I] think we cannot help being left behind – but in this particular context, there may not be drawbacks.<sup>341</sup>

**27.236** Commenting on Dr Forrester’s minute, Dr Moir, Director, CSO, noted that he had discussed matters with Dr Jeremy Metters of the DHSS who had advised that his DHSS colleagues with policy interests felt particularly vulnerable. They were aware that there were some Scottish data on the prevalence of the problem whereas there was no comparable data in England and Wales.<sup>342</sup> Dr Moir noted:

[Dr Metters] also felt that a substantial part of his policy colleagues’ interests in funding this “research” study was that it would allow them to “play for time” in the hope that instead of ALT a more suitable screening assay could be found which would act as a marker for [NANB] Hepatitis.<sup>343</sup>

**27.237** At their meeting on 12 April 1988 the SNBTS Directors confirmed that it had been agreed not to introduce ALT testing in Scotland until it had become UK policy.<sup>344</sup> The Directors, however, wished to reserve their position in light of reports of ALT testing in at least one RTC in England and Wales.<sup>345</sup> It was noted that imported commercial products were being marked ‘ALT tested’.

---

<sup>340</sup> See minute dated 15 April 1988 by Dr Moir, Director, CSO [SGF.001.2059]

<sup>341</sup> Dr Forrester’s minute of 14 April 1988 [SGH.002.8058] at 8059

<sup>342</sup> Minute dated 15 April 1988 by Dr Moir [SGF.001.2059]. The reference to ‘Scottish data’ is, presumably, a reference to Dr Dow’s study into NANB hepatitis in the West of Scotland

<sup>343</sup> Ibid [SGF.001.2059].

<sup>344</sup> Minutes of the SNBTS Directors’ Meeting, 12 April 1988 [SNB.002.7321] at 7324

<sup>345</sup> At the next meeting of the SNBTS Directors, on 14 June, it was reported by Professor Cash that it was the intention of the Birmingham RTC to begin ALT and anti-HBc testing routinely within the next months. Minute [SNB.002.7333] at 7337 as corrected at the meeting on 27 September 1988 [SNB.002.7344] at 7345

**27.238** Studies continued to be reported that showed a low prevalence of ALT and anti-HBc in the general population. In 1988 Dr Alan Kitchen and colleagues reported on a study to determine the incidence of anti-HBc in donors at the North East Thames Regional Transfusion Centre.<sup>346</sup> In the study, 1893 donors were tested, of whom 35 (1.85%) were repeatedly positive. The authors commented that, at that time, there was likely to be very little benefit in the introduction of anti-HBc screening of blood donors. The loss of approximately 2% of available donors because of deferment would cause problems for those transfusion centres facing shortages of donors, especially those serving the Greater London Area. The costs of testing donations for the presence of anti-HBc were high and, in the prevailing financial climate, would be hard to justify. A further consideration was the need to counsel those donors found to be anti-HBc positive. Although the authors accepted that the introduction of surrogate testing might eventually be unavoidable, they believed that only a controlled prospective study would provide the necessary information to determine the significance of donor anti-HBc levels in relation to post-transfusion hepatitis, especially NANB Hepatitis, in the UK.

**27.239** At the annual meeting of the SNBTS Directors and the Scottish Haemophilia Centre Directors on 5 May 1988, Dr Forrester reported that the multi-centre study into NANB Hepatitis surrogate screening was being carried out in England and that a decision whether to introduce screening would probably wait upon its outcome.<sup>347</sup> Dr McClelland and Professor Cash were both uncomfortable with the delay involved. In effect, the funding process had excluded the SNBTS from participation in continuing research by the NBTS into the effectiveness of surrogate screening of blood donations.

### The Chiron announcement

**27.240** This was the position reached in the UK immediately before Chiron Corporation, USA, made the important announcement, on 10 May 1988, that had identified, cloned and expressed proteins from an NANB Hepatitis virus and had developed a prototype immunoassay that might lead to a screening test.<sup>348</sup>

**27.241** The announcement heralded the beginning of a transitional period between the discovery and the production of a marketable test during which surrogate testing for NANB Hepatitis remained of significant interest. The issue at this stage, in 1988, was whether it was appropriate to postpone a decision on the introduction of surrogate testing for NANB Hepatitis, using the assays then available.

**27.242** The SNBTS Directors noted the Chiron announcement, at their meeting on 14 June 1988.<sup>349</sup> Professor Cash was to enquire about the availability of the test in the UK; at that stage, he thought that 'specific NANB testing kits will be available in about 2 years'.<sup>350</sup> A subsequent letter from Ortho Diagnostic Systems Ltd, which had entered into an agreement to manufacture the test kits under licence from Chiron, advised that the kits might be available 'towards the end of 1989'.<sup>351</sup> The 1988 SNBTS PES bid, which

<sup>346</sup> Kitchen et al, 'Incidence and significance of hepatitis B core antibody in a healthy blood donor population', *Journal of Medical Virology*, 1988; 25(1):67-75 [LIT.001.3817]

<sup>347</sup> Minutes of meeting of SNBTS Directors and Haemophilia Directors, 5 May 1988 [SGH.001.7505] at 7508-9

<sup>348</sup> News Release dated 10 May 1988 by Chiron Corporation [PEN.016.0290]. Dr McClelland gave evidence that 'the breakthrough, if I can use that term, that led to [the Chiron group] discovering the Hepatitis C test was dependant entirely on what was very novel technology, which I and most of my colleagues didn't know anything about at the time. You know, the sort of reverse engineering of a virus from - starting off with an antibody was science fiction, as far as I was concerned.' Day 64, page 120

<sup>349</sup> Minutes of SNBTS Directors' Meeting, 14 June 1988 [SNB.002.7333] at 7336-7337

<sup>350</sup> Note of SNBTS Directors' Meeting, 14 June 1988 [SGH.002.8034]

<sup>351</sup> Letter dated 19 July 1988 from Allan J Follett, Managing Director, Ortho Diagnostics Systems Ltd, to Professor Cash [SNB.008.3586]

appears to have been prepared in June 1988, sought funding for ALT testing in 1989–90 and funding for use of the Chiron/Ortho test in 1990–91.<sup>352</sup> In particular, PES bids for funding for testing were submitted by the CSA as follows:

- (i) 1989–90 ALT £85,000
- (ii) 1990–91 ALT £25,000; NANB<sup>353</sup> £300,000

**27.243** There was discussion of the Ortho anti-HCV test when the SNBTS Directors met on 27 September 1988.<sup>354</sup> The test had been the subject of a workshop at the International Society of Blood Transfusion Conference in July 1988. As understood by the Directors, the availability of the test was not imminent and the data presented had been inconclusive. The antibody was a late-developing one which would present similar problems in relation to the ‘window’ between infection and the production of measurable antibodies, as was the case with HIV. In the SNBTS Directors’ view, ALT remained the earliest available indicator of infection. Notwithstanding the Chiron discoveries, therefore, there was likely to be a period, of indefinite duration, in which surrogate testing for ALT or anti-HBc remained a relevant and material issue for the SNBTS. The Directors agreed not to plan any medium-term policy on the basis of the successful introduction of Chiron technology and that ALT would remain the test of choice in the meantime.

**27.244** At the end of 1988, however, the SNBTS Directors continued to take the view that Scotland should not commence surrogate testing, pending the outcome of the UK study. At their meeting on 13 December 1988, Dr Wagstaff informed the Directors that the DHSS had funded three centres to carry out a study of ALT technology and of anti-HBc screening. Professor Cash confirmed that the Scottish Directors would not commence surrogate testing ‘until the Department of Health and the SHHD supported and funded the project’, which would be a task for the soon-to-be-formed UK blood transfusion services’ Advisory Committee on Transfusion Transmitted Diseases (ACTTD).<sup>355</sup> The issue would also engage the Advisory Committee on the Virological Safety of Blood (ACVSB). The topic had moved into a new phase, with advice being taken from duly constituted expert bodies.

**27.245** Dr Gunson had, early in 1988, discussed with Dr McClelland and Dr Pickles the formation of a UK group to determine policy with respect to transfusion-transmitted diseases.<sup>356</sup> In the event, two groups were formed. The ACTTD was a UK BTS group on transfusion-transmitted diseases. The ACVSB was a DoH group on the virological safety of blood. The ACVSB had a wider remit than blood transfusion medicine, embracing transplantation and other aspects of disease transmission. It was a UK advisory committee and included Scottish members. The establishment of the ACVSB and the ACTTD and the groups’ initial discussions relating to the introduction of anti-HCV testing in the aftermath of Chiron’s discoveries, are described in Chapter 31, *The Introduction of Screening of Donated Blood for Hepatitis C*. In this chapter, it is necessary to trace only the fate of the investigations into the use of surrogate testing that continued into the period from 1989 onwards.

<sup>352</sup> SNBTS PES Programme Narrative, 1988 [SNB.003.3078] at 3103–3104

<sup>353</sup> This appears to be a reference to the Chiron/Ortho anti-HCV test

<sup>354</sup> Extract from minutes of the SNBTS Directors Meeting, 27 September 1988 [SGH.002.8027]

<sup>355</sup> Minutes of SNBTS Directors’ Meeting, 13 December 1988 [SNB.002.7350] at 7353

<sup>356</sup> Minutes of ACTTD on 24 February 1989 [SNB.006.1975]; Dr McClelland’s Witness Statement [PEN.017.2491]

**1989**

**27.246** The ACTTD had among the terms of reference agreed at its first meeting on 24 February 1989: 'To consider the epidemiological, clinical and laboratory aspects of diseases which may be transmitted by the transfusion of blood and blood products.'<sup>357</sup>

**27.247** The continuing three-centre study of ALT technology and anti-HBc screening in England and Wales was also within the group's remit.

**27.248** At that meeting, Dr Contreras (North London RTC) outlined the results of the study to that date. Notwithstanding the decisions on funding already discussed, research continued in Scotland. Dr Mitchell reported on the study of 5000 donations in Glasgow, in which 2.8% of donors had elevated ALT levels. With respect to anti-HBc tests, in a separate study 17 out of 2000 donations were found positive, of which 15 results were reproducible. Professor Cash reported that the methodology for ALT testing and follow-up had been examined in Scotland and that a standardised method had been agreed. This would be available to the RTCs if the general introduction of ALT testing was agreed.<sup>358</sup> It was again agreed that there should be no recommendation to institute ALT testing until the current study in England was completed.<sup>359</sup> It was noted, however, that there was a degree of inevitability about the introduction of the test, which was required by regulatory authorities in other countries to determine the acceptability of fractionated plasma products. That would be discussed with the BPL in the near future.<sup>360</sup> At this stage, therefore, the ACTTD was resolved to continue research into surrogate testing, but with acknowledgement that external marketing considerations would come to drive the agenda (that having been recognised to be the case for some time).

**27.249** In the meantime, steps had been taken to implement the decision of the UK health ministers, originally proposed the year before, to set up the ACVSB. The decision was intimated in a letter of 8 March 1989 sent out by Dr E Harris.<sup>361</sup> The ACTTD and other committees would report through the ACVSB, which would provide formal scientific advice to the UK Government and its agencies. The terms of reference of the ACVSB were:

To advise the Health Departments of the UK on measures to ensure the virological safety of blood, whilst maintaining adequate supplies of appropriate quality for both immediate use and for plasma products.<sup>362</sup>

**27.250** The ACVSB became the main advisory committee to the UK Government on whether surrogate testing of blood donors for NANB Hepatitis and screening of donors for Hepatitis C should be introduced. The first meeting of the group took place on 4 April 1989 under the chairmanship of Dr Harris.<sup>363</sup> The intention was that the next meeting would concentrate on viral hepatitis.

<sup>357</sup> Meeting minutes [SNB.006.1975], Terms of Reference [SNB.006.1923]

<sup>358</sup> Meeting minutes [SNB.006.1975] at 1978

<sup>359</sup> Repeating the position of the SNBTS Directors on 13 December 1988. See paragraph 27.242

<sup>360</sup> The interests of the NBTS and SNBTS were not necessarily the same. In each case the safety claims for imported products based on screening were relevant. However, in foreign markets regulation had an impact and this appears to have affected the BPL and to some extent the PFC rather than the Blood Transfusion Services as such.

<sup>361</sup> Letter from Dr Harris to Dr Perry dated 8 March 1989 [SNF.001.1263]

<sup>362</sup> Terms of Reference [SNB.001.9366]

<sup>363</sup> Meeting minutes [SNF.001.1219]

**27.251** The multi-centre study of ALT and anti-HBc testing, funded by the DHSS (see paragraphs 27.230–27.233), and coordinated by Dr Gunson, had proceeded with surrogate test trials, though impending developments relating to the Chiron discoveries were anticipated. Progress was reported in a paper subsequently submitted to the ACVSB at its second meeting on 22 May 1989.<sup>364</sup> The paper (ACVSB 2/7) stated:

This study (supported by the Health Departments) is being co-ordinated by Dr Gunson on behalf of the UKBTS. It is too early to report on this yet, but all the samples have now been collected and screened for ALT and anti-HBc. Much of the follow-up has been done, but this is not yet complete. It is hoped that in June a review of the study will take place although conclusions cannot be drawn until the results of the Chiron tests are known.<sup>365</sup>

**27.252** The paper gave up-to-date information on Chiron's progress as published, including information on the cloning of cDNA and the development of a specific assay for NANB Hepatitis. The paper concluded:

At present there does not appear to be any urgent need to introduce routine surrogate testing for NANB hepatitis among voluntary blood donors in the UK in respect of public health.

The position should be reconsidered by this Committee [the ACTTD] when the results of the UKBTS NANB study are available .... The availability of the Chiron test will help with interpretation of the data obtained. The Chiron test may also make surrogate testing obsolete ....<sup>366</sup>

**27.253** Professor Zuckerman's Taipei paper was also before the ACVSB; it continued to present the possibility of more than one agent of transmission of NANB Hepatitis. He commented that several 'non-specific' (surrogate) tests had been recommended for screening units of blood, until specific tests became widely available for NANB Hepatitis. Of these, the non-specific indicator which had received most attention was said to be ALT levels in blood donors. Several studies had shown that the risk of post-transfusion NANB Hepatitis was directly related to the ALT level of the donor. However, lack of sensitivity and the variability of ALT levels with age, sex, alcohol use and geographical region were factors. His view was that ALT levels would therefore not be useful as a surrogate marker of NANB Hepatitis.<sup>367</sup>

**27.254** The minute of the meeting of the ACVSB on 22 May 1989 noted that:

The Department would keep the issue of testing under review. The use of Chiron or surrogate testing would be influenced by Chiron data once released; MRC might be asked to consider. Members regarded the matter to be a priority.<sup>368</sup>

**27.255** At this stage, it was the consistent position of both the ACVSB and the ACTTD that surrogate testing for NANB Hepatitis should not be introduced by the transfusion services before Dr Gunson's study had been completed.

---

<sup>364</sup> Meeting minutes [SNB.001.9416] at 9418

<sup>365</sup> Paper (ACVSB 2/7) [SNB.001.9483]

<sup>366</sup> Ibid [SNB.001.9483] at 9484

<sup>367</sup> Taipei Paper [SNB.001.9490]

<sup>368</sup> Meeting minutes [SNB.001.9416] at 9418

**27.256** The minutes of the next meeting of the ACVSB, on 3 July 1989, record the Advisory Committee's understanding that the results of Dr Gunson's NBTS study of ALT and anti-HBc testing had shown that raised ALT levels were identified in 25% of the donors sampled.<sup>369</sup> Members expressed concern that this type of study 'revealed nothing of specificity'. The figure of 25% appears to have reflected the information made available at the meeting. It was not a correct indication of the proportion of donors who would have been rejected on the grounds of elevated ALT. In subsequent reports, the average was given as 3.2%, with results from individual centres of 3.06%; 4.56% and 1.97% (see, for example, the entries for 3 November 1989 below).<sup>370</sup>

**27.257** Dr Gunson's paper for the Council of Europe's Committee of Experts in Blood Transfusion and Immunohaematology, analysing replies from ten countries to a questionnaire on NANB Hepatitis, was also available.<sup>371</sup> As already noted, routine ALT testing of donations was carried out in four countries: Germany, France, Malta and Switzerland. France also routinely performed anti-HBc testing. Denmark, Norway, the UK and France were undertaking studies to determine their policies. Members of the ACVSB supported the Council of Europe view that anti-HCV testing alone was not sufficient to eradicate post-transfusion hepatitis.<sup>372</sup> Members cautioned against the overtly commercial stance of test manufacturers. It was reported that first time recipients of Factor 8Y had been screened by the Chiron test and had shown no positive results. Further study of stored sera from haemophilia patients was advocated. Dr Phillip Mortimer, Public Health Laboratory Service (PHLS), thought that there was a persuasive case that the Chiron test results were reliable. The outcome was that the (new) Chairman, Dr Metters, considered that all the available data should be compiled and provided for the next meeting. Members were asked to forward all contributions on NANB Hepatitis to the Committee's secretariat.<sup>373</sup>

**27.258** On 3 November 1989 Dr Gunson produced the final report of the multi-centre study in England and Wales into surrogate markers for NANB Hepatitis in donors.<sup>374</sup> The study was carried out between September 1988 and April 1989, during which time a total of 9741 blood donors at the North London, Bristol and Manchester RTCs were tested for elevated ALT and the presence of anti-HBc. In summary, the report stated:

- Taken overall, 3.2% of donors would have been rejected for raised ALT and 0.63% for anti-HBc seropositivity. However, if only donors with a raised ALT on two successive samples were rejected, the number would have been reduced to 1.1%. A 'disturbing finding' was the variability of ALT testing in the three centres.
- It was difficult to conclude how many of the donors with a raised ALT, or who were seropositive for anti-HBc, might have transmitted NANB Hepatitis. To determine that, a prospective study would have to be performed.
- However, it was evident that the ALT test was non-specific since the correlation with alcohol intake and obesity was striking. Similarly, the significance of a positive anti-HBc result was unknown.

<sup>369</sup> Meeting minutes [SNB.001.9513] at 9514

<sup>370</sup> See paragraph 27.257

<sup>371</sup> See paragraph 27.63

<sup>372</sup> Meeting minutes [SNB.001.9513] at 9514

<sup>373</sup> Dr Metters succeeded Dr Harris as DCMO and chairman of the ACVSB on 31 July 1989: Minute of ACVSB meeting of 3 July 1989 [SNB.001.9513]

<sup>374</sup> Appended to the agenda for the ACVSB meeting on 6 November 1989 [SNF.001.1383] at 1387. A further, fuller, report was produced in April 1990 [PEN.016.0075] and a formal report was published in the journal *Transfusion Medicine* in 1992 [PEN.017.0831]

- Following the introduction of the anti-HCV test the only justifications for routinely performing the ALT and anti-HBc tests were:
  - The possibility that ALT (in particular) would identify a 'window' of infectivity prior to seroconversion to anti-HCV.
  - The possibility that anti-HCV identified only one of a number of viruses which caused NANB Hepatitis.
- The introduction of other specific viral markers and increased sensitivity of the anti-HCV test might in due course render the subject of surrogate testing of academic interest. Meanwhile, the desirability of introducing these tests remained an issue of health economics.<sup>375</sup>

**27.259** Dr Gunson's report was considered at the fourth meeting of the ACVSB on 6 November 1989.<sup>376</sup> Dr Gunson drew members' attention to the non-specificity of ALT testing brought out in the report. He also reported discussion at a meeting in Rome sponsored by Chiron. The debate on use of the Chiron test is discussed in Chapter 31, *The Introduction of Screening of Donated Blood for Hepatitis C*. So far as surrogate tests for ALT and anti-HBc are concerned it is reported that Dr Gunson commented that there was a question mark hanging over their status. After discussion of the Chiron test, it was the feeling of the Advisory Committee that there was no case for using surrogate tests for NANB Hepatitis. That was largely the end of the issue of general surrogate testing in the UK as consideration turned instead to the evaluation and eventual introduction, on 1 September 1991, of the Chiron/Ortho test for antibody to Hepatitis C.

### *UK Postscript–1990s*

**27.260** Apart from sporadic references to surrogate screening for specific purposes, there was no independent consideration given in Scotland at this time to the introduction of surrogate testing, consistent with the decision that the procedures would not be introduced before the DHSS and the SHHD, on the advice of the expert advisory bodies, supported and funded them.<sup>377</sup> On 12 March 1990, Mr David McIntosh (General Manager, SNBTS) wrote to Dr McIntyre (SHHD) on the subject of ALT donation testing.<sup>378</sup> Subject to advice from the ACVSB, Mr McIntosh's understanding was that neither the SNBTS nor the NBTS would be introducing ALT testing for the time being and that neither the SHHD nor the DoH recommended that such testing should be introduced. Equally, however, it was anticipated that there could be a need to start new testing procedures, probably including ALT testing, in conjunction with another test or tests. There was a possibility of having to take rapid steps during the course of the summer. Consistent with that possibility in July 1990, a revenue bid for funding for ALT and anti-HBc testing was submitted by the SNBTS for 1991–92.<sup>379</sup> It was, however, considered highly unlikely that ALT and anti-HBc tests would be introduced into routine practice in the forthcoming financial year and the provisions were carried forward to the next year. In the event, the introduction of HCV testing superseded the need for provision of surrogate testing.

<sup>375</sup> Report (ACVSB version) [SNF.001.1383] at 1388–1389

<sup>376</sup> Meeting minutes [SNB.001.9563] at 9566–9567

<sup>377</sup> See Preliminary Report paragraphs 9.188 and 9.189

<sup>378</sup> Letter [SGH.002.7958]

<sup>379</sup> Public Expenditure Survey, bid number PES90 1.2.a.ii [SNB.002.7426] at 7433. The date for the bid is taken from the Agenda [SNB.002.7404] for the SNBTS management meeting of February 1991.



**27.261** The NBTS and the SNBTS were awaiting the outcome of the Ortho anti-HCV trial in progress before taking a decision but the broad policy issues had by this time been referred to the ACVSB. It was that body's advice that, in November 1989, effectively brought to an end the active consideration of general surrogate testing of blood donations and blood donors in the UK. By that time the practice had already been adopted in the USA and in some European countries.

**27.262** On 8 February 1990 the American Association of Blood Banks, the American Red Cross and the Council of Community Blood Centres issued a joint statement: 'Guidelines for planning the implementation of anti-HCV testing of blood and components for transfusion'.<sup>380</sup> The statement recommended that ALT and anti-HBc screening of blood donations should continue until it could be demonstrated that NANB Hepatitis agents other than the Hepatitis C virus were not a significant cause of transfusion-associated hepatitis.

**27.263** In this respect, however, practice in the USA does not provide guidance. Pragmatic considerations dictated the continuance of established practice in the USA and there was nothing to suggest that the decision had been driven by new insights into the efficacy of surrogate testing.

**27.264** Professor Cash drew the Inquiry's attention to evidence that consideration had been given in England in the early- and mid-1990s to the ALT testing of plasma sent to the BPL for the manufacture of albumin and intravenous immunoglobulin.<sup>381</sup> While it is unclear whether ALT testing of plasma for the BPL was actually introduced in England,<sup>382</sup> it appears that the consideration given to such testing was based solely on economic factors (as such testing would allow excess fractionated products manufactured by the BPL to be sold abroad rather than destroyed) and it was expressly disavowed that the use of ALT testing of plasma that was to be used for the manufacture of blood products implied any safety benefit.<sup>383</sup>

### Studies conducted after the Ortho anti-HCV test became available

**27.265** It is convenient at this stage to consider various studies that were carried out after the Ortho anti-HCV test became available. In short, while studies indicated that ALT screening of donors is likely to have materially reduced the incidence of transfusion-transmitted NANB Hepatitis, it is not possible to quantify that reduction with any degree of accuracy. Furthermore, the results of these studies were not available until after anti-HCV screening had been introduced in the UK, in September 1991.

**27.266** In common with the rest of the UK, Scotland introduced anti-HCV screening on 1 September 1991. In the first six months of testing the prevalence of HCV infection among blood donors was 0.088%.<sup>384</sup> Of the 159 HCV positive donors identified, 151 responded to the invitation for further counselling and follow-up and 59% (89) of these

<sup>380</sup> Guidelines for Planning the Implementation of Anti-HCV Testing of Blood and Components for Transfusion [SNB.001.9825]

<sup>381</sup> Additional statement from Professor Cash [PEN.017.1885] at 1889–1890

<sup>382</sup> See the supplementary statements by Professor Cash [PEN.017.2635], Dr Foster [PEN.017.2636] and Dr Perry [PEN.017.2777]

<sup>383</sup> See, for example, the discussion in the September 1994 revised report of the NBS working group on ALT testing of plasma [SGH.008.7021] and the discussion of that report at the third meeting of the Advisory Committee on the Microbiological Safety of Blood and Tissues for Transplantation (the successor committee to the ACVSB) on 29 September 1994 [DOH.001.0021] at 0026–0028

<sup>384</sup> Crawford et al, 'Prevalence and epidemiological characteristics of hepatitis C in Scottish blood donors', *Transfusion Medicine*, 1994; 4:121 [PEN.002.0582]

151 HCV-positive donors had ALT levels above the upper limit of normal.<sup>385</sup> This was not a random sample, however, but a self-selected group and, importantly, it could not be inferred that excluding all donors with elevated ALT (ie above the upper limit of the laboratory's reference range) would have prevented 59% of cases of transfusion-related Hepatitis C infection. As Dr Gillon explained:

[T]he vast majority of the carriers of Hepatitis C were at levels below the cut-offs that were proposed. And looking at this 59[%] figure, that was based on a relatively low cut-off – well, in Edinburgh it was 40 units per litre. It was probably the same elsewhere, which is not what we would have used in practice.<sup>386</sup>

**27.267** Once more sensitive HCV tests became available, Dr Dow and colleagues tested samples stored from his study undertaken between 1980 and 1984.<sup>387</sup> In the study, a total of 54 donations – 50 from prison donors and four from other donors – were found to have ALT values in excess of 2.5 times the upper limit of normal. Thirty-two of these samples were stored frozen and tested with various HCV tests including the Polymerase Chain Reaction (PCR) test. Twenty-one of the 32 stored samples (65.6%) were positive on PCR testing. This was a relatively high proportion on any view. However, it probably reflected the higher incidence of Hepatitis C in the prison population in the first half of the 1980s and cannot be held to be representative of the correlation between surrogate markers and HCV infection generally.

**27.268** The 1989 evaluation study of the first generation Ortho anti-HCV test by Dr Dow and colleagues should also be noted.<sup>388</sup> Granted the insensitivity of this test, it is interesting nevertheless to note that only 15 of the 2745 donations tested (0.54%) were positive on initial screen test and, of these, 13 were repeatedly reactive on repeat testing in duplicate. All 2745 donations had been tested for ALT levels in the earlier exercise in 1987 and 1988. Only one of the 15 initial screen positive donations had an abnormal ALT level.

**27.269** Later studies have indicated that, in some countries at least, surrogate testing was more effective in screening out HCV from donor blood than the UK study and, indeed, the early TTV and NIH studies in the USA had suggested it might be. Once anti-HCV tests became available, the NIH and TTV study groups tested stored sera collected from a relatively small number of patients in whom NANB Hepatitis had developed after transfusion.<sup>389</sup> The NIH group estimated that in their study ALT and anti-HBc screening would have detected approximately one half of the anti-HCV positive donors involved in the transmission of hepatitis.<sup>390</sup> The TTV group reported that just over 70% of cases of post-transfusion Hepatitis C in their study were associated with the presence of surrogate markers in donors.<sup>391</sup> The tests used were of the first generation, however, and lacked sensitivity, as discussed in Chapter 31, *The Introduction of Screening of Donated Blood for Hepatitis C*.

<sup>385</sup> Ibid [PEN.002.0582] at 0583. Dr Dow gave evidence that 'we were aware that 25% of all HCV confirmed positives were anti-HBc reactive', although it is not clear what the source of that information was: Statement [PEN.017.1925] at 1930

<sup>386</sup> Day 65, pages 106–107

<sup>387</sup> Dow et al, 'Failure of 2nd- and 3rd-generation HCV ELISA and RIBA to detect HCV Polymerase Chain Reaction-Positive donations', *Vox Sanguinis*, 1994; 67:236 [PEN.014.0072]

<sup>388</sup> SNBTS Evaluation of the Ortho HCV Antibody Elisa Test System-Preliminary Report – October 1989 [SNB.006.1596]

<sup>389</sup> Alter et al, 'Detection of antibody to hepatitis C virus in prospectively followed transfusion recipients with acute and chronic [NANB] hepatitis', *New England Journal of Medicine*, 1989; 321:1494 [SNB.001.9854] and Aach et al, 'Hepatitis C virus infection in post-transfusion hepatitis', *New England Journal of Medicine*, 1991; 325:1325 [LIT.001.0851]

<sup>390</sup> Alter et al, 'Detection of antibody to hepatitis C virus in prospectively followed transfusion recipients with acute and chronic [NANB] hepatitis', *New England Journal of Medicine*, 1989, 321:1494 [SNB.001.9854], Abstract

<sup>391</sup> Aach et al, 'Hepatitis C virus infection in post-transfusion hepatitis', *New England Journal of Medicine*, 1991; 325:1325 [LIT.001.0851] at 0854

**27.270** Another large US study (carried out in Baltimore and Houston) found that the introduction of surrogate testing had reduced by 60% the risk of patients developing anti-HCV.<sup>392</sup> In particular, of 912 patients undergoing cardiac surgery who received transfusions between April 1985 and September 1986, at a time when donors were not screened for surrogate markers, 35 patients seroconverted<sup>393</sup> to anti-HCV (an attack rate of 3.84%). Of 976 patients who received transfusions after surrogate testing was introduced in October 1986, only 15 seroconverted to anti-HCV (an attack rate of 1.54%).<sup>394</sup> In interpreting the data from this study, however, one must bear in mind that, even without the introduction of surrogate testing in the USA, rates of post-transfusion hepatitis may have reduced as a result of the HIV exclusion measures taken from 1984 onwards. In his evidence to the Inquiry, for example, Dr McClelland noted that the authors of the Canadian paper discussed below had observed that there had been a similar reduction in the prevalence of post-transfusion hepatitis in Canada over the same period, in the absence of the introduction of surrogate testing.<sup>395</sup>

**27.271** That Canadian study into post-transfusion hepatitis was carried out between 1988 and 1992.<sup>396</sup> In one group of patients who received blood transfusion, units which were positive for NANB Hepatitis surrogate markers were withheld, while in the other group of patients such units were not withheld. Samples from 2277 patients in the group in which units positive for surrogate markers were not withheld were tested retrospectively when the anti-HCV test became available. It was found that 10 patients (0.44%) had developed Hepatitis C. Of 2311 patients in the group in which units positive for surrogate markers were withheld, only three patients (0.13%) developed Hepatitis C.<sup>397</sup> The authors concluded that withholding blood containing surrogate markers reduced by 70% the rate of post-transfusion HCV in their study.<sup>398</sup> Interpreting the study, however, may be complicated by the fact that Canada introduced screening of donors for anti-HCV in May 1990, part way through the study.<sup>399</sup>

**27.272** In Finland, a prospective study was carried out between 1987 and 1989 which aimed, as one of its goals, to determine the predictive value in donor screening of surrogate marker candidates.<sup>400</sup> Stored samples were tested with first generation anti-HCV tests once these tests became available. Six of the 145 recipients (4.14%) of at least one unit of blood with raised ALT levels<sup>401</sup> developed NANB Hepatitis (as measured by elevation of ALT levels post-transfusion). That figure is in contrast to five of the 540 recipients (0.93%) who received only blood with normal ALT levels.<sup>402</sup> The positive predictive value of ALT (the percentage of cases of NANB Hepatitis among all recipients of blood with elevated

<sup>392</sup> Donahue et al, 'The declining risk of post-transfusion hepatitis C virus infection', *New England Journal of Medicine*, 1992; 327:369 [PEN.017.2672] at 2675

<sup>393</sup> Seroconversion is the development of antibodies as a result of infection

<sup>394</sup> Donahue et al, 'The declining risk of post-transfusion hepatitis C virus infection', *New England Journal of Medicine*, 1992; 327:369 [PEN.017.2672] at 2674, Table 2 and Abstract

<sup>395</sup> Day 64, pages 62–63

<sup>396</sup> Blajchman et al, 'Post-transfusion hepatitis: impact of [NANB] hepatitis surrogate tests', 1995, *The Lancet*, 345:21 [LIT.001.3223]

<sup>397</sup> Ibid [LIT.001.3223] at 3224, Table 2

<sup>398</sup> Ibid [LIT.001.3223] at 3223, Summary

<sup>399</sup> Ibid [LIT.001.3223] at 3223, Introduction. Dr McClelland, for example, stated, 'I would stress that this is not a simple paper and the more I looked at it, the more I felt less confident in the conclusions I can draw from it.' Day 64, Page 67

<sup>400</sup> Ebeling et al, '[ALT], gamma-glutamyltransferase, [anti-HBc] and [anti-HCV] in blood donor screening', *Vox Sanguinis*, 1991; 60:219 [PEN.017.1763]

<sup>401</sup> ie  $\geq 58$  U/l

<sup>402</sup> Ebeling et al, '[ALT], gamma-glutamyltransferase, [anti-HBc] and [anti-HCV] in blood donor screening', *Vox Sanguinis*, 1991; 60:219 [PEN.017.1763] at 1764

ALT) was only 4.1%.<sup>403</sup> No correlation was found between the presence of anti-HBc in donors and the development of NANB Hepatitis in recipients.<sup>404</sup>

## Discussion

### *Prospective study of post-transfusion NANB Hepatitis in the UK*

**27.273** At any time during the period 1981–88, the introduction of surrogate testing for NANB Hepatitis virus infection of donor blood, or of blood components and products, would have involved significant expenditure. It would have been considered a matter of such importance at the time to have required ministerial approval.<sup>405</sup>

**27.274** Ministerial decisions might have involved political considerations and almost certainly would have required the balancing of competing demands for funding. Before that stage was reached, however, the preliminary course that had to be negotiated, before ministers were consulted, would have included scientific and medical input and administrative discussions and decisions.

**27.275** The benefit of surrogate testing would have depended on the efficacy of the test or tests used in identifying blood and blood components that carried risk for the recipient. A decision to introduce testing would have required information and advice on a number of interrelated factors, including:

- The prevalence of infection in the relevant donor population or populations.
- The sensitivity of the tests as applied to those people (a measure of the efficiency of the test in identifying people with the target disease).
- The specificity of the tests as applied to those people (a measure of the efficiency of the test in identifying people without the target disease).
- The incidence of post-transfusion hepatitis.
- The clinical significance of post-transfusion NANB Hepatitis.
- The impact of testing on the donor population or populations.
- The cost/benefit balance found on analysis of all relevant information.

**27.276** The issue of whether or not to introduce surrogate testing of blood donors for NANB Hepatitis was never put to ministers and the reasons for that changed through the 1980s. This section deals with events at the beginning of the period that had long-lasting consequences. Those events, involving discussions within scientific and medical advisory groups, prevented research into the first three factors listed above: the prevalence of infection and the sensitivity and specificity of available tests.

**27.277** The MRC report of the Maycock Group study into post-transfusion hepatitis carried out between 1969 and 1971, was published in 1974.<sup>406</sup> As previously noted, it carried the authority of Professor Zuckerman and Professor Sherlock in addition to that of Sir William Maycock. The findings were influenced by the approach adopted: elevated ALT values alone were not regarded as providing sufficient evidence of hepatitis. The

<sup>403</sup> Ibid [PEN.017.1763] at 1765

<sup>404</sup> Ibid at 1766

<sup>405</sup> Mr Macniven – Day 65, page 140

<sup>406</sup> Medical Research Council, 'Post-transfusion hepatitis in a London hospital', *Journal of Hygiene*, 1974; 73:173–188 [LIT.001.0116]

overall incidence of icteric and anicteric hepatitis (that is, hepatitis with or without clinical jaundice) was calculated to be 1% – lower than in other countries, at least in part due to the factors stipulated by the authors as prerequisites of diagnosis. A range of factors that might have influenced the result were considered in the discussion part of the paper but none of them was thought to undermine the overall assessment. The MRC study was regarded for many years as proof that the incidence of post-transfusion NANB Hepatitis in the UK was not a significant problem whereas, when properly analysed and having regard to the limitations of the study, it could offer no such assurance.

**27.278** As was the case with Dr Rosemary Biggs' report of the incidence of episodes of jaundice among haemophilia patients treated with blood products, also published in 1974,<sup>407</sup> the data discussed in the MRC report were collected before the existence of NANB Hepatitis was postulated. The seminal article by Alfred Prince and others was published on 3 August 1974.<sup>408</sup> Dr Biggs' data were drawn from returns from Haemophilia Centres for the period 1969 to 1971 and reflected the perception at that time that jaundice was the appropriate focus for assessment of the incidence of transmitted virus infection.<sup>409</sup>

**27.279** When the MRC ad hoc meeting took place on 12 February 1979<sup>410</sup> to discuss, amongst other matters, growing anxiety about the threat of NANB Hepatitis, it was recognised that ALT (referred to by its alternative name, SGPT in the minute) testing could be a useful pointer to NANB Hepatitis infection. The views of Dr Tom Cleghorn and Professor Sherlock that post-transfusion hepatitis 'must now be rare' were countered by Professor Zuckerman's observation that much NANB Hepatitis might be anicteric and might progress to chronic liver disease, however mild the initial infection. It is also clear that Sir William Maycock recognised that there was a lack of data on the prevalence of post-transfusion hepatitis. His proposal that a survey of post-transfusion hepatitis be set up was, however, rejected. The prevailing view was that until there were specific markers, a survey of post-transfusion hepatitis was not justified.

**27.280** Having regard to the published data from 1974, the effect of the decision, so far as the MRC was concerned, was that other research concerning viral hepatitis should proceed in the absence of relevant data about the prevalence of NANB Hepatitis in the UK. Dr McClelland's evidence to the Inquiry that the report of the 1974 MRC study did not, in his view, provide the information required, is accepted as accurate generally.<sup>411</sup>

**27.281** The outcome of the meeting of 12 February 1979 included a decision to set up the Working Party on Post Transfusion Hepatitis which met on 14 February 1980.<sup>412</sup> Its agreed functions included investigations to assess the incidence of NANB Hepatitis in the UK, particularly as associated with blood transfusion, the characterisation of the agent of transmission and the development of diagnostic tests. There was discussion of the intelligence available to the participants about cases of NANB Hepatitis. Against that background, Dr McClelland who to the other members of the Working Party was then a

<sup>407</sup> Biggs, 'Jaundice and antibodies directed against Factors VIII and IX in patients treated for haemophilia or Christmas disease in the United Kingdom', *British Journal of Haematology*, 1974; 26:313–329 [LIT.001.0099]

<sup>408</sup> Prince et al, Long-incubation Post-transfusion Hepatitis Without Serological Evidence of Exposure to Hepatitis-B Virus, *The Lancet*, 3 August 1974 [LIT.001.0363]. See Chapter 14, paragraph 14.64.

<sup>409</sup> Biggs, 'Jaundice and antibodies directed against factor VIII and IX in patients treated for haemophilia or Christmas disease in the United Kingdom', *British Journal of Haematology*, 1974; 26:313- 329 [LIT.001.0099]

<sup>410</sup> Meeting minutes [PEN.017.1737]

<sup>411</sup> Day 63, page 71. Comments on the study were made in the Preliminary Report at paragraphs 6.23 and 6.24. See chapter 14, *Knowledge of Viral Hepatitis 1*, paragraphs 14.19-14.22

<sup>412</sup> Meeting minutes [PEN.017.1710]

colleague without an acknowledged reputation in developing and directing large complex studies, suggested that a multi-centred study of transfusion-associated NANB Hepatitis might be sponsored by the Working Party. The minute of the meeting is rather perplexing in that, on the one hand, it noted that it was agreed that Dr McClelland's proposal should be deferred until candidate laboratory tests were available (an agreement that he did not remember)<sup>413</sup> and, on the other hand, it records agreement that there should be epidemiological surveys to assess the size of the problem in relation to blood transfusion. The minute also reported that MRC studies had already received a grant for research into the incidence, epidemiology and clinical features of NANB Hepatitis.<sup>414</sup>

**27.282** Dr McClelland clearly did not consider that he had been precluded from developing his proposal and discussed it with the SNBTS Directors on 23 June 1981 before presenting a draft protocol for a multi-centre study to the MRC Working Party on 25 June 1981.<sup>415</sup> It is not necessary to resolve the questions that arise from the minute of 14 February 1980; what happened at the meeting on 25 June 1981 is of greater significance. Significantly, as recollected by Dr McClelland, Professor Zuckerman insisted that a study into post-transfusion hepatitis had already been carried out (a reference to the MRC study reported in 1974) and 'it didn't need to be done again'.<sup>416</sup> The minute of the meeting noted that Professor Zuckerman commented on the earlier study, noted that the sera collected were available for evaluation of candidate tests for NANB Hepatitis and said of Dr McClelland's proposal: 'A careful evaluation of the need for such a project should be carried out before the Working Party could recommend to the MRC that a fresh study should be sponsored.'<sup>417</sup> Professor Zuckerman left the meeting before the discussion was concluded. The remaining members of the Working Party decided that Dr McClelland's proposals could be reconsidered later. They clearly believed that the group had a future. However, the MRC Working Party did not meet again and the prospect of an MRC sponsored study along the lines proposed by Dr McClelland disappeared.

**27.283** The initiative passed to the transfusion services' Working Party on Transfusion Associated Hepatitis which, as discussed above, met on 27 September 1982 and on three occasions in 1983 before lapsing and being reconvened on 24 November 1986. While Dr McClelland had continued to advocate a large-scale prospective study into NANB Hepatitis in the UK when the Working Party met in 1982 and 1983, by the time the Working Party was reconvened in late 1986 the view of the members was that a prospective study was impracticable on the grounds of both cost and the requirement for a large sample group.

**27.284** As more fully set out above, the view of the Scottish and English transfusion services in the late 1980s (and which was supported at various times by officials in the SHHD and the DHSS) remained that it was not feasible to carry out a large-scale prospective study of NANB Hepatitis and that, instead, there should be a limited study into the incidence of surrogate markers in donors. Such a study would not include the follow-up of recipients and thus would be of little or no assistance in determining the efficacy of surrogate screening in reducing the incidence of post-transfusion NANB Hepatitis.

---

<sup>413</sup> Day 63, page 63

<sup>414</sup> This was a reference to the MRC study reported in 1974.

<sup>415</sup> Meeting minutes [PEN.017.1478]; draft protocol [PEN.017.1486]

<sup>416</sup> Day 63, page 66

<sup>417</sup> Meeting minutes [PEN.017.1478] at 1480

**27.285** Despite the best efforts of Dr McClelland, no sufficiently large-scale prospective study was ever carried out on a coordinated basis to determine the likely prevalence of post-transfusion NANB Hepatitis in the UK. Without such a study having been carried out it was, and remains, difficult to come to an informed view on the likely prevalence of post-transfusion NANB Hepatitis in the UK generally and in Scotland in particular.<sup>418</sup>

**27.286** In his oral evidence Professor Leikola commented, with reference to the later 1980s:

I think that what was regrettable was that no ... large study was performed in the UK in order to find out what would be the value of especially ALT, both in recipients of blood and donors of blood .... We [in Finland] did not introduce ALT testing before our study was done ....<sup>419</sup>

**27.287** If he had a criticism of events in Scotland, it related to the failure to carry out a prospective study into post-transfusion NANB Hepatitis involving the follow-up of recipients (in the UK as a whole), rather than the failure to introduce surrogate testing.<sup>420</sup>

**27.288** However, in considering Professor Leikola's criticism a number of matters ought to be borne in mind. The first is that the Finnish study, 'Post-transfusion hepatitis after open-heart surgery in Finland – a prospective study' states that it was carried out between 1987 and 1989, and the second is that the Finnish Red Cross Blood Transfusion Service charged the hospitals for their products and services and could, therefore, finance the study themselves. The SNBTS was dependant on funding from the SHHD or other bodies for such a study, and that had a material effect on its ability to carry it out. Professor Leikola indicated that the catalysts for the Finnish study (which started in December 1987) were the decision made in the USA in 1986 to introduce surrogate testing and the discussions at the Council of Europe in 1987. The Council's Committee of Experts on Blood Transfusion and Immunohematology had not then recommended the introduction routinely of non-specific tests for evidence of NANB Hepatitis infectivity of blood donors but had indicated that '[i]ndividual countries would have to assess the situation locally and decide on the appropriate action to take'.<sup>421</sup> By March 1987 the SNBTS Directors had agreed to recommend to the SHHD that surrogate testing for NANB Hepatitis should be implemented with effect from 1 April 1988 as a national development requiring strictly new funding. In their letter of 4 July 1987 to *The Lancet*, entitled 'Testing blood donors for (NANB) Hepatitis: irrational, perhaps, but inescapable' they explained why they considered the introduction of surrogate testing, despite the absence of relevant data, to be 'virtually inescapable'. In particular, they adverted to forthcoming legislation that would provide for strict liability for harm caused by products unless all known measures had been taken to avoid the risk, to the possibility that such testing would reduce the level of infectivity of pooled plasma products and to consumers' wishes to be supplied with 'NANB tested' products, in light of the fact that commercial manufacturers were now doing such testing and would be likely to market their products as being safer. Haemophilia Directors had unrestricted clinical freedom to opt either for NHS fractionated products or commercially fractionated products. Had surrogate testing been introduced then blood used for blood products, blood components and whole blood would have been screened.

<sup>418</sup> This is of continuing significance in relation to estimates of HCV prevalence at the present time: see Chapter 3, *Statistics*.

<sup>419</sup> Day 71, pages 61–62

<sup>420</sup> Ibid page 63. For the Finnish study, see Ebeling et al, 'Post-transfusion hepatitis after open-heart surgery in Finland – a prospective study', *Transfusion Medicine*, 1991; 1:103–108 [PEN.017.1777]

<sup>421</sup> Council of Europe: Extract from the report of the Committee of Experts on Blood Transfusion and Immunohaematology, 19–20 May 1987 [SNB.001.9445] at 9450

**27.289** It is regrettable that Dr McClelland's proposals in the early 1980s were dismissed and that they were not taken up by others. Whilst the results of a large scale prospective study might not have led to the introduction of surrogate testing, data about the prevalence of NANB Hepatitis and the likely efficacy of surrogate testing in reducing the incidence of post-transfusion NANB Hepatitis would have led to more informed decision making. In addition, a library of samples might have been available for preservation to use in subsequent research into the Chiron anti-HCV test. In short, there were adverse long-term consequences of the decisions made by the wider scientific and medical community, first, not to follow the initial suggestion of Sir William Maycock in 1979 and, secondly, not to follow Dr McClelland's proposals in the early 1980s. However, it must be borne in mind that in Finland, despite the existence of the small 1979 study, a new, larger study was considered necessary in 1987 in consequence of the international developments described above and the effect of the AIDS risk in 1983 and 1984 on donor selection criteria. Had the SNBTS undertaken a study in 1987, as occurred in Finland, it is unlikely that it would have been completed before May 1988, when Chiron announced that they had identified, cloned and expressed proteins from an NANB virus and had developed a prototype immunoassay that might lead to a screening test. According to the Directors' letter in *The Lancet*, the study would produce no 'answer' for three to four years.

#### The administrative context

**27.290** The ultimate responsibility for deciding whether surrogate testing should have been introduced lay with the UK Government.<sup>422</sup> The Secretary of State for Scotland had cabinet responsibility, but ordinarily the junior Scottish minister, whose remit at the relevant time included Scottish health matters, would have been involved before an issue was referred to the Secretary of State. The minister would have acted on advice received from appropriate committees and from officials including, in particular, SHHD medical officers. However, apart from issues raised at ministerial level in the first place, it was for SHHD administrators to decide what issues should be referred to ministers for decision. In that context, there could be a material difference in approach depending on whether or not positive action was proposed.

**27.291** In the SHHD, the issue of surrogate testing was dealt with on a day-to-day basis by Dr Forrester, Senior Medical Officer, and Dr Archibald McIntyre, Principal Medical Officer. On occasion Dr Scott, DCMO, was also involved in considering the issue. Dr Macdonald, CMO, said in oral evidence that he was kept informed of the issue.<sup>423</sup> On the administrative side of the SHHD, surrogate testing was dealt with at a day-to-day level by Mr Alexander Murray, Senior Executive Officer, and by Mr Macniven, Assistant Secretary. On occasion, the issue reached the level of Mr Hugh Morison, Under Secretary.<sup>424</sup>

**27.292** In his evidence to the Inquiry Mr Macniven agreed that the introduction of a new screening test, such as surrogate screening with its significant financial implications, would have required ministerial approval. He was asked whether a decision not to introduce a screening test, in particular one that was recommended by the SNBTS Directors, was also a matter of such importance that a ministerial decision ought to have been sought. He replied:

<sup>422</sup> See chapter 17, *Blood and Blood Products: Management* for the statutory structure and administrative background.

<sup>423</sup> Day 66, pages 63–64

<sup>424</sup> See, for example, Dr McIntyre's minute of 6 June 1987 to Dr Scott, Mr Morison et al [SGH.002.8127] and the evidence of Mr Macniven – Day 65, pages 174–175



Not necessarily. Obviously, although the Secretary of State ... had at that time statutory responsibility for the health service in Scotland, and a great many other things beside, it would have been impracticable for the Secretary of State personally or indeed a junior minister personally to take a decision on every question that the Scottish Office, as it was then called, was considering. It's a matter of judgment when a topic should be put to ministers, and it looks as if our judgment at the time, certainly the documentary evidence suggests that our judgment at the time was that that did not need to be put to ministers.<sup>425</sup>

**27.293** In addition to matters arising from the general administrative structure, applications for major research funding might require formal review by the CSO Biomedical Research Committee.

**27.294** While the views of SNBTS staff were an important element in the picture, the question as to whether or not surrogate testing should be introduced was not put to Scottish Ministers for decision and, on the evidence as a whole, was never resolved at official level.

**27.295** A decision was not taken by anyone, whether an official of the SHHD or a minister, not to introduce surrogate testing but, instead, SHHD officials took the view that there was not sufficient evidence to recommend to ministers that such testing should be introduced.<sup>426</sup> Dr Macdonald's evidence suggested that there never was a resolution:

I'm not quite sure that a final decision was ever taken. I think we were still agonising over the question of setting up research. Frankly, I just don't quite remember the end of it, except that we didn't do it.<sup>427</sup>

**27.296** SHHD officials, in particular medical officers, considered that there were good reasons for not introducing surrogate testing.<sup>428</sup> The fact that the Department of Health did not support the introduction of surrogate testing was also an important factor in their consideration.

**27.297** Dr Macdonald said:

If departmental medical staff had been persuaded, after consulting colleagues with relevant expertise, that surrogate testing for NANBH was a reliable procedure which would give few false results (positive or negative) and be free from adverse effects, they would have advised administrators accordingly and it would have been highly likely that funding would have been provided. In the event departmental medical staff were not sufficiently persuaded and advice reflected this.<sup>429</sup>

**27.298** Dr Macdonald was not personally involved in the consideration being given in the Department to surrogate testing<sup>430</sup> but he was kept informed of what was happening and did not see any need to intervene.<sup>431</sup> He further explained that if the advice from his colleagues appeared to be veering towards introducing surrogate testing, he would have found it necessary to intervene. He explained his reasons:

---

<sup>425</sup> Day 65, Page 140. See also Day 78, page 30

<sup>426</sup> Ibid page 141

<sup>427</sup> Day 66, page 64

<sup>428</sup> Day 65, pages 137 and 156–157

<sup>429</sup> Dr MacDonald's Witness Statement [PEN.017.1702] at 1704

<sup>430</sup> The matter being dealt with by Dr Scott, DCMO, Dr McIntyre, PMO and Dr Forrester, SHO

<sup>431</sup> Day 66, pages 63–64

One is that ... it wouldn't be the complete answer to the problem as far as the recipients of blood and blood products were concerned, but it would also have repercussions on the donors. Testing the donors ... would undoubtedly have yielded a fairly appreciable number of positives, some of which would be false and, at the other end, a fair number of negatives, some of which would be false.

If you then – what are you going to do about the positives? You won't know which are false and which are genuine ... there was some risk that we would find that donors would be disturbed by this situation and I think that was something which we really should not have risked doing. That's one side of it.

The other is a point ... about DHSS ... the point that I think has to be made is that DHSS and the Scottish Office, which included SHHD, and for that matter, the Welsh Office, were three different departments of the same government, each responsible to a Secretary of State in that government and the Secretaries of State were sitting together round the same cabinet table.

On an issue of this kind, where there was a group, the Haemophilia Society, and perhaps others, watching all our moves carefully, if one of us – and it might have been us – ... decided to institute testing and the other didn't, that would be extremely difficult to explain. One of us must be right, one must be wrong, would be the reaction.

But it goes a little further than that because, as I recall it, we were facing a situation in which the Scottish [D]irectors were pressing for the introduction of testing and the English [D]irectors – I think pretty unanimously at that stage, the English Directors were against it. I don't think we could ignore the fact that there was a well informed body of opinion, not very far away, with a different view.

So I think in that situation I would certainly need to have become involved.<sup>432</sup>

**27.299** It was suggested to Dr Macdonald that the primary consideration of the SHHD throughout the relevant period was that there should not be any divergence in practice between England and Wales and Scotland. He replied:

I don't think that that – it was an important consideration, certainly, but I think that the staff in SHHD did attempt to form an opinion of their own and that opinion was that we should not go ahead. I think that, if we had agreed with the Scottish [D]irectors' view, Dr Scott would have said so, even if the outcome eventually ... had been different.<sup>433</sup>

**27.300** Dr Macdonald also said that, if he had intervened in the middle of 1987 on the question of surrogate testing, his involvement would have been to say to his medical colleagues that such testing should not be introduced rather than simply to say that there were wider issues which required to be considered.<sup>434</sup>

---

<sup>432</sup> Ibid pages 65–67

<sup>433</sup> Ibid page 157

<sup>434</sup> Ibid pages 67–68

**27.301** Dr Macdonald's succinct explanation as to why surrogate testing was not introduced was that: 'Essentially, there was too much uncertainty about various aspects of surrogate testing to justify introducing it.'<sup>435</sup> He referred to these concerns as relating to 'the quality of the testing'<sup>436</sup> and that 'the screening method was not really good enough'.<sup>437</sup>

**27.302** That explanation is acceptable as an accurate reflection of the factual position at the end of November 1987: the poor sensitivity and specificity of the proposed surrogate tests were likely to give rise to significant difficulties if used for mass screening of blood donors.

### The relationship between the DHSS and the SHHD

**27.303** Dr Macdonald was asked whether it would have been open to Scotland to introduce surrogate testing in the event that the SHHD had taken the view that it was justified but had been unable to persuade colleagues in the DHSS of that justification. He replied:

I think in a very theoretical sense. This was never tested. I think what would have happened, I can, I believe, have advised Scottish ministers that testing should be introduced in Scotland. The CMO and DHSS could have advised his ministers that it should not be tested in England. I think we would have been bound, each of us, to tell our ministers that the other minister was being given the opposite advice. I don't know what would have happened then.<sup>438</sup>

**27.304** He said that it could have become a matter for ministerial decision, possibly at cabinet level.<sup>439</sup> Before pressing matters that far, officials would have had to ask themselves whether they felt so strongly in favour of it that they really wanted their minister to press it.<sup>440</sup>

**27.305** Realistically, the introduction of surrogate testing was not, and was most unlikely ever to have become, an issue requiring a cabinet decision at this time. So far as officials were concerned – and in the first instance the initiative lay with them – it never reached the level of requiring Scottish ministerial decision. Scottish officials were far from convinced that there was an issue worth pressing. However, the possibility of independent action in Scotland led to a discussion of the relationship between the SHHD and the DHSS.

**27.306** There were issues of external perception that would have influenced ministers. Internally, the DHSS would have been expected to take a lead on major policy matters. It was the biggest department and, as Dr Macdonald put it:

SHHD and the Welsh Health Department, would have been expected to fit their policy around that. In other words, there can be a bit of a variation for local circumstances, but broadly the policy would be evolved in DHSS.<sup>441</sup>

---

<sup>435</sup> Dr MacDonald's Witness Statement [PEN.017.1702] at 1709

<sup>436</sup> Day 66, page 87

<sup>437</sup> Ibid pages 116–7

<sup>438</sup> Ibid page 82

<sup>439</sup> Ibid page 83

<sup>440</sup> Ibid page 84

<sup>441</sup> Ibid pages 80–81

**27.307** Practical expedients were adopted to avoid problems. Often an expert group would be assembled, sometimes very formally by ministers, and sometimes by the departments. There would usually be Scottish members who would contribute and would be able to give an account of the views of colleagues in Scotland, and an iterative debate would take place. Dr Macdonald thought that on the whole it worked reasonably well. The profession in Scotland was content with it but would have been less content if the DHSS involved only their English colleagues, though the DHSS was sensitive to the issue.<sup>442</sup>

**27.308** Dr Macdonald's view would not necessarily be shared by everyone who had ever participated as a sole Scottish representative on a UK committee dominated by English colleagues. Professor Cash could never have imagined Scotland being allowed by the SHHD 'to go off on our own'. In any event, he considered that there were good reasons relating to seeking to avoid legal liability, team work and the sharing of information for centres, or at least groups of centres, to act in unison in relation to introducing a new test.<sup>443</sup> While acknowledging the positive reasons for collaboration, his assessment of the prospects of Scotland being permitted to take independent action on a matter of this kind is accepted.

**27.309** Dr McClelland took a typically practical view of the position:

I think the decision probably rested with ... the Scottish minister responsible for health, ultimately, as it were, delegated down the line through the department and the [CSA], which was the channel through which our funding arose. But I think that's oversimplistic. I think the minister would inevitably be heavily dependent on the burden of the advice that he or she was given, and if there was very strong, clear, consistent, well-argued and rational advice coming from, say, the clinical and scientific community through the [SHHD] to the minister, I find it hard to believe that most ministers would not have acted according to it. And it's perfectly clear that the advice that was, as it were, coming from the relevant professional community was not clear and consistent.<sup>444</sup>

**27.310** He thought that while there were many obvious advantages in having a coordinated approach throughout the UK. If that meant that something he felt was important to patient safety, such as surrogate testing, was not going to be done, he would have given that a higher priority over 'keeping things tidy and avoiding problems of cross-border differences in practice'. He did, however, consider that surrogate testing could not have been introduced in Scotland without government funding and approval.<sup>445</sup>

**27.311** Dr McClelland's final observation reflected the ultimate reality: where UK government funding was required for major projects, the SHHD had limited scope for major independent initiatives.

**27.312** However, for immediate purposes, it was not a live issue: Scottish administrative officials never promoted for ministerial approval an independent Scottish scheme of surrogate testing. While influenced by the thinking of DHSS colleagues, that was a Scottish decision based on local advice.

---

<sup>442</sup> Ibid pages 80–81

<sup>443</sup> Day 70, pages 186–187

<sup>444</sup> Day 63, page 133

<sup>445</sup> Ibid pages 131–133

## The state of knowledge of NANB Hepatitis in the SHHD

**27.313** There is an issue whether the SHHD had the resources to form views on the threat posed by NANB Hepatitis generally or in particular relation to Scotland. In considering the state of knowledge expected of medical officers in the SHHD at the time Dr Macdonald said:

Generally speaking, we were not individuals who were taking up anything resembling specialist positions. There were one or two examples at variance with that, but broadly speaking we ... would have regarded ourselves as generalists.

....

[I]t is this kind of – relative lack of specialisation, maintaining a degree of generality that is what we wanted.<sup>446</sup>

**27.314** Dr Macdonald was asked what he would have expected his medical officers to do to inform themselves on a particular subject:

In broad terms, I would have expected them to keep up-to-date. I would – how shall I put this? I would perhaps warn him, if I was giving advice, that he has always to remember that the people he is dealing with in the subject know a lot more than he does and he is not going to get himself on to that level.

....

I think they have to go some way towards mastering the subject, but I think what we really expect of them is to be able to come in and tell us what people out there are thinking and be able to explain, to some extent, why they are thinking it, but not to go too deeply into the subject itself .... I think our function was to know enough about medical matters to know what we ought to be asking.<sup>447</sup>

**27.315** He and his colleagues would keep up to date with developments in medicine by reading journals, such as the *British Medical Journal*, *The Lancet* and several public health journals and by attending conferences.<sup>448</sup> As regards NANB Hepatitis, another source of information would be physicians who specialised in the diagnosis and treatment of patients with the disease. They might also have obtained information from the SNBTS Directors, the Scottish Haemophilia Directors and Professor Cash, as National Medical Director of the SNBTS.<sup>449</sup> In addition, SHHD medical officers attended meetings of various advisory committees and working parties as observers and, in that way, would also be able to obtain expert views and advice.<sup>450</sup>

---

<sup>446</sup> Day 66, pages 94–95

<sup>447</sup> Ibid pages 96–98

<sup>448</sup> Ibid page 102

<sup>449</sup> Dr Macdonald – Day 66, pages 130–132. Professor Cash resigned as Consultant Advisor to the SHHD in March 1986 – see his statement in that regard [PEN.017.2767]. Dr Macdonald was not of the view, however, that that changed his relationship with the SHHD in practice: Day 66, page 133. While that also appears to have been the view of Professor Cash in his oral evidence to the Inquiry (Day 72, pages 51–52), in his written evidence he stated that the position he had adopted in 1983 in respect of industrial action at the SNBTS ‘was the cause of an almost complete disruption in professional relations between some important and senior members of the SHHD’s medical team and me’ for a decade and had ‘irreparably damaged’ his professional relationship with Dr Scott, DCMO [PEN.017.2767].

<sup>450</sup> Witness Statement of Dr Scott, DCMO [PEN.017.1854] at 1855 and Witness Statement of Dr McIntyre, PMO [PEN.017.1858] at 1859.

**27.316** In his evidence to the Inquiry Dr Forrester stated that when he joined the SHHD he did not have a great deal of knowledge of problems among haemophilia patients. He explained that he was 'a relayer of information and the gatherer of information from the different sources it could come in'.<sup>451</sup> He did not 'attempt to fulfil the role of a free-standing authority in these matters at all'.<sup>452</sup> Dr McIntyre, Principal Medical Officer, had more experience and expertise in matters relating to the blood transfusion service. Dr Forrester considered that Dr McIntyre 'was always in a position of overlooking what I had done and I put it to him in writing and if there was anything amiss he would have told me'.<sup>453</sup>

**27.317** In various notes and minutes made at the time Dr Forrester commented on the clinical significance of NANB Hepatitis.<sup>454</sup> The general tenor of his comments in documents between 1986 and 1988 was to the effect that the disease was 'relatively benign', at least in the short term. Notwithstanding the risk of serious liver disease, he said that the expression 'relatively benign' was 'a numerical question'. A disease could be 'relatively benign in most cases – in practically all cases'.<sup>455</sup> In a follow-up e-mail to the Inquiry Dr Forrester explained:

Among the meanings of the word "benign" there are two that I believe apply. The first is that in medical and medico-scientific circles, if one form of a fatal disease takes much longer to prove fatal, and does so in fewer cases than another, it is usually termed "benign" in comparison. [Dr Forrester's minutes were directed at such circles.] But in ordinary discourse, and especially if oneself or one's relations are involved, no form of a disease that may prove fatal or disabling can be called "benign".<sup>456</sup>

**27.318** Dr Forrester's view on the prevalence and clinical significance of NANB Hepatitis was influenced by Dr Dow's PhD thesis and by advice received from Dr Reid of the Communicable Diseases Centre. Unfortunately, the Inquiry has been unable to obtain Dr Reid's written replies to Dr Forrester and can only rely on Dr Forrester's record made at the time of his understanding of Dr Reid's views.<sup>457</sup> As regards Dr Dow's thesis, its inadequacy as a means of estimating the true incidence of post-transfusion NANB Hepatitis has already been discussed.

**27.319** Dr Dow's study did not include as one of its purposes an attempt to investigate the clinical significance of NANB Hepatitis. As Dr Dow said to the Inquiry: 'There was no attempt to evaluate the seriousness of the disease, which would have required clinical evaluation by gastroenterologists.'<sup>458</sup> Dr Dow agreed with the suggestion made to him that one would have required to read his thesis along with the wider literature to obtain a more informed view of NANB Hepatitis.<sup>459</sup> He was surprised that a copy of his thesis had been sent to the SHHD but said:

<sup>451</sup> Day 66, page 11

<sup>452</sup> Ibid page 12

<sup>453</sup> Ibid page 13

<sup>454</sup> See note dated 12 June 1986 [SGH.002.8142]; short note dated 26 January 1987, 'Material for PMO Report' [SGH.003.1657]; minutes of meeting of SNBTS and Scottish Haemophilia Directors on 9 February 1987 [SGF.001.2261] at 2263; minute dated 30 August 1988 to the CMO and others [SGH.002.4672] at 4673

<sup>455</sup> Day 66, page 31

<sup>456</sup> E-mail from Dr Forrester dated 3 December 2011 [PEN.018.1481]

<sup>457</sup> See, in particular, Dr Forrester's note of 12 June 1986 [SGH.002.8142]

<sup>458</sup> Day 67, page 17

<sup>459</sup> Ibid pages 59 and 65

[I]t was probably the only study done on Scottish patients ... and it probably did give a grass roots level [view] of what was actually happening. It may have given the wrong impression but it was what we actually saw at the time and it was mild in comparison to Hepatitis A and Hepatitis B which really are very severe diseases in their acute form.<sup>460</sup>

**27.320** For his PhD thesis, Dr Dow had the benefit of supervision by Dr Follett, and of his expertise. No criticism is made by the Inquiry of that thesis which was, inevitably, of limited scope and influenced by the state of medical knowledge at the time, for example in relation to the association then made between 'infective jaundice' and NANB Hepatitis. It covered a discrete topic and was never intended to be an exegesis of the whole of contemporary knowledge of NANB Hepatitis.

**27.321** His surprise that the thesis was submitted to the SHHD was both admirable and realistic. Since he himself went on to conduct further research, it can reasonably be inferred that he would have indeed been surprised to learn of the degree of authority accorded within the SHHD to his original work.

**27.322** In his evidence to the Inquiry Dr Macdonald was asked whether there was a greater awareness of NANB Hepatitis among SHHD medical officers than the relatively brief comments contained in Dr Forrester's notes and minutes and said that he thought there was.<sup>461</sup> Dr Macdonald agreed with the suggestion that what was set out in the 7th edition of Patrick Mollison's standard textbook on blood transfusion medicine in the UK in 1983<sup>462</sup> represented the standard or level of knowledge that one would expect of a medical officer in the SHHD who was considering the subject (whether or not that knowledge was derived directly from Mollison's book). He suggested a need for caution when making statements in 1986, for example, about the seriousness of NANB Hepatitis.<sup>463</sup> Dr Macdonald was taken to the statement in the Preliminary Report that '[f]rom about 1985 onwards there appears to have been a growing awareness that [NANB] Hepatitis was a potentially serious and progressive disease which could lead, over time, to cirrhosis of the liver, hepatocellular cancer and death'.<sup>464</sup> He was asked whether that statement was consistent with the statement by Dr Forrester in his note dated 26 January 1987, 'Material for PMO Report', that '[t]his "hepatitis" is a residual rag-bag when Hepatitis B and Hepatitis A are excluded, and consequently no specific test can detect it. It is relatively benign'.<sup>465</sup> Dr Macdonald replied: 'Yes. Well, I think perhaps something should be added to the relatively benign statement to qualify it. Yes, I think a little more could have been said.'<sup>466</sup>

**27.323** In his evidence to the Inquiry Dr McClelland stated:

I think it's entirely reasonable that the relatively small cadre of medical staff in the Scottish Home and Health Department at that time couldn't be expected to be experts in hepatitis.

It does seem ... looking with the wisdom of the retrospectoscope [with the benefit of hindsight] that they were guided very much by one single piece of

---

<sup>460</sup> Ibid page 66

<sup>461</sup> Day 66, pages 119–120

<sup>462</sup> See comments on Mollison in chapter 15, *Knowledge of Viral Hepatitis 1975–1985*, from paragraph 15.130

<sup>463</sup> Day 66, pages 99–100

<sup>464</sup> Preliminary Report, paragraph 9.1

<sup>465</sup> Dr Forrester's note [SGH.003.1657]

<sup>466</sup> Day 66, pages 135–136

work, which was the Dow and Follett research, and didn't show – there wasn't much to see in the documentation that they had actually seriously tried to take a more independent look at the literature and the information that was available.<sup>467</sup>

**27.324** When considering Dr Forrester's contemporaneous comments about NANB Hepatitis one must be cautious. First, the records recovered are often relatively brief and may not represent a complete account of Dr Forrester's knowledge at the time. Secondly, Dr Forrester was a generalist public health doctor who would be reliant on the views of experts in particular fields. Thirdly, he was the most junior level of SHHD medical officer (and there is no documentation available to the Inquiry from a more senior medical officer correcting his understanding of the disease). Fourthly, at the material time, Dr Forrester was relatively new in position. Lastly, Dr Forrester's notes must be seen in their wider context – namely, that views in the medical profession about the potential long-term seriousness of NANB Hepatitis did not change overnight, but instead, evolved over time, from about 1985 onwards, as more evidence became available of the risk of progression to cirrhosis. As Dr Forrester put it in relation to his own understanding of the position: 'My impression was this was the way it did seem to able minds at the time. It doesn't mean it was true in the end.'<sup>468</sup>

**27.325** Of course, the available textbooks were slightly out of date: Sherlock had last published her standard textbook in 1981 and Mollison in 1983, and their views were widely relied on in more general textbooks of the period. English colleagues of Dr Forrester used Dr Dow's work as a peg on which to hang their own applications for funding, implicitly suggesting that it contained authoritative data on the position in Scotland.

**27.326** It is clear that Dr Dow came to appreciate that further study was necessary: the Dow, Mitchell and Follett letter to *The Lancet* on 13 June 1987<sup>469</sup> demonstrated that. They drew particular attention to the result of introducing abnormal ALT levels to the diagnosis of post-transfusion NANB Hepatitis in the USA where, when this was done, the rate of infection rose from 0.1–0.2 cases per 1000 units transfused to the significantly higher rate of 10–28 cases per 1000 units transfused. Furthermore, 99% of hepatitis cases were never brought to the attention of transfusion centres. In advocating a prospective study, they demonstrated that they had realised that the conclusions drawn earlier might have been wrong. It is unfortunate that SHHD officials did not adopt this view of the situation but, rather, persisted in according Dr Dow's original work such a high degree of authority.

**27.327** It is regrettable that the preliminary conclusions of Dr Dow's thesis became so firmly established as received wisdom within the SHHD until at least late 1987. Dr Forrester appears by 20 August 1987 to have understood the limitations of the study and clearly sought to influence the terms of the Biomedical Research Committee decision (on the Gillon/McClelland application for funding to join the UK multi-centre study) in his memorandum to Mr Macniven of 1 October 1987 to ensure that the need for new research was not excluded by that decision.<sup>470</sup> It is unclear whether others in the SHHD took the same view. Adherence to the view that the Dow research was a sufficient basis for a decision can only have been because relevant medical officers did not have the

---

<sup>467</sup> Day 64, page 47

<sup>468</sup> Day 66, page 14

<sup>469</sup> Dow et al, [NANB] 'Hepatitis surrogate testing of blood donations', *The Lancet*, 13 June 1987 [LIT.001.0346]

<sup>470</sup> See paragraphs 27.225–27.226 above



knowledge or experience required to assess and understand its limitations in the context of NANB Hepatitis. Given that they were essentially generalists, Medical Officers in the SHHD might have been expected to be less inclined to form and to express views on the highly specialist issues that arose. Instead, they might have been expected to take more formal, structured advice from experts, perhaps engaging a technical committee to advise them in the way indicated by Dr Macdonald and/or by liaising with their counterparts in the DHSS to form a UK committee such as the Advisory Committee on the Virological Safety of Blood, which was eventually set up in April 1989. However, it would be pure conjecture, at this juncture, to attempt to speculate what any advice from such a hypothetical committee would have been.

### ***Clinical significance of post-transfusion NANB Hepatitis***

**27.328** Apart from issues relating to the specificity, sensitivity and general effectiveness of surrogate screening tests as perceived in November 1987, other matters influenced official thinking. The clinical significance of NANB Hepatitis was among these. The evolving state of medical and scientific knowledge in respect of NANB Hepatitis/Hepatitis C is discussed more fully elsewhere in this report.<sup>471</sup> At the beginning of the 1980s NANB Hepatitis was considered to be a generally mild disease with an ‘uncertain but probably benign’ prognosis.<sup>472</sup> From the mid-1980s onwards there was a gradual move away from that assessment towards NANB Hepatitis being viewed as a potentially serious and progressive disease that could, for some patients at least, lead over time to cirrhosis of the liver, hepatocellular cancer and death.<sup>473</sup>

**27.329** There remained a persistent view throughout the 1980s in some quarters, however, that despite an increasing body of evidence to the contrary, NANB Hepatitis was only rarely transmitted by blood and was usually not particularly serious.<sup>474</sup>

**27.330** For administrators, however, the question was not whether one or other view of the risk of transmission or of the seriousness of the disease was correct in absolute terms. Rather, the issue was whether there was a sufficient body of reliable opinion that NANB Hepatitis did present a serious risk, to bring that into account in determining whether research was required and should be funded and what the scope of that research should be. It is clear that SHHD officials, including medical staff, were not competent to make that judgment themselves. They were confronted by conflicting views from people they were entitled to look to for expert advice. That was an additional factor pointing to the need for structured study of the problem, with the benefit of an expert committee to advise them. It is a matter of regret that by late 1987 sufficient information had not been gathered to reach an informed view.

**27.331** Apart from the fundamental question of the natural history of NANB Hepatitis, however, two further factors came to prominence in 1988: the impact of surrogate testing on the blood supply and the problems associated with counselling of donors.

---

<sup>471</sup> See Chapter 15, *Knowledge of Viral Hepatitis 2 – 1975–1985*

<sup>472</sup> Sherlock, S. *Diseases of the Liver and Biliary System*, 6th edition, 1981, page 259 (Preliminary Report, paras 6.110–6.114)

<sup>473</sup> See, for example, the publications listed in footnote 1 in Chapter 9 of the Preliminary Report. See also Chapter 16, *Knowledge of Viral Hepatitis 3 – 1986 onwards*.

<sup>474</sup> Dr McClelland’s C2 witness statement [PEN.017.0754]; see also Dr McClelland’s oral evidence – Day 63, pages 14–15 and 24–25

***Impact on the blood supply***

**27.332** Several studies were carried out into the likely loss of donations in the event surrogate testing was introduced.

**27.333** Dr Gillon's study of Edinburgh blood donors found that 2.4% of a cohort of regular donors had elevated ALT levels<sup>475</sup> and 2% was positive for anti-HBc. There was no overlap between these two donor groups with the result that, based on these findings, combined screening would have led to an initial loss of 4.4% of donations (from this cohort).<sup>476</sup> It was concluded that:

In view of the medical and economic implications of the introduction of these screening tests, and the poverty of data on the clinical significance of post-transfusion [NANB] hepatitis ... such a screening programme cannot be justified at present. Further studies are required, including a prospective controlled trial of the effects of screening.<sup>477</sup>

**27.334** The evaluation of ALT testing equipment by the SNBTS Microbiological Validation Group found that a cut-off of 2.5 standard deviations above the mean would lead to the exclusion of approximately 1.5% of donations and that a cut-off of 2 standard deviations above the mean would lead to the exclusion of approximately 5% of donations.<sup>478</sup>

**27.335** The multi-centre study in England found that 3.2% of donors would have been rejected using ALT screening, that 0.63% of donors would have been rejected using anti-HBc screening and that there was little overlap between these groups of donors.<sup>479</sup>

**27.336** Looked at overall, had both ALT and anti-HBc screening been introduced in Scotland it seems likely that between 3% and 5% of donations would have been excluded on initial screening.<sup>480</sup> In the case of regular donors, the loss would remain as long as they continued to have elevated test results.

**27.337** As noted by Dr McClelland:

These numbers may have underestimated the longer term effect on donor attendances, because later research has shown – perhaps not surprisingly – that donors who are rejected on one occasion are unlikely to return to volunteer again, and this tends to have a cumulative effect that is not measured by the initial rate of deferral.<sup>481</sup>

**27.338** At the time of the SNBTS Directors' recommendation on 3 March 1987<sup>482</sup> that surrogate testing should be introduced with effect from 1 April 1988, there was no recorded discussion of the effect on the blood supply of introducing such testing.

**27.339** By 1988, a fall in donor attendances had become a matter of concern. In the introduction to the SNBTS 1988 PES bid (prepared around June 1988), Professor Cash stated:

<sup>475</sup> ie above 45 units per litre

<sup>476</sup> Gillon et al, 'Post-transfusion [NANB] hepatitis: significance of raised ALT and anti-HBc in blood donors', *Vox Sanguinis*, 1988; 54:148 [SNB.008.3536]

<sup>477</sup> Ibid [SNB.008.3536] at 3536

<sup>478</sup> SNBTS/NIBTS Microbiological QA Group, *Evaluation of ALT Testing – Final Report*, 25 August 1988 [SNB.002.4423] at 4424

<sup>479</sup> Advisory Committee on the Virological Safety of Blood, meeting of 6 November 1989 [SNF.001.1383] at 1388

<sup>480</sup> In their evidence to the Inquiry, Dr McClelland thought 3-4% [PEN.017.2651] at 2654 and Professor Cash thought between 1-3% [PEN.017.1885] at 1889

<sup>481</sup> Supplementary statement [PEN.017.2651] at 2654

<sup>482</sup> Minutes of the SNBTS Directors' meeting, 3 March 1987 [SGH.001.6653] at 6658

1987/88 has been the year when, perhaps, for the first time since its foundation in the early 1940s, serious doubts have arisen with regard to the ability of the SNBTS to sustain the quantity and volume of its service to the [Scottish Health Service] and meet the needs of the future.<sup>483</sup>

**27.340** The problems included a decline in total donor attendances, an escalation in demand for blood products and resulting problems in supply and self sufficiency.

**27.341** As regards the decline in donor attendances, Professor Cash noted that there had been a 'sustained decline' in attendances since 1985 which had 'become more evident in the last 18 months'.<sup>484</sup> The total annual donor attendances showed that, from a high of 338,278 in the year ended 31 March 1985, there was a decline to 333,112 attendances in 1986, 331,089 in 1987 and 315,845 in 1988.<sup>485</sup> Investment totalling £221,000 was sought in the 1988 PES to appoint a national donor recruitment and blood collection manager, to fund a permanent media publicity programme and to improve the conduct of blood donor sessions.<sup>486</sup>

**27.342** As regards the escalation in demand for blood products, Professor Cash explained in the 1988 PES that '[t]here has been a significant and substantial increase in the clinical demand/use of SNBTS blood and blood products over the last decade' which was 'out of control'.<sup>487</sup>

**27.343** As far as supply and self-sufficiency were concerned, the 1988 PES noted that 'major difficulties' had emerged for RTCs in meeting demand centred primarily on the provision of platelet concentrates and supporting the fresh plasma needs of the PFC.<sup>488</sup> It was noted that 'further significant increases in fresh plasma for PFC cannot be obtained from the existing blood donation input (which is falling in any event)' and that the major contribution to any planned increases in plasma were likely to be by a mixture of plasmapheresis and optimal additive solution (OAS).<sup>489</sup> Investment of £650,000 was sought in the PES to address these concerns.<sup>490</sup>

**27.344** In a letter to Mr Donald of 25 July 1988, Professor Cash ranked the various bids in the 1988 PES in order of priority.<sup>491</sup> The sums sought to address escalating demand, supply and self-sufficiency and falling donor attendances were included in the highest priority category. In contrast, the sums sought for ALT testing were in the medium priority category.

<sup>483</sup> SNBTS PES Programme Narrative, 1988 [SNB.003.3078] at 3088

<sup>484</sup> Ibid [SNB.003.3078] at 3089

<sup>485</sup> Ibid [SNB.003.3078]. The total number of donations collected in these years, although not shown in the 1988 PES, fluctuated from 304,914 in 1985, 309,748 in 1986, 289,006 in 1987 and 310,785 in 1988. SNBTS paper on Blood Collection 1975-1991 [PEN.010.0026] at 0029. Compare Chapter 3, *Statistics*, Table 14

<sup>486</sup> SNBTS PES Programme Narrative, 1988 [SNB.003.3078] at 3090

<sup>487</sup> Ibid [SNB.003.3078] at 3090 and 3091. The 1988 PES contained figures showing that the demand for albumin had trebled between 1978 and 1988, and between 1985 and 1988, had increased by a quarter; the demand for Factor VIII had risen almost six-fold between 1978 and 1988, and between 1985 and 1988 had risen by over a quarter; the demand for Factor IX in 1988 was almost 16 times that in 1978 and had doubled between 1985 and 1988, [SNB.003.3078] at 3091. The PES narrative stated that while the increase in demand for blood products was not unique in Scotland, there was circumstantial evidence of over-prescribing of products and a sum of £73,300 was sought for the establishment of an academic department of Transfusion Medicine whose primary purpose would be to develop research directed towards defining the appropriate treatment of disease using blood and blood products: [SNB.003.3078] at 3092 and 3093.

<sup>488</sup> SNBTS PES Programme Narrative, 1988 [SNB.003.3078] at 3093

<sup>489</sup> Ibid [SNB.003.3078] at 3095. When plasma is removed from a donation of collected whole blood it is replaced with OAS which optimises red cell preservation and lowers viscosity. The use of OAS allows more plasma to be taken from the donation.

<sup>490</sup> The £650,000 sought comprised £250,000 in respect of a new staffing structure at the PFC and £400,000 in respect of RTC 'plasma procurement' – that is, the implementation of plasmapheresis and OAS [SNB.003.3078] at 3098

<sup>491</sup> Letter [SNB.011.4790]

**27.345** In his evidence to the Inquiry, Dr Mitchell was asked whether a loss of 4% or 5% of donors in the west of Scotland would have created a problem for the blood supply and he replied that it would.<sup>492</sup> He was then asked whether that would have been an insurmountable problem and replied:

With sufficient drive perhaps it could have been overcome ....

And so the answer to that is, yes, we could probably have overcome the problem. It would have taken a lot of additional advertising, and it's difficult to see how you would recruit donors faced with the knowledge that you were imparting through their colleagues at the workplace, who were not infected, but had a marker which was putting them off-service. They would be saying to themselves "Well, I'm not going. If you are not going to go, I'm not going because I might be turned down the same as you". And once you are turned down, then you have a problem. I have said to you many, many times, a donor becomes a patient ....<sup>493</sup>

**27.346** Dr Gillon stated:

The situation became serious to the extent that a substantial injection of resources was necessary around 1990, with most of the money and effort going into a television advertising campaign which reversed the decline in donor numbers. Whether it would have been possible to weather a loss of donations of the order of at least 4-5% and so maintain self-sufficiency with or without such funding is doubtful, but this is speculative in the extreme.<sup>494</sup>

**27.347** Professor Cash was asked whether, given the difficulties in blood collection in the second part of the 1980s, it would have been feasible to introduce surrogate testing at any time between 1987 and 1990. He replied that, had he been asked about surrogate testing at the end of 1987, his position would probably have been: 'Go away ... forget it in the meantime.' He stated that in 1988/89, 'we would have been struggling a little.' Progress was, however, being made in that unnecessary use was being reduced, stocks were being moved around and the problems in the west of Scotland were eventually resolved.<sup>495</sup>

**27.348** Although these problems were dealt with, it appears that the Scottish service was not well placed at this time to withstand any further reductions in donations, in particular if self-sufficiency in blood products was to be maintained. The potential sensitivity of donors to the implications for them of surrogate testing added to the difficulty.

### *Counselling of donors*

**27.349** As noted above, surrogate tests such as ALT and anti-HBc markers were non-specific indicators of the presence of NANB Hepatitis.

**27.350** In his written evidence to the Inquiry Dr McClelland stated:

Low test specificity ... has serious consequences when a test is used to screen a member of a healthy population. A substantial proportion of the individuals

---

<sup>492</sup> Day 65, pages 47-48

<sup>493</sup> Ibid page 48

<sup>494</sup> Statement [PEN.017.1931] at 1938

<sup>495</sup> Day 72, pages 38-42. He also gave evidence on his concerns that the donor panel may have 'collapsed' as a result of excluding a large number of donors on the basis of a non-specific surrogate test for which there was no confirmatory test: Day 72, pages 63-64

who test “positive” and who therefore will be rejected as donors because of the risk of transmitting [NANB Hepatitis], will not in fact, have [NANB Hepatitis] nor will their blood contain the relevant infectious agent. Nevertheless, such individuals have to be informed that their donations can no longer be accepted and the risk that their blood could transmit hepatitis must be part of the explanation. This can have the effect of converting a person who correctly considers themselves to be in good health into one who has been given information that indicates that they may be afflicted with a serious infection. This problem can only be avoided if there is some form of additional test (often termed a confirmatory test) that can reliably demonstrate the presence or absence of infection.<sup>496</sup>

**27.351** Until the Hepatitis C virus was identified in 1988, and a test for antibody to Hepatitis C became available the following year, there was no direct test – far less a confirmatory test – for the agent or agents responsible for NANB Hepatitis.

**27.352** Taking Dr McClelland’s oral evidence as a whole, it is clear that there was concern as to how the SNBTS would have managed donors who were rejected on the basis of a surrogate test. It was suspected that in most cases a positive test would not indicate infection.<sup>497</sup> Effective counselling of donors who tested positive for surrogate markers would have been a ‘challenging problem’ for the service. Further thought required to be given to the practical arrangements for counselling the many thousands of donors who would test positive for surrogate markers and the SNBTS had little practical experience of such counselling to draw on.<sup>498</sup> The numbers involved in Hepatitis B and HIV testing had not been large and, furthermore, in relation to these infections confirmatory tests were available.

**27.353** On reflection, Dr McClelland accepted that the SNBTS Directors ‘certainly had not ... prepared a systematic sort of management plan and costed out the stuff involved’. He remained ‘absolutely confident’, however, that, looking at the implications for the other hospital departments and GPs, the issue of donor counselling ‘could and would have been addressed’.<sup>499</sup>

**27.354** Dr Mitchell was altogether less confident. He emphasised the uncertainties that arose from the fact that ALT levels could fluctuate and that elevated ALT had many different causes, many or most of which had nothing to do with hepatitis.<sup>500</sup> In his view, a donor who tested positive for a surrogate marker would become a patient.<sup>501</sup> Asked whether that would not have been a reason to avoid testing, Dr Mitchell commented:

No, provided the basis on which you make him a patient is justifiable ....

What do you say, “Go and see your GP”? The GP immediately phones us and says, “What does this mean?”, “I don’t know what it means, but I know what you are getting at”, but he says to me, “But this chap is sitting in front of me and he is dead scared, he’s worried, “What’s going to happen to me?” I can’t tell him anything”. I say, “Neither can I”.<sup>502</sup>

<sup>496</sup> Dr McClelland’s statement on surrogate testing [PEN.017.0754] at 0759–0760

<sup>497</sup> Day 64, pages 18–19

<sup>498</sup> Day 63, pages 155–159

<sup>499</sup> Day 64, pages 19–20

<sup>500</sup> Day 65, pages 15–16

<sup>501</sup> Ibid page 48

<sup>502</sup> Ibid pages 64–65

**27.355** On Dr Mitchell's approach, there were many questions for which practitioners had to have answers before proceeding to implement surrogate testing.

**27.356** Dr Gillon's experience with donors supported the view that there was a problem with counselling. Donors in his study into surrogate markers who were found to have elevated ALT levels 'were quite anxious, they were very keen to know the next set of results, and they were really quite concerned about this'.<sup>503</sup> Dr Gillon also had experience of counselling plasmapheresis donors with elevated ALT and stated:

As soon as you see somebody, sit them down and say, "There may be something wrong with your liver, you may be carrying some nasty virus that may or may not cause chronic liver disease. We may have to send you to a specialist. They may stick a needle in your liver". It was not trivial. It is absolutely not trivial.<sup>504</sup>

**27.357** Dr Macdonald said:

It's not simply a matter of counselling and advice but there would be a number of donors identified who would have to be referred to a physician, subjected to laboratory tests, reviewed for a period of at least some months, I would have thought, before it would be possible to offer them an opinion as to whether they were infected or not. In other words, whether they were the false positives or genuine positives. Yes, there is quite a lot involved in this.<sup>505</sup>

**27.358** Notwithstanding Dr McClelland's confidence that a solution would have been found, and quite irrespective of the numbers involved, the introduction of surrogate testing would have required resolution of the many issues relating to informing donors, providing counselling and regulating follow-up, all of which were inherent in using a mass screening test of such poor specificity and sensitivity.

**27.359** The scale of the problem – the number of donors who might have required counselling and investigation – added to the underlying difficulty. In the mid- to late-1980s approximately 300,000 blood donations were collected annually in Scotland.<sup>506</sup> The number of donors is likely to have been considerably lower. As noted in Chapter 18, *Collection of Blood in Scotland: General*, paragraph 18.14, at the date of the Inquiry's hearings 80% of donors bled were not 'new' and return donors contributed about 85% of all donations. These percentages must fluctuate and a 'new' donor in January may become a return donor in May and September. On the evidence, a return donor might give 1.06 donations a year on average. It is not possible to extrapolate on any reliable basis from the findings of a limited study to an estimate of the potential loss to the blood supply. However, for illustrative purposes only, total donors for 300,000 donations might be the sum of new donors ( $300,000 \times 15\% = 45,000$  individuals) and return donors ( $255,000/1.06 = 240,566$ ), a total of 285,566 individuals. If ALT testing had been introduced then, on the best current estimates, approximately 3% of donors might have been expected to have had elevated levels, just over 8500 donors per year. Dr Gillon's study had found that about 80% of donors with elevated ALT had a 'non-viral' explanation, such as obesity or alcohol.<sup>507</sup> Based on Dr Gillon's findings, about 6800 might

---

<sup>503</sup> Ibid page 125

<sup>504</sup> Ibid page 124

<sup>505</sup> Day 66, pages 136–137

<sup>506</sup> SNBTS paper on Blood Collection 1975–1991 [PEN.010.0026] at 0029

<sup>507</sup> Gillon et al, 'Post-transfusion [NANB] Hepatitis: significance of raised ALT and anti-HBc in blood donors', *Vox Sanguinis*, 1988; 54:148 [SNB.008.3536]

be expected to have had a 'non-viral' explanation for their condition, leaving 1700 – 0.6% of the total number presenting with a view to donation – who would have elevated ALT for which a viral explanation was possible. In a Finnish study by Freja Ebeling and colleagues, the authors considered that the positive predictive value (the number of true positive results amongst the 'positive calls') of an elevated ALT level in identifying those donors who transmitted NANB Hepatitis was about 4%.<sup>508</sup> While for a number of reasons one must be very cautious about relying on that figure, for purely illustrative purposes it would suggest that if about 1700 donors a year in Scotland were found to have elevated ALT levels deemed to be associated with NANB Hepatitis, about 68 donors would be infective and the remaining 1632 would be 'false positives'.

**27.360** The concerns about the impact on donors, often advanced by practical transfusion doctors, were significant. Giving a label of uncertainty to individuals who were likely in the nature of things to be immediately anxious would have been a serious matter. Had it been intended to introduce surrogate testing of donated blood generally, it would have been necessary to have developed clear guidance on how donors found to have elevated ALT or to be positive for anti-HBc were to be dealt with and, in particular, counselled. The risk of false positive results would have presented a particular challenge. That stage was not, in the event, reached. The evidence of Dr Mitchell, Dr McClelland and Dr Gillon made it clear that finding a satisfactory solution that would have had general support would not have been easy.

#### *The perceived benefits of surrogate testing*

**27.361** The preceding discussion has considered the various difficulties with using surrogate tests to screen donors for possible NANB Hepatitis infection. One must also, however, consider the evidence that was available at the time in respect of the advantages of surrogate testing including, in particular, the extent to which surrogate screening may have reduced the incidence of transfusion-transmitted NANB Hepatitis infection. A full cost/benefit analysis does not appear to have been carried out, and, indeed, such an analysis could not have been carried out in any meaningful way in the absence of a large-scale prospective study of the prevalence of NANB Hepatitis in Scotland and of the efficacy of surrogate testing here. As discussed above, such a study would have been required to extend beyond the investigation of the prevalence of surrogate markers in donors and to have included investigation of the link, if any, between such surrogate markers and the development of post-transfusion NANB Hepatitis in recipients. A study of that scope was never properly considered or carried out in the UK. The perceived benefits of surrogate testing in the late 1980s can therefore be considered only on a more general basis.

**27.362** Dealing, first, with patients with blood disorders, the size of pools (containing many thousands of donations) used to manufacture Factor VIII and Factor IX meant that most were likely to have contained at least one donation containing HCV (which donation would potentially have infected the whole pool). Given the poor sensitivity of surrogate testing as a screening test, it was never likely to have been effective in identifying and excluding all infective donations. The safety of factor concentrates, therefore, depended not on surrogate screening of donations but on the development and introduction of manufacturing processes that inactivated any virus in the pool. By the end of 1987 the PFC had already issued products sufficiently heated to inactivate HCV-infecting source

---

<sup>508</sup> Ebeling et al, '[ALT], gamma-glutamyltransferase, [anti-HBc] and [anti-HCV] in blood donor screening', *Vox Sanginis*, 1991; 60:219 [PEN.017.1763] at 1765, Table 4

plasma. In particular, heat-treated Factor IX concentrate (DEFIX) was issued in August 1985 for routine clinical use in the treatment of Haemophilia B.<sup>509</sup> The PFC's heat-treated FVIII concentrate, Z8, was issued for routine clinical use in the treatment of Haemophilia A in April and May 1987.<sup>510</sup> Patients receiving factor concentrate therapy with NHS products after those dates would not have been infected due to the inactivation procedures. Surrogate testing of blood donations would not have added to the security of recipients of these products in haemophilia therapy.

**27.363** Further, most patients who had routinely received blood products before the introduction of the heat-treated concentrates had almost certainly already been infected with NANB Hepatitis/HCV. That was the conclusion of a number of studies: most haemophilia patients, whether treated with NHS concentrates or concentrates produced by commercial companies, were likely to have developed NANB Hepatitis on first exposure to concentrates that had not been virally inactivated.<sup>511</sup> Only haemophilia patients receiving single or small numbers of doses of cryoprecipitate (made from pools of around 10 donations), who were in broadly the same position as medical and surgical patients receiving transfusions of blood or blood components, might have benefited. The topic of relevance is primarily in those cases.

**27.364** As regards transfusion of whole blood and its components,<sup>512</sup> the TTV and NIH studies suggested in 1981 that in the USA (and therefore in the context of the specific characteristics of that country's blood donor population), ALT testing might have reduced the incidence of post-transfusion NANB Hepatitis by 30–40%.<sup>513</sup> The same studies, reporting in 1984 and 1986, suggested that anti-HBc testing might reduce the incidence of post-transfusion NANB Hepatitis by about one third.<sup>514</sup> The ALT and anti-HBc tests largely identified different groups in the donor population. However, even if these predictions had been correct, on average two-thirds of the pre-screening risk of transmission would have continued despite screening.

**27.365** Importantly, the TTV and NIH estimates of the extent to which surrogate testing might have reduced the incidence of post-transfusion NANB Hepatitis were predicted efficacies (based on an historical analysis of existing data) rather than actual efficacies (based on a randomised prospective study whereby one group of patients was given blood which had been screened for surrogate markers and the other was given blood that had not been so screened). Very few randomised prospective trials were carried out and published before the late 1980s to establish the actual efficacy of surrogate testing in reducing the incidence of post-transfusion NANB Hepatitis. Those that were published in the early- to mid-1990s were too small for reliable conclusions to be drawn from their results.

<sup>509</sup> SNBTS Briefing Paper on the Development of Heat Treatment of Coagulation Factors. November 2010 [PEN.013.0045] at 0078; Written statement from Dr Foster, [PEN.012.1797] at 1803

<sup>510</sup> SNBTS Batch Issue History log sheets [PEN.017.1451]; [PEN.017.1470]

<sup>511</sup> Fletcher et al, 'Non-A non-B hepatitis after transfusion of factor VIII in infrequently treated patients', *British Medical Journal*, 1983; 287:1754-1757 [LIT.001.0239]; and Kernoff et al, 'High risk of non-A, non-B hepatitis after a first exposure to volunteer or commercial clotting factor concentrates: effects of prophylactic immune serum globulin', *British Journal of Haematology*, 1985; 60:469-479 [LIT.001.0800]

<sup>512</sup> eg mainly red cells, platelets and plasma

<sup>513</sup> Aach et al, 'Serum alanine aminotransferase of donors in relation to the risk of non-A, non-B hepatitis in recipients', *New England Journal of Medicine*, 1981; 304:899 [LIT.001.0753]; Holland et al, 'Post-transfusion hepatitis and the TTVs', *New England Journal of Medicine*, 1981; 304:1033 [LIT.001.1630]; Alter et al, 'Donor transaminase and recipient hepatitis', *Journal of American Medical Association*, 1981; 246:630 [LIT.001.1817]

<sup>514</sup> Stevens et al, 'Hepatitis B virus antibody in blood donors and the occurrence of non-A non-B hepatitis in transfusion recipients', *Annals of Internal Medicine*, 1984; 101:733 [LIT.001.3755]; Koziol, et al, 'Antibody to hepatitis B core antigen as a paradoxical marker for [NANB] hepatitis agents in donated blood', *Annals of Internal Medicine*, 1986; 104:488 [LIT.001.1869]



**27.366** The letter from Dr Gillon and his colleagues published in *The Lancet* on 13 June 1987 commented on the published literature as at mid-1987:

Of the four small prospective studies, two using ALT screening and two using anti-HBc, three<sup>515</sup> failed to demonstrate any reduction in post-transfusion NANB hepatitis as a result of donor screening and one<sup>516</sup> found an apparent association between anti-HBc in donor units and recipient hepatitis.<sup>517</sup>

**27.367** The information available at the time on the likely benefits of surrogate testing therefore remained inconclusive. The majority of small-scale prospective studies had failed to demonstrate the reduction in post-transfusion NANB Hepatitis that was predicted by the TTV and NIH studies when blood with surrogate markers was withheld.

**27.368** There was an additional difficulty in relying on these data. Prevalence in the US donor population could not be assumed to be representative of the prevalence of NANB Hepatitis elsewhere. Prevalence in the USA was generally believed to be relatively high and, as Professor Leikola said, most countries that elected to introduce surrogate testing in 1987 first conducted research to find out the situation in their own donor population and did not simply follow the US example.

**27.369** There are other difficulties in trying to estimate the extent to which surrogate testing might have reduced the incidence of post-transfusion Hepatitis C in Scotland. Dr Gillon, for example, took the view that predictions of a reduction of cases of post-transfusion NANB Hepatitis by 30% or 40% following ALT testing would almost certainly have been too high for a number of reasons, including that donors rejected on surrogate screening would have to be replaced with new donors. The introduction of anti-HCV screening had shown that new donors had an increased prevalence of HCV when compared with existing donors. That factor, unknown and unknowable in extent, would require to be taken into account when calculating the efficacy of surrogate testing. Dr Gillon explained: 'I know Harvey Alter talked about a corrected efficacy to try to accommodate that, and that dropped his predicted efficacy from 40% to 20%, but it was totally speculative.'<sup>518</sup>

**27.370** Developing knowledge of other causes of elevated ALT became significant. Hepatitis C causes liver damage and elevated ALT is an indicator of liver damage (from whatever cause). It was reasonable to infer that donors with Hepatitis C were more likely to have elevated ALT than donors who were not infected. Elevated ALT is, however, also associated with other factors, such as obesity and alcohol intake, and these required to be excluded before an inference of Hepatitis C infection could be drawn from the finding. In addition, as Dr Gillon explained:

The segment of the population with the highest mean [ALT] levels is in males aged 30 to 40 ....

<sup>515</sup> Alter, H 'Post-transfusion hepatitis: clinical features, risk and donor testing', in *Infection, Immunity and Blood Transfusion*, 1985, Alan R. Liss, pages 47–61, at 55 [LIT.001.0811], Steinbrecher et al, 'Abnormal alanine aminotransferase level in blood units from donors in Montreal does not indicate high risk of transmitting hepatitis', *Clinical and Investigative Medicine*, 1983; 6:327 [LIT.001.2207] and Aynard et al, 'Post-transfusion [NANB] Hepatitis after cardiac surgery: prospective analysis of donor blood anti-HBc antibody as a predictive indicator of the occurrence of [NANB] hepatitis in recipients', *Vox Sanguinis*, 1986; 51:236 [LIT.001.3810]

<sup>516</sup> Sugg et al, 'Antibodies to hepatitis B core antigen in blood donors screened for alanine aminotransferase level and hepatitis [NANB] in recipients', *Transfusion*, 1988; 28:386 [LIT.001.3813]

<sup>517</sup> Gillon et al, '[NANB] hepatitis surrogate testing of blood donations', *The Lancet*, 13 June 1987:1366 [LIT.001.0346]

<sup>518</sup> Day 65, page 77

In most studies of HCV-positive blood donors, there is found to be a preponderance of males, typically in the age range 30-40. There is therefore a coincidental association between higher ALT levels and the donors most likely to have been exposed to HCV. It is therefore likely that ALT is to some extent an epiphenomenon in statistical or epidemiological terms [that is, a secondary phenomenon without a necessary causal relationship to the primary disorder] as Alter and Holland suggested.<sup>519</sup>

**27.371** The information available from later investigations suggests that, viewed exclusively in terms of efficacy, surrogate testing for elevated ALT would probably have reduced the incidence of transfusion-transmitted hepatitis for some recipients of blood, blood components and single donor preparations such as cryoprecipitate, if introduced between 1988 and 1991. The extent to which that would have happened cannot be quantified, given the difficulties with the evidential material previously discussed.

### *Product liability*

**27.372** Council Directive 85/374/EEC, imposing strict liability for harm caused by defective products came into force in the UK on 1 March 1988 under the Consumer Protection Act 1987.<sup>520</sup> In *A v The National Blood Authority and Others*, Mr Justice Burton decided on 26 March 2001 – for the time being conclusively – that as of 1 March 1988 recipients of blood or blood products which transmitted HCV infection, had suffered harm for which a remedy was available under the terms of the Directive. The circumstances of the case are discussed in Chapter 31, *The Introduction of Screening of Donated Blood for Hepatitis C*, at paragraphs 31.432–31.437.

**27.373** SNBTS officials, particularly Professor Cash but including the Transfusion Directors generally, anticipated that there would be strict liability under the Directive and engaged that risk by contending that surrogate testing should be introduced. The ‘irrational but perhaps inescapable’ conclusion was perhaps most clearly expressed in the letter to *The Lancet* dated 4 July 1987 and discussed at paragraphs 27.206–27.207.

**27.374** As originally argued by Professor Cash, the risk of strict liability, for the SNBTS in particular, was presented as a reason for the UK to attempt to exclude blood and blood products from the scope of the legislation. That argument failed to achieve support from the DTI and it was accepted by the SHHD that blood and blood products would remain within the scope of the act. Once that position was accepted, the success of the UK public sector producers of blood products and of the transfusion services in escaping liability, inevitably depended on the view taken by the court of the effect of the legislation and, in some respects more critically, of the facts found by the court on the evidence before it.

**27.375** The facts found in *A v The National Blood Authority and Others* are not determinative of the factual issues that arise on the evidence before the Inquiry which remain facts for the Inquiry to determine. In particular why surrogate testing was not introduced and whether it should have been introduced are issues the Inquiry must deal with on the evidence now available.

---

<sup>519</sup> Ibid page 98. The reference to Alter and Holland is a reference to their December 1984 editorial discussed above at paragraphs 27.40–27.41 [PEN.018.1156]

<sup>520</sup> See paragraphs 27.150–27.154

***Why surrogate testing was not introduced and whether it should have been introduced***

**27.376** Central to this discussion are questions as to whether the UK Government departments, particularly the DHSS and the SHHD, were wrong to have first delayed and then failed to institute general surrogate testing of blood donations for high ALT levels and anti-HBc. Since HCV screening was introduced generally on 1 September 1991, the relevant period for considering these questions can be taken to have ended on that date: there was no general safety issue to be addressed by surrogate screening thereafter, whatever commercial reasons fractionators might have had for continuing with the practice. The issue had, however, already changed in the course of the period ending on that date. It is relevant and material to note that as the period proceeded it became clear (and was certainly clear by the date of the introduction of HCV screening) both that the large majority of cases of post-transfusion NANB Hepatitis/HCV were attributable to a single virus and that screening and confirmatory tests for HCV were increasingly of reasonable sensitivity and specificity. As the tests improved, particularly in relation to those genotypes of HCV prevalent in the UK, the potential relevance of surrogate testing diminished.

**27.377** There is, however, a short and compelling answer, at least from March 1989 onwards, when the ACVSB was set up: given the advice of the committee, the appropriate expert advisory group established to provide objective and independent advice to government, that the blood transfusion services should not introduce surrogate testing, there was no medical or scientific basis on which the DHSS and the SHHD could properly have done otherwise.

**27.378** The issue is not whether, having regard to subsequent developments in medical and scientific knowledge, the expert advice tendered was correct or incorrect. The members of the ACVSB included eminent experts of national and international repute who were leaders in their fields. Professor Zuckerman, for example, appears from the record to have been a significant voice influencing the direction of thought throughout this important period. It would be inappropriate with the benefit of hindsight to analyse his advice and, in comparison with others' views, comment on the validity of his opinions. The Inquiry is not tasked with an assessment of professional opinions responsibly held and expressed as guidance to government. At the time, the NHS, the Scottish agencies, the SHHD and the government generally were entitled to rely on the advice given by appropriate experts and to act accordingly. Ministers would have required clear and powerful scientific advice to the contrary before taking a different course. At no point was there clear and powerful advice in favour of the introduction of surrogate testing in Scotland or the rest of the UK.

**27.379** Before the ACVSB was set up, however, the question was more open. Until the decision of the AABB (in the USA) in August 1986, there was no consensus anywhere that surrogate testing was appropriate as a method of screening blood for NANB Hepatitis. In the UK, there was never a medical and scientific evidential basis to justify the introduction of a mass screening test of such poor sensitivity and specificity. The lack of sound medical and scientific reasons for the introduction of surrogate testing was recognised by the SNBTS Directors who instead, in their letter to *The Lancet* of July 1987, pointed to other factors which they considered meant that surrogate testing was 'irrational, perhaps, but inescapable'. These other factors included forthcoming product liability legislation already referred to and pressures arising from the practice of commercial manufacturers.

**27.380** It was suggested in closing submissions to the Inquiry that the SNBTS Directors failed to explain properly to the SHHD their reasons for recommending the introduction of surrogate testing, including the benefits to patient safety and that, for their part, the SHHD failed in not asking the SNBTS Directors to clarify the reasons for their recommendation.<sup>521</sup> The Directors' reasons for making their recommendation were stated at the time to be based on the fact that blood banks and fractionators elsewhere, in particular in the USA, were introducing ALT testing and because of new product liability legislation. The SHHD officials were aware of the SNBTS Directors' concerns in that regard, even if they did not agree with them.

**27.381** Given the lukewarm support of the SNBTS Directors for surrogate testing and the lack of data in the UK as to its efficacy in preventing or reducing transfusion-transmitted NANB Hepatitis, it would be unrealistic to proceed on the basis that the Directors should have been expected to provide much more by way of clarification of their reasons for 'recommending' the introduction of surrogate testing. It was not a fully reasoned response to the problem, which remained that surrogate testing was a controversial topic which did not command widespread scientific support outwith the USA. The Directors' reasons for their recommendation, so far as they were developed and expressed, were known to the SHHD. They were not persuasive without the backing of relevant research.

**27.382** There was, at least potentially, an independent question for the SHHD: whether, having regard in particular to the impending product liability legislation, a full cost/benefit analysis would have tended to support surrogate testing, notwithstanding its limitations. That was, however, never carried out. It would have been a complex exercise, not least because of the incalculable impact on donors and the blood collection complex of inefficient screening technology. It would not be appropriate to speculate on what the outcome of such an analysis might have been.

**27.383** In his written evidence Professor Leikola commented on the fact that surrogate testing for NANB Hepatitis was not introduced in the UK. Even on the basis of all that is now known, it was reasonable and correct, in his view, for the UK not to have introduced surrogate testing.<sup>522</sup> So far as anti-HBc testing was concerned, its use as a surrogate marker could not be validated. He considered that ALT testing might have been more logical but observed that it was used in some countries, not because of a scientific basis and logical reasoning but because of public pressure.<sup>523</sup>

**27.384** As noted above, Dr Macdonald explained that surrogate testing was not introduced because, '[e]ssentially, there was too much uncertainty about various aspects of surrogate testing to justify introducing it.'<sup>524</sup> He referred to these concerns as relating to 'the quality of the testing'<sup>525</sup> and that 'the screening method was not really good enough'.<sup>526</sup>

**27.385** Dr Macdonald was also asked whether, with the benefit of current knowledge of Hepatitis C, he would be any more positive towards surrogate testing; he replied that he did not think he would be, given the non-specific nature of surrogate testing, the number

<sup>521</sup> Closing submission on behalf of patient interest core participants [PEN.019.0605] at 0622–32

<sup>522</sup> Professor Leikola's statement on surrogate testing [PEN.017.1837] at 1841

<sup>523</sup> Prior to the research carried out by Dr Ebeling and others surrogate testing for ALT or anti-HBc had not been routine practice in Finland: Ebeling et al, 'Post transfusion hepatitis after open-heart surgery in Finland – a prospective study', *Transfusion Medicine*, 1991; 103: 108. [PEN.017.1777] at 1780

<sup>524</sup> Dr MacDonald's Witness Statement [PEN.017.1702] at 1709

<sup>525</sup> Day 66, page 87

<sup>526</sup> Ibid pages 116–7

of false positives that would arise and the fact that such testing would not be able to completely eliminate infection.<sup>527</sup> He was also asked whether, hypothetically speaking, if it was reasonably believed that the introduction of surrogate testing was likely to reduce the incidence of post-transfusion hepatitis by, say, 30–40%, he considered there then arose a reasonable case for introducing surrogate testing. He replied:

No, I think I would still have argued against it. I think too much uncertainty still remained and I would have put considerable weight on the possibility that donors would find it disturbing. I think the one thing that we really had to avoid, almost at any cost, was disturbing donors because the whole enterprise depended on them.<sup>528</sup>

**27.386** While in his evidence to the Inquiry, Dr McClelland stated that patient safety was ‘the’ reason why he favoured the introduction of surrogate testing,<sup>529</sup> that can only have been in a very general and inchoate way, given the fundamental problem that one could not make a fully reasoned and scientific case for its introduction, including quantifying any benefit in recipient safety, because of the lack of adequate evidence and research in the UK into the prevalence of post-transfusion NANB Hepatitis and the likely efficacy of surrogate screening in reducing the transmission of the disease through transfusion. Furthermore, the issues identified by Dr Mitchell and Dr Gillon around the risk of turning thousands of healthy donors, found to have elevated ALT levels on surrogate testing, into patients concerned about the implications of test results for their long-term health that could not be resolved, were real obstacles to the introduction of the tests on a routine basis. The impact on the blood supply was also a legitimate concern, in particular against the background of a fall in donor attendances around this time, an increase in demand for blood products and the resulting difficulty in maintaining a policy of self-sufficiency in blood products.

**27.387** From May 1987, the general European position was that each country should ascertain the prevalence of NANB Hepatitis infection in its own region and take a decision on that basis. In Finland, a decision to carry out a study was implemented, the study beginning in December 1987 and lasting a year. Had Scotland followed the Finnish pattern, the results of such a study would not have been available before the ACVSB was established. The timescale anticipated by the SNBTS in their letter to *The Lancet* in July 1987 was three to four years. However, Dr McClelland had been pressing for such a study since 1981. As narrated, his early efforts failed in consequence of decisions taken by the MRC and the transfusion services’ Working Party on Transfusion Associated Hepatitis. Had his early efforts received a positive response then it is likely that the results of such a study would have been available before the AABB decision in 1986. Whether an additional study would have been required in consequence of the effects of the AIDS risk on donor selection policies cannot now be known. Professor Leikola, however, was clear that he was not critical of the decision not to introduce surrogate screening into Scotland and his opinion on this matter is accepted.

**27.388** Importantly, while such a study would have led to more informed decision-making, given the difficulties discussed above that arise from using a test of such poor sensitivity and specificity to screen hundreds of thousands of donors, it cannot be concluded that had such a study been carried out at some point in the 1980s in Scotland, or in the UK, surrogate screening would, or should, have been introduced.

---

<sup>527</sup> Ibid pages 76–77

<sup>528</sup> Ibid page 77

<sup>529</sup> Day 63, page 143

## Conclusions

### *The relevant period*

**27.389** The period during which consideration of the introduction of surrogate screening of blood for possible signs of NANB Hepatitis infection was a significant issue for the SNBTS and Scottish Government officials, began with the recommendations of the Council of Europe Committee of Experts on Blood Transfusion and Immunohaematology in May 1987.

**27.390** The period ended with the introduction of specific testing for antibodies to HCV on 1 September 1991.

### *Recipient populations potentially affected by the lack of surrogate testing*

**27.391** By May 1987, blood products used in Scotland for the treatment of patients with blood coagulation disorders did not expose recipients to a risk of transmission of HCV that might have been removed or alleviated by surrogate testing because:

- Commercial products imported from the USA were prepared from blood donations that were subject to surrogate testing.
- PFC Factor VIII and Factor IX concentrates were already heat-treated in such a way as to effectively inactivate any virus in the product (Factor IX DEFIX with effect from October 1985 and Factor VIII 8Y with effect from April/May 1987).

**27.392** The recipient populations potentially exposed to risks following the failure to carry out surrogate testing of donations during the relevant period were surgical, medical and other patients receiving transfusions of whole blood or blood components from donations that were not screened for elevated ALT or for anti-HBc.

### *The surrogate tests available and their effectiveness*

**27.393** Before the relevant period, research studies, mainly carried out in the USA, reported a correlation between elevated ALT levels in blood donors and an increased risk of transfusion recipients developing NANB Hepatitis.

**27.394** Other research from that time also reported an association between the presence of anti-HBc in blood donors and an increased risk of NANB Hepatitis transmission to transfusion recipients.

**27.395** These findings supported the view that elevated ALT and/or anti-HBc might be useful 'surrogate markers' for NANB Hepatitis in donated blood.

**27.396** No acceptable scientific basis for a correlation between the presence of anti-HBc in donated blood and the transmission of HCV was established on the evidence before the Inquiry and the failure to institute routine anti-HBc screening is not significant.

**27.397** In individuals, ALT levels fluctuate from time to time. There are different causes of ALT elevation, many of which have nothing to do with hepatitis, including obesity and the effects of the excessive consumption of alcohol. A single, isolated elevated test is not a reliable indicator of underlying infection.

**27.398** Generally, the poor sensitivity and specificity of ALT tests meant that the majority of infected donations were unlikely to be detected and, of the many thousands of donations that tested positive, the vast majority were likely to be false positives.

**27.399** The likelihood that ALT testing would provide an acceptable surrogate test varied from country to country. There was no guarantee that, in a given country, ALT testing would result in a significant reduction in the transmission of NANB Hepatitis.

**27.400** It was recognised in Europe that individual countries would have to assess the situation locally and decide on the appropriate action to take. In particular, the prevalence of NANB Hepatitis in the local population generally, and in the blood donor population in particular, was a significant consideration.

### *Decision-making in Scotland*

**27.401** Subject, ultimately, to Parliament's over-riding control, the decision as to whether or not to introduce ALT testing in Scotland was a matter for ministers with responsibility Scottish affairs, based on the advice of officials.

**27.402** Scottish officials were not obliged to submit the introduction of ALT testing to ministers unless they were satisfied that there was evidence and expert advice justifying the introduction of the procedure. It was part of their function to consider the evidence and advice available to them and to form a view as to whether or not to seek a ministerial decision on the issue.

**27.403** In the event, SHHD officials were not persuaded of the merits of surrogate testing and did not put the issue to ministers for a decision. As a result, ministers did not take part in the decision-making process, for which they were responsible.

### *The lack of a decision on surrogate testing*

**27.404** After the AVCSB was set up in early 1989, government, at the UK and Scottish levels, had a source of guidance from well reputed experts on which ministers and officials were entitled to rely for scientific and medical advice in formulating policy on surrogate testing. Before that time, Scottish officials had to rely on local expertise and such indirect sources as were available from the DoH.

**27.405** Scottish officials never had adequate information on the prevalence of post-transfusion NANB Hepatitis in the Scottish population or any material cohort of that population. Further, the predictive value of raised ALT levels in donors was limited, due to its known lack of specificity.

**27.406** The lack of data was the result of decisions taken in the 1980s that there should not be a large-scale prospective study of the prevalence of post-transfusion NANB Hepatitis in the UK as a whole or in Scotland in particular.

**27.407** On the evidence before the Inquiry, it was too late by the beginning of the relevant period to initiate such a large-scale prospective study. Such an exercise could not have been expected to have produced reliable results in time to inform decisions on the introduction of surrogate testing. It appears that those reliable results would not have been available before early 1990 at the earliest.

**27.408** There were conflicting expert views on many of the factors relevant to surrogate testing, including the prevalence of post-transfusion NANB Hepatitis, its potential seriousness for patients infected by the virus and the different viruses postulated as infective agents.

**27.409** It was, however, generally acknowledged that the available tests had poor sensitivity and specificity for their effective use in the mass screening of donors and that the lack of a confirmatory test meant that it would be difficult or impossible to distinguish between a true and false positive result.

**27.410** These difficulties would, in turn, have given rise to real difficulties in counselling donors and in maintaining a sufficient blood supply.

**27.411** While surrogate testing is likely to have prevented some cases of transfusion-transmitted NANB Hepatitis, it is not possible to quantify the percentage reduction with any degree of confidence, given that the prevalence of NANB Hepatitis at the time was not known and the likely efficacy of surrogate testing in reducing the transmission of NANB Hepatitis was speculative.

**27.412** With the establishment of the ACVSB in early 1989, it was reasonable for government to act on the expert advice received from that committee. The ACVSB did not, in the event, recommend the introduction of surrogate testing.

**27.413** In the final outcome, there was no definitive decision by Scottish officials whether or not to recommend the introduction of surrogate testing.

#### *Practical consequences*

**27.414** While it seems likely, on the balance of probabilities, that ALT testing would have reduced the incidence of transfusion-transmitted Hepatitis C to some extent, given all of the difficulties set out in this chapter it was not possible at the time, nor is it possible now, to say to what extent the incidence of post-transfusion Hepatitis C would have been reduced in recipients of blood and blood components by transfusion, or at what 'cost' in terms of impact on donors and impact on the blood supply.

**27.415** The Inquiry does not attribute blame for the fact that surrogate testing was not introduced, given the diversity of respected medical and scientific views over the period 1986–91. There was no consistent support for the procedure on tenable scientific or medical grounds that would have made it possible to conclude that officials should have recommended the introduction of ALT testing, or that the question was so narrowly balanced that it required to be referred to ministers for decision.





## CHAPTER 28

### DONOR SELECTION – AIDS

#### Introduction

**28.1** As indicated in Chapter 12, *HIV/AIDS: Response and Clinical Practice*, ‘donor selection’ was among the several approaches taken to minimise the emerging risk of AIDS transmission. ‘Donor selection’ refers to the steps taken by the Scottish National Blood Transfusion Service (SNBTS) and others, before testing of donations was available, to prevent the donation of blood which might carry a risk of transmission of the cause, or postulated cause, of AIDS. These steps consisted mainly of public information, to make ‘higher-risk’ prospective donors aware of the disease and the risk that it could be transmitted through blood transfusion and treatment with blood products. The intention behind the dissemination of such information was to discourage from giving blood those donors perceived to be at higher risk of carrying the infective agent. This chapter discusses donor selection in the AIDS period, 1982–85. The questions for the Inquiry included, particularly, whether these efforts went far enough and began early enough.

#### First steps taken in 1983

**28.2** It was evident that steps to deal with the perceived threat from infected donations were first taken in Scotland in the spring of 1983. In his statement,<sup>1</sup> Dr Brian McClelland, Director of the Edinburgh and South East Scotland Blood Transfusion Service (BTS) at the material time, explained that he received a copy of the *Mortality and Morbidity Weekly Report (MMWR)*, published by the Centers for Disease Control (CDC) in the USA, dated 4 March 1983. The section on ‘Current Trends’ contained an article entitled ‘Prevention of Acquired Immune Deficiency Syndrome (AIDS): Report of Inter-Agency Recommendations’.<sup>2</sup> Background information on the condition, as understood at that time, was given: over 1200 cases had been reported to the CDC from 34 states and the District of Columbia in the USA, and from 15 other countries. Over 450 people had died, the fatality rate being greater than 60% for cases first diagnosed over one year previously. Reports had gradually increased in number. Latterly, 11 cases of unexplained, life-threatening opportunistic infections and cellular immune deficiency had been diagnosed in patients with haemophilia. The article included the following recommendation:

As a temporary measure, members of groups at increased risk for AIDS should refrain from donating plasma and/or blood. This recommendation includes all individuals belonging to such groups, even though many individuals are at little risk of AIDS. Centers collecting plasma and/or blood should inform potential donors of this recommendation. The Food and Drug Administration (FDA) is preparing new recommendations for manufacturers of plasma derivatives and for establishments collecting plasma or blood. This is an interim measure to protect recipients of blood products and blood until specific laboratory tests are available.<sup>3</sup>

<sup>1</sup> Dr McClelland’s Witness Statement [WIT.003.0036]. See also Day 12, pages 3–7

<sup>2</sup> ‘Current Trends: Prevention of Acquired Immune Deficiency Syndrome (AIDS): Report of Inter-Agency Recommendations’, *Morbidity and Mortality Weekly Report*, 04 March 1983 [LIT.001.0568]

<sup>3</sup> *Ibid* [LIT.001.0568] at 0569

**28.3** The reference to ‘groups at increased risk for AIDS’ was expanded in the article. The groups were described as follows:

[P]ersons who may be considered at increased risk of AIDS include those with symptoms and signs suggestive of AIDS; sexual partners of AIDS patients; sexually active homosexual or bisexual men with multiple partners; Haitian entrants to the United States; present or past abusers of IV drugs; patients with hemophilia; and sexual partners of individuals at increased risk for AIDS.<sup>4</sup>

**28.4** It was suggested that the approach to dealing with the risk of AIDS from transfusion revealed by this article seemed to be to cast the net wider than might be strictly necessary when highlighting groups at risk, because of the priority of including those people who had to be identified. Dr McClelland agreed: it appeared to have been accepted that the criteria applied would result in the exclusion of healthy donors who happened to belong to the broadly defined groups of those being asked not to donate blood.<sup>5</sup> He explained that the inter-agency recommendation quoted was unusual and had ‘quite a tortured origin’. The FDA had not been enthusiastic to issue a statement. The prime instigator of the statement was Dr Bruce Evatt of the CDC, whom Dr McClelland described as ‘essentially the focal point of the discovery of the occurrence of AIDS in patients with haemophilia’.<sup>6</sup> Dr Evatt’s role in promoting wider knowledge of the aetiology of AIDS and encouraging an appropriate clinical response has been discussed in Chapter 11, *HIV/AIDS Aetiology*, and, briefly, in Chapter 12, *HIV/AIDS – Response and Clinical Practice*.

**28.5** In addition to the influential *MMWR* publication, Dr McClelland described the evidence which had started to emerge in July 1982, that AIDS was transmissible by blood and was therefore more likely to be due to a transmissible infectious agent than to any of the other causes then being considered. He also referred to an additional, local factor. During 1983 one or two local newspapers had taken up the suggestion that Edinburgh could become the ‘AIDS capital of the North’, relating this claim to the Edinburgh Festival and a supposed relationship between gay men and the arts.<sup>7</sup>

**28.6** In this regard, Dr McClelland was asked if, at the time of first drafting a leaflet discouraging potentially high-risk donors from giving blood in 1983, he had knowledge of possible AIDS cases in Edinburgh. He answered:

From May 1983 or possibly a little earlier, Dr Anne Smith and I were meeting with Dr Sandy McMillan, a GU [genitourinary] medicine Consultant in the Royal Infirmary of Edinburgh and Mr Derek Ogg of the Scottish Homosexual Rights Group to work out ways of communicating to gay men the message that they should refrain from donating blood. Dr McMillan would have been restrained by clinical confidentiality from mentioning any specific cases, but it is my recollection that he was aware that some of his male patients who were known to be gay were showing clinical features that suggested that they could be suffering from this new form of immune deficiency disorder.<sup>8</sup>

---

<sup>4</sup> Ibid [LIT.001.0568] at 0569

<sup>5</sup> Day 12, pages 5–6

<sup>6</sup> Ibid page 7

<sup>7</sup> Witness statement [WIT.003.0036] at 0037. See also the summary of the accumulating evidence in the Preliminary Report at paragraphs 8.12–8.31.

<sup>8</sup> Ibid [WIT.003.0036] at 0039

**28.7** Dr McMillan's remit as Consultant at the Royal Infirmary of Edinburgh (RIE) included sexually transmitted diseases and he was well known to and respected by the gay community. His recollection of events, after more than 25 years, was understandably hazy but in a letter to the Inquiry he also described meetings with members of the SNBTS, in particular Dr McClelland, and Mr Ogg of the Scottish Homosexual Rights Group (SHRG), to discuss how best to dissuade men who had sex with men from donating blood.<sup>9</sup> Open discussion in this group was to be of some importance as matters proceeded.

**28.8** Against this background, Dr McClelland began work on a leaflet.<sup>10</sup> He explained that the obvious approach at the time was to follow the principles of the US Public Health Services Interagency Guidelines, as reported in the *MMWR*, slightly adapted for use in Edinburgh.<sup>11</sup> By 24 May 1983, when the SNBTS Coordinating Group met, Dr McClelland had prepared a draft, which he tabled at the meeting.<sup>12</sup> The leaflet stated:

What is AIDS?

It is a disease called

(A) (I) (D) (S)  
acquired immuno deficiency syndrome

which is thought to be caused by an infectious agent, perhaps a virus. So far the cause is unknown. It is a rare disease but it can have serious consequences.

....

Who can get the disease?

AIDS has been occurring, particularly in the USA, in certain people who are apparently susceptible to the disease:

- 1) Homosexual men, particularly those with multiple partners;
- 2) Drug abusers;
- 3) Sexual contacts of people with AIDS – women can be infected if the males are bisexual;
- 4) Haitian immigrants to USA;
- 5) Haemophiliacs – who may be more susceptible or may become infected by their use of blood products which may have come from a blood donor with AIDS.

Most (but not all) cases have occurred in the homosexual male population. Why this should be is not yet known. A small number of young children have been affected.

....

<sup>9</sup> See Dr McMillan's comments to this effect in his letter at [PEN.014.0102]

<sup>10</sup> A newspaper article dated 20 November 1984 [DHF.001.6009] was shown to Dr McClelland, and he was asked about the comments in it by a Dr John Seale that the UK was slow in 'clamping down' on higher-risk donors. Dr McClelland did not agree, and referred to the near simultaneous commencement of the issuing of similar advice in the UK and the USA in 1983 – Day 12, pages 68–70 and Dr McClelland's Witness Statement [WIT.003.0036] at 0044.

<sup>11</sup> Day 12, page 10; Witness Statement [WIT.003.0036] at 0038. See also: 'Current Trends: Prevention of Acquired Immune Deficiency Syndrome (AIDS): Report of Inter-Agency Recommendations', *MMWR*, 04 March 1983 [LIT.001.0568]

<sup>12</sup> Meeting minutes [SNB.003.7116] at 7120

### Can it be Transmitted by Blood Transfusion?

It appears it can. This might cause the disease in people who are not normally at risk. It may have infected clotting factors that caused AIDS in Haemophiliac men in USA.

We have not had any definite cases of AIDS in Haemophiliacs in UK. If the clotting factor concentrate (factor VIII) can be infected, then cases could occur in UK because much of the factor VIII is imported to UK from USA.

The disease cannot be taken lightly. Those getting AIDS may die, because they are more susceptible to serious infections and cancer due to their impaired immune system.

The Blood Transfusion Service is therefore concerned to try and stop any chance of infection spreading by blood transfusion.

We want to ask people who may be at risk from the disease to avoid giving blood until we have a suitable screening test. Many donors will remember we did this with hepatitis until we had screening tests for the hepatitis virus.

### Whose Blood Could be a Risk?

All our information about at risk groups comes from the USA. However, until more is known about the cause and spread of AIDS, we would ask the following groups to refrain from donating blood:

- 1) Homosexual men;
- 2) Women who continually have multiple sexual partners;
- 3) Partners of bisexual men;
- 4) Anyone who abuses drugs;
- 5) Anyone who has been in contact with a case of AIDS.

We hope that if we take precautions now, we can prevent the problem of AIDS which has become serious in USA.

Remember it is a rare disease but an important one.<sup>13</sup>

**28.9** For comparison, the Inquiry examined some of the text from an early leaflet produced by the American Red Cross and apparently intended to be available at donation centres in the USA. The leaflet was entitled 'An important message to all blood donors'. The relevant section of the text is quoted at the end of a Council of Europe Recommendation, No. R(83) 8:

What are these illnesses?

Some persons may feel in excellent health but have viruses or other infectious agents in their blood that could cause illness in persons receiving a transfusion of their blood. If you think any of the following information pertains to you, please do not donate blood today:

1. *Acquired Immune Deficiency Syndrome (AIDS)*. This newly described illness of unknown cause is believed to be spread by intimate personal contact and possibly by blood transfusion. Persons with AIDS have reduced

---

<sup>13</sup> Leaflet: 'AIDS AND BLOOD TRANSFUSION: Some background to the recent publicity' [SNB.003.7153]. (Note the handwritten note in the top right hand corner which reads 'Item 15 of 24.5.83'). Council of Europe Recommendation, No. R(83) 8 [DHF.001.4550]

defences against disease and as a result may develop infections such as pneumonia, or other serious illnesses. At this time there is no laboratory test to detect all persons with AIDS. Therefore we must rely on blood donors' health histories to exclude individuals whose blood might transmit AIDS to patients who will receive that blood.

The Office of Biologics of the Food and Drug Administration has identified groups at an increased risk of developing AIDS. These groups are:

- Persons with symptoms and signs suggestive of AIDS. These include severe night sweats, unexplained fevers, unexpected weight loss, lymphadenopathy (swollen glands) or Kaposi's Sarcoma (a rare cancer);
- Sexually active homosexual or bisexual men with multiple partners;
- Recent Haitian entrants into the United States;
- Present or past abusers of intravenous drugs;
- Sexual partners of persons at increased risk of AIDS.

....

What should I do?

If you believe that you may be carrying one of the above-mentioned illnesses, or if you are an individual in a group at increased risk of developing AIDS, we ask that you refrain from donating blood at this time. You may leave now without providing an explanation. Or, if you prefer, you may proceed to be deferred confidentially, without further questioning, by the health history interviewer.<sup>14</sup>

**28.10** Dr McClelland was asked about the detail of the drafting of successive versions of the early leaflets in Scotland. He pointed out that there were various reasons for adjusting the wording:

I think ... we were probably trying to make some adjustments in the wording for two separate reasons. One was, in successive drafts, trying to come up with wording which was not more offensive to people than it had to be. Secondly, wording that was as unambiguous as we could make it, and thirdly that where we felt there might be some areas that perhaps hadn't been adequately identified in the very first version, which had come from the United States, we were prepared to try and extend a little bit more because we had the advantage of coming second, if you like.

....

[T]he fourth one, of course, was that as the months went on, new information was becoming available quite rapidly, which also we attempted to reflect as accurately as we could in successive drafts of the document.<sup>15</sup>

**28.11** At the meeting of the Coordinating Group on 24 May 1983, other Directors were asked what, if any, steps they had taken to address the AIDS risk. Dr Ruthven Mitchell, Director of the Glasgow and West of Scotland BTS, reported that he had introduced into the standard health questionnaire issued to prospective donors at West of Scotland sessions a question inviting those who were worried about AIDS to consult the doctor at the

<sup>14</sup> Information leaflet [DHF.001.4550] at 4551–52. Dr McClelland could not recall if he saw this leaflet in 1983: Day 12, page 109

<sup>15</sup> Day 12, pages 13–14

session. Professor Stan Urbaniak, then Director of the Aberdeen centre, had decided, after consideration, not to do anything locally, his view being that once a donor had entered the session it was too late to make an approach. He also thought that the problem was ‘minor’ in north east Scotland.<sup>16</sup> The responses underlined the extent to which Dr McClelland’s leaflet preparations were ahead of other regions, although as it transpired, the problem in the Edinburgh area at that time was indeed more serious than elsewhere in Scotland.<sup>17</sup>

**28.12** In the course of his oral evidence, Dr Mitchell was shown a copy of a leaflet produced by the Glasgow and West of Scotland BTS which appeared to include an early reference to AIDS. It took the form of a label or sticker attached to the bottom of the leaflet, with the following wording:

HAVE YOU HEARD OF A.I.D.S. (ACQUIRED IMMUNE DEFICIENCY SYNDROME).  
IF YOU HAVE ANY DOUBTS ABOUT GIVING A DONATION CONSULT THE  
DOCTOR AT THIS SESSION OR YOUR OWN G.P. OR WRITE IN CONFIDENCE TO  
THE REGIONAL DIRECTOR.<sup>18</sup>

**28.13** The date ‘16/6/83’ had been written at the bottom of this leaflet. Dr Mitchell had checked with his then donor manager and she could not produce any other leaflets from that time. It appears that this copy leaflet reflected the information provided by Dr Mitchell at the meeting of the Coordinating Group on 24 May 1983 and was evidence of the question added for donors in the west of Scotland in the first half of 1983.<sup>19</sup> The advice to donors concerned about giving blood was to consult the doctor at the session, as mentioned by Dr Mitchell, or to follow one of the alternatives proposed in the leaflet.

### Reaction to draft leaflets in Edinburgh

**28.14** It was apparent to the Inquiry that the text of Dr McClelland’s draft leaflet changed shortly after the meeting on 24 May 1983 and he was asked about the circumstances leading to those changes.

**28.15** A press release on AIDS had been issued by the SHRG on 21 May 1983.<sup>20</sup> One of its headlines was ‘Gays say “no” to ban on blood donors’. In its text, the release referred to AIDS as ‘an American disease epidemic’ and also recorded concern about the possible infection of haemophilia patients in the UK who relied on blood products ‘supplied in part from the United States which may be infected by AIDS’. It continued: ‘The disease has become known, wrongly, as “the gay plague”, and has also been described erroneously as sexually transmitted’. There followed a statement that there were no confirmed cases of AIDS among people with haemophilia in the UK. Under the heading ‘GAYS OPPOSE BAN ON GAY DONORS’, the release stated:

SHRG in particular and, it is thought, the majority of the gay population reject any proposals for a voluntary or compulsory ban on British gays giving blood. This last proposal is the most panic-stricken of the many strange proposals aired in recent weeks.<sup>21</sup>

<sup>16</sup> Meeting minutes [SNB.003.7116] at 7120

<sup>17</sup> The first positive HIV test results obtained in the Grampian Health Board area were from blood samples taken in 1984. By contrast, samples taken in the Lothian Health Board area in 1983 yielded 68 positive results. See table 3, page 32 within <http://www.documents.hps.scot.nhs.uk/general/review-of-communicable-diseases-1999.pdf> (last accessed 24 December 2014)

<sup>18</sup> Label on information leaflet [PEN.013.1395] (Caps in original)

<sup>19</sup> Day 9, page 171

<sup>20</sup> Press statement [SGH.002.6759]

<sup>21</sup> Press statement [SGH.002.6759] at 6760

**28.16** Characterising descriptions of the disease as sexually transmitted as ‘erroneous’ was unfortunate: it was wrong in fact. The statement that there were no confirmed cases of AIDS in people with haemophilia in the UK was made in a number of different contexts in May 1983<sup>22</sup> but this, too, was incorrect. The Communicable Disease Report of the Public Health Laboratory Service (PHLS) for the week ending 6 May 1983 recorded that AIDS had been reported in a 20-year-old man with haemophilia in Cardiff.<sup>23</sup> That information was not widely known. Dr McClelland had no recollection of being aware of it at the time.<sup>24</sup> The gay community felt unfairly targeted as a vector of disease, in the USA and in the UK, but adopting an extreme position of denial was unlikely to have been helpful to their position, if maintained. It is to the credit of all involved in Edinburgh and the South East of Scotland that it was not maintained.

**28.17** The SHRG press release called for research and screening in relation to AIDS to be given greater priority and greater funding. It also called on the press to exercise restraint. Dr McClelland agreed that there had already been alarmist reports in the UK press.<sup>25</sup>

**28.18** The stance of the SHRG was modified in relation to what must have been an early version of Dr McClelland’s leaflet. A follow-up comment was published in the July/August 1983 edition of *Gay Scotland* at page 10:

SHRG secured a major success in its consultations with medical authorities by having a proposed leaflet withdrawn because it was seen as anti-gay and likely to cause panic. A revised leaflet drawn up jointly by SHRG and the South-East Scotland Blood Transfusion Service has now been agreed.<sup>26</sup>

**28.19** An agreed form of words for the leaflet was a major step forward.

**28.20** The magazine also reported that AIDS had, in fact, arrived in Scotland, with two cases ‘highly suspected’. Much of the report narrated cooperation between gay organisations in Scotland and the medical profession, both in relation to people who might have symptoms of AIDS and in relation to blood donation. It reported that a monitoring group was being set up involving Dr McMillan, the SHRG and the Blood Transfusion Service.

**28.21** Dr McClelland described the relationship between the gay community in Edinburgh and the blood transfusion service over this issue as follows:

At some point in the period between May/June of 1983 we became very much aware that there was a major issue among the gay community in Edinburgh, that they felt they were going to be stigmatised by this and that’s an issue that persists to this very day. We felt that the only way to approach this was to very positively engage with the gay community, and the people who were the spokesmen were Derek Ogg ... and a colleague of his, Nigel Cook. We actually brought in somebody who had a very good working relationship with them, which was Dr Alexander McMillan who was one of the consultants in the sexually transmitted disease department. As a result of that, we tried to work with them on the creation of a wording that they were able to endorse. As you

<sup>22</sup> See Chapter 9, *Knowledge of the Geographical Spread and Prevalence of HIV/AIDS 1*.

<sup>23</sup> PHLS bulletin for week ending 6 May 1983 [DHF.001.4349]. See discussion in Chapter 9, *Knowledge of the Geographical Spread and Prevalence of HIV/AIDS 1*, paragraphs 9.95–9.97.

<sup>24</sup> Day 12, page 17

<sup>25</sup> Ibid page 19

<sup>26</sup> *Gay Scotland*, July/August 1983 [SGH.002.6698]. A summary of the revised leaflet is set out in the magazine.



can see from this piece on the screen, they eventually did, and I think we were fairly clear that we were trying to get the best out of a difficult situation, and rather than producing a leaflet which perhaps had the wording that we would have chosen, that would be totally rejected by the gay community, we were trying to strive for something that could not only be accepted but endorsed, and quite a lot of work was done over that summer to ... promote this leaflet and the general approach within the gay community in Edinburgh.

So I'm sure the wording was amended possibly more than once as a result of dialogue – actually sitting round a table with these guys.<sup>27</sup>

**28.22** In a paper on donor selection produced for the Inquiry, Dr John Gillon, Edinburgh and South East Scotland BTS, observed:

This [dialogue] was extremely productive in securing the co-operation of the Scottish homosexual community, and gave rise to formal collaboration in the establishment of the Scottish AIDS Monitor Group (SAMG), an information sharing group consisting of representatives of SHRG, SNBTS and a consultant genito-urinary medicine (GUM) physician, on 22 June 1983.<sup>28</sup>

### Revised leaflet

**28.23** A leaflet dated June 1983 was the first to be deployed for use at donor sessions.<sup>29</sup> In comparison with the first draft, a simpler approach had been adopted in the leaflet to the definition of the groups at risk of the disease and the groups asked not to give blood. There was a single list of groups that appeared to be at risk of AIDS, including men who had multiple partners of the same sex, and it was said to be unknown why the members of these groups were more susceptible to the disease. The tone of the leaflet had been softened. It stated:

[U]ntil more is known about the cause and spread of AIDS, we would ask people in any of the high risk groups described above to avoid giving blood until we have a suitable screening test.<sup>30</sup>

**28.24** Dr McClelland was asked about a possible difficulty of interpretation in the reference to the group, 'men who have multiple partners of the same sex'. Dr McClelland said that there was no guidance as to what 'multiple' might mean and explained that this was a problem 'that has been discussed and explored again repeatedly'.<sup>31</sup> He emphasised the need to avoid a situation in which the precautions adopted ruled out the majority of potential donors; the question of 'how many sexual partners is too many' posed the same difficulty with heterosexual transmission.<sup>32</sup>

**28.25** The geographical concentration of AIDS in particular parts of the world also raised issues of potential racial discrimination. Dr McClelland described these questions of what to include in publications as 'the tip of a huge iceberg of unresolvable problems'.<sup>33</sup>

<sup>27</sup> Day 12, pages 20–21

<sup>28</sup> Report [SNB.014.3125] at 3132

<sup>29</sup> The leaflet [SNF.001.3397]; Dr McClelland – Day 12, page 26

<sup>30</sup> Leaflet [SNF.001.3397] at 3398

<sup>31</sup> Day 12, page 27

<sup>32</sup> Ibid page 28

<sup>33</sup> Ibid page 28

**28.26** Another noteworthy aspect of the leaflet was that the answer to the question, 'Who can get the disease?' included in its list 'haemophiliacs' and 'recipients of blood transfusion'. When asked about this, Dr McClelland said:

I think by this time Dr Anne Smith and myself who drafted this, we had little doubt that the evidence that had been assembled by the CDC had to be interpreted as showing that this was a blood transmissible disease. We think we really had no doubt about that.<sup>34</sup>

**28.27** There were striking differences between the tone of this material and the information being given to people with haemophilia at this time, however, in particular a letter containing text drafted by Professor Bloom which was sent to members of the Haemophilia Society on 4 May 1983.<sup>35</sup> Dr McClelland was asked for his view:

Q. [T]he question which has been posed to us and which I'm therefore posing to you is: is there not an inconsistency between, on the one hand, people involved in blood transfusion saying that those with haemophilia, those receiving blood transfusion are at risk, even to the extent that they are asked not to donate their own blood, and the tone of this letter and other similar material, which is actually quite reassuring? This is all contemporaneous material. Is there an inconsistency?

A. Absolutely, clearly, there is.

Q. Yes.

A. I think this [the Bloom letter] is extraordinarily reassuring advice and it is one example of many very reassuring statements, as it were, risk-minimising statements, that were made over this period, which – I can't honestly say – I can't recall whether at the time I sort of scrutinised these statements and said, 'Gosh, that's very – that's a bit too reassuring'. I think our preoccupations were probably with doing our bit actually.

I think, if I was or had I been aware of this, I don't think it would have modified the text that we put in our leaflet because I think we felt our priority was trying to do whatever the available information could guide us to do to minimise the risk to patients. That was really our priority at that time.<sup>36</sup>

**28.28** The contrast in approach between transfusionists, acutely aware of their responsibility for the collection of blood, processing donations and supplying blood, blood components and therapeutic products, on the one hand, and haemophilia clinicians torn between the need to treat potentially fatal conditions and recognising the risks associated with therapy, on the other, which arises at many points in this Report, is particularly clear in the present context.

---

<sup>34</sup> Ibid pages 28–29

<sup>35</sup> Letter [DHF.001.4474] – discussed in Chapter 9, *Knowledge of the Geographical Spread and Prevalence of HIV/AIDS 1*, paragraphs 9.89–9.95.

<sup>36</sup> Day 12, pages 30–31. See also Day 12, page 94 where Dr McClelland tempered his comments slightly, saying he should perhaps have said 'in my opinion inappropriately reassuring' rather than 'extraordinarily reassuring'.

### Circulation of revised leaflet

**28.29** Leaflets were again discussed at the meeting of the SNBTS Directors on 14 June 1983.<sup>37</sup> Dr McClelland is recorded as having tabled a revised version of the leaflet he had distributed at the Coordinating Group meeting on 24 May 1983.<sup>38</sup> Dr Mitchell circulated his blood donor questionnaire into which he had inserted the invitation to donors who were worried about AIDS to discuss it with the doctor at the blood donor session or to follow one of the other approaches suggested.

**28.30** At this meeting, Dr Harold Gunson<sup>39</sup> reported to the Scottish Directors on developments in England and Wales, where a leaflet drafted by Dr John Barbara was in circulation for comment and amendment and arrangements for distribution of the leaflet were under discussion. Dr McClelland updated the other Directors on his liaison with the SHRG. The meeting discussed the need to deter certain donors without causing offence to others. The Directors are recorded as noting that the Department of Health and Social Security (DHSS) were closely involved in discussions about the approach to take to high-risk donors in England and Wales and recommending that the Scottish Home and Health Department (SHHD) should have a similar involvement in Scotland.

**28.31** The next day Dr Albert Bell of the SHHD, who had attended the meeting, wrote a memorandum to Dr Archibald McIntyre, copied to Mr John Wastle, reporting on the discussions. According to the memorandum, Dr Gunson was still drafting the leaflet for England and Wales. The memorandum continued:

All the Directors present are now more aware of the complexity of the issues involved particularly in relation to the views of the homosexual community, the scope for misrepresentation by the press and the public, and the diplomacy required in presenting the AIDS issue in donor centres.<sup>40</sup>

**28.32** Dr Bell also referred to continuing issues about distribution and advised Dr McIntyre that there was no doubt that the SHHD would have to involve their Minister and could not rely solely on the views of the SNBTS. When Dr McClelland was asked specifically about the comments in the memo, he did not accept the implication that, at some earlier point, the Directors had been unaware of the complexities of the situation. He wondered if the memo instead reflected a previous lack of awareness within the SHHD of the complexity of the situation.<sup>41</sup>

**28.33** Later that day, Dr Bell wrote a second memorandum, this time to Mr Wastle in the SHHD and copied to Dr McIntyre.<sup>42</sup> Dr McClelland had informed Dr Bell that the leaflet tendered at the meeting the day before had now commenced circulation through the SHRG network. It was suggested that this appeared to have happened through some misunderstanding between the SHRG and the Edinburgh Regional Transfusion Centre. Dr Bell commented, however, that publication would seem to have demonstrated 'the acceptability of that particular presentation' to the SHRG.

---

<sup>37</sup> Meeting minutes [SNF.001.0085] at 0086–87

<sup>38</sup> Meeting minutes [SNB.003.7116] at 7120

<sup>39</sup> Chairman of the Regional Directors of the NBTS in England and Wales

<sup>40</sup> Memorandum [SGH.002.6755]

<sup>41</sup> Day 12, pages 106–107

<sup>42</sup> Memorandum [SGF.001.0960]

**28.34** In his evidence, Dr McClelland expressed his view that the circulation of the leaflet was not based on a misunderstanding.<sup>43</sup> Even if the leaflet was issued earlier than some people intended or expected, he felt it was a good thing that it had happened: ‘it was the right thing [to do] to get it out there’.<sup>44</sup>

### United Kingdom-wide leaflet

**28.35** Meanwhile, work continued on a UK-wide leaflet, prepared in the DHSS, though ‘progress ... was slow’.<sup>45</sup> The NBTS version had said that ‘a person in any of the high risk groups of developing AIDS ... should not give blood even though they are in normal health ...’.<sup>46</sup> That had been amended to ask that anyone who thought they might have the disease or be at risk from it should refrain from giving blood. However, the first reaction of Mr Norman Fowler, then Secretary of State for Health and Social Security, had been that the wording was ‘too strong’ and that further revision might be required.<sup>47</sup> A meeting took place on 6 July 1983 involving the Minister of State for Health and the Under Secretary of State.<sup>48</sup> Further revision occurred and debate ensued about appropriate methods of distribution.<sup>49</sup> Ministers appeared keen on a ‘low key’ approach. When it was suggested, however, that the leaflet ‘cannot be seen as a leaflet which you read and then change your mind about giving blood’,<sup>50</sup> a medically qualified civil servant<sup>51</sup> was provoked to intervene:

I am afraid I cannot accept that the leaflet should not be seen “as a leaflet which you read and then change your mind about giving blood.” To my mind this is precisely what it is intended for although the message has had to be slightly obscured for obvious reasons. Clearly we must bow to Ministers’ wishes on the matter of handling the distribution ... but ... I am not sure that Ministers have fully understood the pros and cons.<sup>52</sup>

**28.36** The civil servant’s own view, on purely medical grounds supported by independent advice which he respected, was that the only sensible course was to send the leaflet out with call-up cards.

**28.37** By contrast, in relation to the question of ministerial involvement in Scotland, Dr McClelland said that he was:

[Q]uite confident that there was never any interference. There may have been a lot of discussion within the SHHD but we were never given any direct or indirect verbal or written instructions not to do what we were doing.<sup>53</sup>

**28.38** It is also evident from the DHSS documentation on this issue that many people were involved in the preparation of the leaflet and discussion of arrangements for its distribution. One memorandum, dated 4 July 1983, was addressed to a Mr Joyce and copied to 26 other people.<sup>54</sup>

<sup>43</sup> Day 12, page 35

<sup>44</sup> Ibid page 36

<sup>45</sup> File note of 28 June 1983 [SGH.002.6752]

<sup>46</sup> Memorandum of 6 July 1983 [SGH.002.6732]

<sup>47</sup> Dr Bell’s memorandum of 6 July 1983 [SGH.002.6732]

<sup>48</sup> That is, Kenneth Clarke and Lord Glenarthur. See minute of meeting [DHF.001.4580] and ensuing memorandum [DHF.002.0412]

<sup>49</sup> Memorandums of 19 July 1983 [DHF.001.9912] and 20 July 1983 [DHF.001.9913]

<sup>50</sup> Memorandum of 21 July 1983 [DHF.001.9914]. In evidence, Dr McClelland stated that this was, in fact, the ‘sole purpose’ of his leaflet – Day 12, page 43

<sup>51</sup> This appears to have been a Dr Oliver – see Day 12, page 47 and memorandum of 4 July 1983 [SGH.002.6736]

<sup>52</sup> Memorandum of 25 July 1983 [DHF.001.9915]

<sup>53</sup> Day 12, page 46. See also pages 107–108

<sup>54</sup> Memorandum [SGH.002.6736]

**28.39** A leaflet for distribution across the UK was ready in September 1983.<sup>55</sup> It was in the following terms:

What is AIDS?

... AIDS is probably caused by a virus, but this is not known for certain.

Who is at risk from AIDS?

Most of the information about AIDS has come from the USA where approximately 1500 patients have been found to be suffering from the disease, up to the middle of 1983. Certain groups of people appear to be particularly susceptible; these are:

1. Homosexual men who have many different partners.
2. Drug addicts, male and female, using injections.
3. Sexual contacts of people suffering from AIDS.

It has also been found in a number of immigrants to the USA from the island of Haiti.

Patients with AIDS also seem more likely to have suffered, at some time, from various other diseases such as hepatitis B, syphilis or other sexually transmitted diseases.

....

Can AIDS be transmitted by transfusion of blood and blood products?

Almost certainly yes, but there is only the most remote chance of this happening with ordinary blood transfusions given in hospital. However, in the USA a very small number of patients suffering from haemophilia, an illness in which the blood will not clot, have developed AIDS. Haemophiliacs are more susceptible to AIDS because they need regular injections of a product called Factor VIII. This is made from plasma obtained from many donors. Should just one of the donors be suffering from AIDS, then the Factor VIII could transmit the disease.

How can the risks be reduced?

At present, there is no screening test the Transfusion Service can use to detect people with AIDS. So, until there is and until more is known about this disease, donors are asked not to give blood if they think they may either have the disease or be at risk from it.<sup>56</sup>

**28.40** In Scotland, this leaflet was issued with a press release by the Scottish Information Office dated 1 September 1983.<sup>57</sup> The press release reiterated that 'there is no conclusive proof that the disease can be transmitted in blood or in blood products'. Dr McClelland thought that the reference to 'no conclusive proof' (a line used in a number of government communications over this period) had an 'internal contradiction' in it.<sup>58</sup>

**28.41** The Inquiry examined some press comment from the summer of 1983. The *New Scientist* of 11 August 1983 referred to the forthcoming leaflet under a headline 'AIDS

---

<sup>55</sup> Leaflet [SGH.002.6675]

<sup>56</sup> Ibid [SGH.002.6675] at 6676

<sup>57</sup> Press Notice [SNF.001.0416]

<sup>58</sup> Day 12, page 51. See the discussion on this form of words in Chapter 9, *Knowledge of the Geographical Spread and Prevalence of HIV/AIDS 1*.

Circular'.<sup>59</sup> *The Sun* of 12 August 1983 covered the same story under a headline 'Docs ban gays' blood.'<sup>60</sup> Dr McClelland agreed that the latter was likely to have been an example of the sort of coverage the SHRG had had in mind when they called for 'press restraint'.<sup>61</sup>

**28.42** It was apparent from the minutes of an SNBTS Directors' meeting on 13 September 1983 that, by that time, the leaflets were in 'fairly wide' circulation in the Scottish transfusion centres, although it was not clear if they were publicly available in Glasgow.<sup>62</sup>

### Reception of United Kingdom leaflet

**28.43** The UK Working Party on Transfusion-Associated Hepatitis discussed leaflets at its meeting on 27 September 1983.<sup>63</sup> Different centres were trying different ways of presenting the leaflets to donors. It was minuted that the Working Party had a preference for deciding a uniform approach as soon as possible.<sup>64</sup> In the course of discussion, it was noted in relation to the lack of a uniform method of distribution:

Dr Lane presented the fractionator's view that a variable approach did not provide material of uniform specification but Dr Mitchell pointed out the problems associated with any infringements of the integrity of the donor.<sup>65</sup>

**28.44** It appears that Dr Mitchell continued to resist any steps that might damage relationships between the blood transfusion service and donors.

**28.45** Further discussion of the leaflet took place at a meeting of the (Scottish) Haemophilia and Blood Transfusion Working Group on 14 November 1983.<sup>66</sup> Dr McClelland was not present at the meeting; Dr Mitchell was the only Transfusion Director present. Members of the Working Group, which comprised Dr George McDonald (SHHD) Professor John Cash, Dr Charles Forbes, Dr Peter Foster, Dr Christopher Ludlam and Dr Robert Perry in addition to Dr Mitchell, were asked for their views on the effectiveness of the UK leaflet. The minute recorded that it was felt generally that the leaflet 'had not been particularly useful'.<sup>67</sup> This comment had surprised Dr McClelland when he read it in preparing for the Inquiry:

[T]his surprised me when I read this again because I hadn't picked up from any ... informal sources a sense that the leaflet was not useful. My impression of the general view, was, 'Yes, this is something that, you know, needs to be done because this is a serious disease and we don't want people to get it'.<sup>68</sup>

**28.46** It was recorded that a few donors had responded to the leaflet by declaring that they were homosexual but that there remained a problem of how to screen out those who might present as donors in spite of the leaflet.<sup>69</sup> It is not clear who, apart from Dr Mitchell and perhaps Professor Cash, Medical and Scientific Director of the SNBTS, would have had occasion to take a practical interest in the usefulness of the leaflet. Professor Cash's

<sup>59</sup> *New Scientist*, 11.08.1983 [DHF.001.4689]

<sup>60</sup> *The Sun*, 12.08.1983 [DHF.001.4690]

<sup>61</sup> Day 12, page 53. See paragraph 28.17 above.

<sup>62</sup> Minutes of meeting [SNF.001.0072] at 0073-4 and Dr McClelland: Day 12, pages 112-113

<sup>63</sup> Meeting minutes [SNB.014.3030]

<sup>64</sup> Ibid [SNB.014.3030] at 3032

<sup>65</sup> Ibid [SNB.014.3030] at 3032

<sup>66</sup> Meeting minutes [SNB.001.5188]

<sup>67</sup> Ibid [SNB.001.5188] at 5189

<sup>68</sup> Day 12, page 55

<sup>69</sup> Meeting minutes [SNB.001.5188] at 5189

view, expressed at the meeting, was that a reprint of the leaflet should include changes and that different ways of bringing it to the attention of donors should be sought but that the method of distribution should be left to the Regional Transfusion Directors (RTDs).

**28.47** At the SNBTS Directors' meeting on 8 December 1983, which was attended by all of the RTDs, SHHD officials and Dr William Wagstaff from Sheffield, it was agreed that a more active approach to the distribution of leaflets was now appropriate.<sup>70</sup> It was felt that each donor should receive a copy, and the donor questionnaire should now include the question, 'Have you read and understood the leaflet on AIDS?'. No further action was to be taken, however, until a revised version of the leaflet had been issued. Dr McClelland agreed to produce a revised version of the leaflet for consideration by the Directors.<sup>71</sup>

### Revision of leaflets

**28.48** On 23 December 1983 Dr McClelland wrote to Professor Cash.<sup>72</sup> He reminded Professor Cash that the leaflet was not at that time being sent out to all donors and he felt that the text needed revision before that was done. The donor questionnaire had now been revised and specific questions and a specific reference to AIDS added. The questionnaire was to be completed and signed by all new and repeat donors.

**28.49** On 3 January 1984, Dr Wagstaff wrote to the DHSS about the leaflet,<sup>73</sup> enclosing a summary of feedback on three months' distribution of it. He also mentioned a perception that revision was necessary and added that Dr McClelland<sup>74</sup> was rewriting the leaflet at that time. He continued:

Since it was his original draft which formed the basis for the present "official" leaflet, I am sure it would be wise to see his new draft before going to the printers.<sup>75</sup>

**28.50** Dr McClelland duly wrote to Dr Wagstaff on 10 January 1984, enclosing his new draft.<sup>76</sup> The suggested changes were his and his alone; he had not, he noted in the letter, discussed the changes with 'the Scottish Transfusion Directors, Harold Gunson's AIDS Working Party of the CBLA Sub-Committee, the Transfusion Directors Hepatitis Working Party, or any of the other numerous groups who appear to be concerned with this problem'. Rather, the revisions had been based on discussions with colleagues at the South East Scotland BTS, of which Dr McClelland was Director, and contacts in the USA. He had also taken some ideas from the leaflet used in the New York Blood Centre. Dr McClelland indicated that he would be discussing the proposals with the Scottish Directors on 17 January 1984 and intended to send a draft to Dr Gunson.

**28.51** In view of his comment about 'numerous groups who appear to be concerned with this problem', Dr McClelland was asked about the effect of the proliferation of contributors or commentators. Whilst he acknowledged that extensive scrutiny of drafts could be very useful, he thought that the number of people involved, 'risked standing in the way of actually doing anything'.<sup>77</sup>

<sup>70</sup> Meeting minutes [SNF.001.0178] at 0179

<sup>71</sup> Ibid [SNF.001.0178] at 0179

<sup>72</sup> Letter [SNB.014.3104]

<sup>73</sup> Letter [DHF.001.5119]

<sup>74</sup> Although the name has been redacted, the identity can be deduced from the rest of the letter.

<sup>75</sup> Letter [DHF.001.5119]

<sup>76</sup> Letter [SNB.014.3185]

<sup>77</sup> Day 12, page 58

**28.52** On 9 February 1984, Dr McClelland attended a meeting at the National Institute for Biological Standards and Control (NIBSC) on the infectious hazards of blood products.<sup>78</sup> At the meeting, he explained the three main strategies for minimising the risk of infection. These were (i) avoidance of high-risk donor communities (such as prisons, ‘known homosexual areas’, etc), (ii) detection of clinical abnormalities by examination and careful questioning and (iii) exclusion of high-risk donors, or their blood, always allowing an ‘escape route’ for a donor who was deemed unsuitable.<sup>79</sup>

**28.53** Further concern about the need for a re-draft was evident from a DHSS memorandum dated 14 February 1984.<sup>80</sup> The memorandum appears to have been written by Dr Diana Walford and contained the observation that, ‘[i]n view of the published evidence of transmissibility of AIDS by blood transfusion, our current advice to donors could seem too lax’. The Inquiry did ask Dr Walford for a statement on these matters but Dr Walford declined to provide one.<sup>81</sup>

**28.54** A revised draft which was current in February 1984 was discussed at a meeting of the SNBTS Directors on 13 March 1984.<sup>82</sup> In their discussion on AIDS, they noted a previous agreement that the current leaflet should be sent to repeat donors with the call-up letter for their next session. Dr McClelland was to revise it and his revised draft had been circulated.<sup>83</sup> It appeared to the Inquiry that the specification of those who should not give blood was becoming simpler, with a request that people in any of the groups at risk not give blood and with the list of those at risk set out as follows:

AIDS has occurred mainly in these groups:

- Intravenous drug users
- Homosexual men
- People from Haiti and some areas of Equatorial Africa
- People who have had sexual contact with persons at risk in the above groups or with a person found to have AIDS.<sup>84</sup>

**28.55** Dr McClelland explained to the Inquiry that the thinking was to identify groups where there was actual epidemiological evidence of transmission and that those should be the groups that the Service was asking to not donate.<sup>85</sup>

**28.56** The text as it stood at 12 June 1984 was attached to the minutes of the meeting of the Directors of that date.<sup>86</sup> Some illustration of the difficulty of achieving an agreed draft is provided by the relevant paragraph in the minutes:

As agreed at the previous meeting Dr McClelland had revised the leaflet which he had drafted for circulation to blood donors with call-up letters. The revised

<sup>78</sup> Draft minutes [SNB.004.8628]

<sup>79</sup> Ibid [SNB.004.8628] at 8634. While not specified in the minutes, it appears that the ‘escape route’ typically involved accepting a suspect donation ‘for research’ or ‘not for clinical use’, enabling the collection of blood to proceed without exposing the donor to embarrassment.

<sup>80</sup> Memorandum [DHF.001.5266]

<sup>81</sup> See correspondence [PEN.019.1279] and letter in reply [PEN.010.0103]

<sup>82</sup> Meeting minutes [SGH.001.0484] at 0485

<sup>83</sup> The revised draft is [SGH.001.0499] which has Dr McClelland’s initials on it and the month ‘2/84’

<sup>84</sup> Draft leaflet [SGH.001.0499] at 0501

<sup>85</sup> Day 12, pages 60–61

<sup>86</sup> Meeting minutes [SGF.001.0150] with the last page, 0155, being the leaflet.



draft had again received comments and a further one had been circulated with the agenda. Dr McClelland tabled another draft in substitute of the one which had been circulated and on the basis of comments made during the meeting this was again revised. (Final version attached.)<sup>87</sup>

**28.57** A printed leaflet, with text very similar to that under discussion at the meeting on 12 June 1984 and called ‘Important message to blood donors’, was published by the SNBTS during 1984, probably as the product of this process.<sup>88</sup> The leaflet explained what AIDS was, including that it was frequently fatal and could be transmitted by blood or blood products, and stated:

For the present therefore, it is important that those who belong to certain groups, who have an above average risk of contracting this condition, should not donate. These groups are:

- residents of or visitors to certain areas such as Chad, Haiti and Zaire
- sexually active homosexual men
- present or past abusers of intravenous drugs
- sexual partners, male or female, of any of the above people.<sup>89</sup>

**28.58** This leaflet is referred to in the Scottish Health Education Group leaflet, ‘Some facts about AIDS’ which bears the date ‘12/84’.<sup>90</sup> A chronology dated 30 November 1984 on actions taken in the South East Scotland to endeavour to make blood safe notes that the leaflet was published in August 1984 and was sent out with all call-up letters from 19 September 1984.<sup>91</sup>

**28.59** Additional steps were taken from November 1984 in relation to advice to donors. From the chronology referred to above, it is evident that some additional measures were implemented in the week beginning 19 November 1984. These included the re-design of the donor questionnaire so that, with effect from 26 November 1984, donors were required to sign a declaration that they had read the leaflet and excluded themselves from the AIDS risk groups. Beside the date 26 November 1984, there is a reference to the ‘established practice’ that all signatures had to be witnessed by the donor attendant.<sup>92</sup> On 29 November 1984, Professor Cash wrote to the RTDs, summarising actions required in relation to the leaflet, including that donors had to sign a statement that they had read the AIDS leaflet and, to the best of their knowledge, were not in one of the risk groups identified.<sup>93</sup> Dr McClelland was asked if these measures in November 1984 were related to the discovery of infection in patients treated only with Scottish products and he told the Inquiry that he was ‘fairly sure’ that this was the case.<sup>94</sup> Later in his evidence, he commented that the introduction of the signed statement by the donor was ‘probably one of the more important ... developments in this procedure’.<sup>95</sup>

<sup>87</sup> Paragraph 3(a) of the minutes [SGF.001.0150]

<sup>88</sup> Leaflet [SGF.001.0932]

<sup>89</sup> Ibid [SGF.001.0932] at 0933

<sup>90</sup> Leaflet [SNB.004.9329]

<sup>91</sup> Booklet [SNF.001.3381] at 3385

<sup>92</sup> Ibid [SNF.001.3381] at 3387

<sup>93</sup> Letter [SGF.001.0908]

<sup>94</sup> Day 12, page 72

<sup>95</sup> Ibid page 80

**28.60** The HIV infection of a group of people with haemophilia who had been treated at the RIE with NHS product ('the Edinburgh Cohort') is discussed elsewhere in this Report.<sup>96</sup> For present purposes, however, it is relevant to note that the 'implicated batch' (the batch of Factor VIII concentrate thought initially to have been associated with all of the cases of infection and latterly to have been associated with all but one or two of them) contained plasma collected from all five Scottish transfusion centres. Manufacture of the batch commenced on 7 November 1983.<sup>97</sup>

**28.61** At the SNBTS Directors' meeting on 11 December 1984, leaflets were again discussed, including the possibility of further re-drafting.<sup>98</sup> Dr McClelland undertook to circulate a leaflet produced by the Terrence Higgins Trust giving to homosexuals a clear explanation that they should not give blood.<sup>99</sup> Dr McClelland described the Trust as 'a very constructive organisation'.<sup>100</sup>

**28.62** By 17 December 1984, Dr McClelland acknowledged that the leaflet required to be revised again, although he considered that it would not be wise or practicable to issue another version just yet.<sup>101</sup> When he reflected on his letter in evidence at the Inquiry, however, he felt that the third proposal in his letter – changing 'sexually active homosexual men' to 'homosexual or bisexual men' – looked 'a bit like tinkering'.<sup>102</sup>

**28.63** The Inquiry also studied the process of re-drafting the leaflet involving the DHSS. The position in England regarding revision of the UK leaflet is set out in various internal memorandums. A submission seeking authority from Ministers for revision of the leaflet was sent on 10 August 1984.<sup>103</sup> That submission was approved on 16 October 1984. The minute recording the approval by the Minister of State for Health of the leaflet being revised and distributed in the manner suggested, also records an apology for the time taken to clear the documents for use.<sup>104</sup> Around this time, the Chief Medical Officer (CMO) for England and Wales requested information about the problems of AIDS and blood donations. A memorandum dated 19 October 1984 was sent in response, detailing the current situation on testing of donations and blood/plasma-related cases of AIDS in the UK. The memorandum ended with the following statement:

A leaflet advising donors from high risk groups for AIDS to desist from giving blood was issued by Regional Transfusion Centres in August 1983. Ministers have just agreed a redraft of this leaflet which strengthens the advise [*sic* – advice] and includes all practising homosexuals as being in the high risk group.<sup>105</sup>

<sup>96</sup> See Chapter 10, *Knowledge of the Geographical Spread and Prevalence of HIV/AIDS 2*.

<sup>97</sup> Report – *Actions Surrounding FVIII Batch 023110090* [PEN.016.1258] at 1263

<sup>98</sup> Meeting minutes [SGF.001.0137] at 0140

<sup>99</sup> Leaflet [SGH.001.0346]

<sup>100</sup> Day 12, page 72

<sup>101</sup> Letter to Professor Cash dated 17 December 1984 [SGH.001.0343]

<sup>102</sup> Day 12, page 67

<sup>103</sup> Memorandum [DHF.002.2192]; Submission [DHF.002.2193]

<sup>104</sup> Memorandum [DHF.002.2208] and leaflet [DHF.001.5849]

<sup>105</sup> Memorandum [DHF.002.0040] at 0041

**28.64** Publication of the revised leaflet was then delayed until it could be discussed at a meeting of the Working Group on AIDS on 27 November 1984. At that meeting, members had only minor comments to make on the draft, which was again submitted to the Minister of State for Health for approval.<sup>106</sup> As this chronology shows, the revised version of the 1983 leaflet did not appear until January 1985.<sup>107</sup> A DHSS Circular accompanied the copy of this leaflet sent to Regional Health Authorities and Special Health Authorities.<sup>108</sup> A copy of the circular was sent to the SHHD and Dr Bell replied to explain that the SNBTS was ensuring that all donors received a copy of the revised AIDS leaflet and were asked to sign a statement that they had read it and were not in one of the risk groups.<sup>109</sup>

**28.65** When a further re-draft was being contemplated in July 1985, a memorandum explicitly recording regret at the delay which had occurred in the revision of the previous leaflet was written by someone in the DHSS.<sup>110</sup> Professor Cash also recorded his views about undesirable delays in the issue of leaflets in letters he wrote to Dr Wagstaff<sup>111</sup> and Dr Kenneth Calman<sup>112</sup> on 14 December 1990.

### Subsequent leaflets

**28.66** When screening of donated blood was introduced in October 1985, a new leaflet was given to donors in Scotland explaining that their blood would be tested and they were asked to sign a form indicating that they understood the new message.<sup>113</sup> The leaflet stated (all emphasis in original):

PLEASE REMEMBER

It is essential that although we are introducing HTLV-III testing you **MUST NOT** volunteer to give a blood donation if you are or have been:

1. A practising homosexual or bisexual man.
2. A drug abuser, either man or woman, who injects drugs.
3. Resident in or a visitor to central African countries.
4. A sexual partner of people in these groups.

**28.67** In England at this time, the standard leaflet said that those in the high-risk groups 'MUST NOT GIVE BLOOD' (capitals as in leaflet).<sup>114</sup> The high-risk groups were said to be:

1. Homosexual and bisexual men.
2. Drug abusers, both men and women, who inject drugs.
3. Haemophiliacs who have been treated with blood products.
4. Sexual contacts of people in these groups.<sup>115</sup>

<sup>106</sup> Memorandum dated 3 December [DHF.002.2233]

<sup>107</sup> Leaflet [DHF.001.8919]

<sup>108</sup> Circular [DHF.001.8929]

<sup>109</sup> Letter dated 21 January 1985 [SGH.002.6907]

<sup>110</sup> Memorandum [DHF.001.7438]

<sup>111</sup> Letter [SNB.012.5019]

<sup>112</sup> Letter [SNB.012.5017]

<sup>113</sup> The final leaflet is [SGH.002.7077]; (A draft of this is [SGH.002.6981]).

<sup>114</sup> Leaflet [SGH.001.8292]. A memo dated October 1985 narrating the introduction of the new leaflet and of testing was prepared for the Advisory Committee to the National Blood Transfusion Service [SGH.001.8295]

<sup>115</sup> Ibid [SGH.001.8292] at 8293

**28.68** By August 1986, the South East Scotland BTS had developed a ‘Flash Card System’, whereby a card was given to donors by a member of the nursing or medical staff to read. The card read (capitals as in leaflet):

AIDS

PLEASE REMEMBER

1. ANY MAN WHO HAS HAD SEX WITH ANOTHER MAN SINCE 1977
2. ANYONE WHO HAS EVER INJECTED THEMSELVES WITH DRUGS
3. ANYONE WHO HAS EVER HAD A SEXUAL RELATIONSHIP WITH ANYONE IN THE ABOVE GROUPS

MUST NOT GIVE BLOOD<sup>116</sup>

**28.69** Dr McClelland explained that the flash card was a response to concern, which the service had held since the first leaflets, about how to ascertain that donors had read and understood the information:

The flash card was an attempt to move on a little bit from that and this was administered at the time when the donor was actually face-to-face with the member of the donor selection staff. You know, it went with the question, ‘Have you clocked this?’ ‘Have you read this?’ And, you know, ‘Are you in any of those categories?’<sup>117</sup>

### **Confidential Unit Exclusion**

**28.70** Dr McClelland was also asked about a system whereby donors could indicate that their blood should not be used. The system – referred to as ‘Confidential Unit Exclusion’ (CUE) – had been devised in the USA and catered for those who realised, once they were at a donating session, that they should not be donating, allowing them to continue through the process but mark their health questionnaire to indicate that their blood should not be used.<sup>118</sup> Although a system of this nature was tried in Edinburgh, Dr McClelland said that it had little effect:

As I recall, our experience with a version of this, which we did implement in Edinburgh, was that we seemed to have an extremely low yield. There were actually very few people who utilised the option. I think we eventually dropped it, actually.<sup>119</sup>

**28.71** Dr McClelland referred to a letter sent to him on 16 January 1985 by Dr Patricia Hewitt of the North London Blood Transfusion Centre.<sup>120</sup> Dr Hewitt commented on the considerable difficulties experienced in their West End Donor Centre in obtaining satisfactory answers to the questions posed in their questionnaire. Men were reluctant to pick up and read a leaflet on AIDS. A new leaflet, ‘Some reasons why you should not give blood’, had proved very popular, however, and the Centre provided a room where the donor could have privacy. Dr McClelland’s ‘escape route’ appears to have had some of the characteristics of the CUE approach in the USA.

---

<sup>116</sup> Flash card [SNB.004.8150]

<sup>117</sup> Day 12, page 74

<sup>118</sup> Ibid pages 76–77

<sup>119</sup> Ibid page 77. Some of the relative documentation is in a memo dated 18 January 1985 [SNB.014.3119]

<sup>120</sup> Letter [SNB.014.3110]

## Rest of Scotland

**28.72** From the narrative of the evidence already set out, in particular relating to the efforts made to achieve progress, it appears to the Inquiry that the lead in drafting and revising leaflets for Scotland was taken by Edinburgh and South East Scotland BTS. It was obvious that the process must have absorbed a great deal of the time and energy of Dr McClelland as Director and others in that region at the time.

**28.73** In the circumstances, the Inquiry was interested to establish the position in the rest of the country. As noted above, at the meeting of the Co-ordinating Group on 24 May 1983, Dr Mitchell outlined action taken in the West of Scotland BTS which probably did not constitute effective communication to donors of risk to the recipient of blood or blood products. Professor Urbaniak explained that he did not feel it necessary to take any action in the north east.<sup>121</sup>

**28.74** Dr Mitchell was asked further questions about the position in Glasgow. He was handicapped by lack of contemporaneous correspondence from Glasgow.<sup>122</sup> In his evidence, he referred to the multitude of leaflets that were around at the time. Unsurprisingly, he remembered the general position concerning public information over the whole period of 1983 onwards, rather than the detail of individual leaflets. He was asked if, on seeing Dr McClelland's draft leaflet at the meeting on 14 June 1983,<sup>123</sup> he might have taken it back for circulation in Glasgow. He answered:

I know that in Glasgow in some places this kind of leaflet would be met with a certain amount of derision from some of the rather hard-working donors who give blood in Glasgow.<sup>124</sup>

**28.75** This response suggests that Dr Mitchell would not have distributed Dr McClelland's leaflet. It seems likely, as Dr Mitchell thought, that before the UK-wide leaflet was issued in the autumn of 1983, Glasgow would probably have been distributing the standard questionnaire with the added question on a label, asking donors if they had heard of AIDS.<sup>125</sup>

## Effect on donors

**28.76** It was evident to the Inquiry that Dr Mitchell was particularly concerned about the integrity of the donor – as he pointed out in terms at the meeting of the UK Working Party on Transfusion-Associated Hepatitis on 27 September 1983.<sup>126</sup> At that meeting it was agreed that it might be helpful if RTDs would provide details of how they got information to the attention of the high-risk groups of donors. As far as the effect of the leaflet on donors in the west of Scotland is concerned, Dr Mitchell was referred to a table prepared around the end of 1983 to record reactions in different parts of the UK. Glasgow was the only Scottish centre included in the table. The entry for Glasgow reads:

Uptake by donors averages one or two leaflets per session. A handful of donors have been resigned after volunteering information about homosexuality.<sup>127</sup>

<sup>121</sup> See paragraph 28.11.

<sup>122</sup> Witness statement [WIT.003.0033] at 0034

<sup>123</sup> See paragraph 28.29.

<sup>124</sup> Day 9, page 173

<sup>125</sup> Glasgow and West of Scotland leaflet [PEN.013.1395]. See Dr Mitchell – Day 9, page 176

<sup>126</sup> Meeting minutes [SNB.014.3030] at 3032

<sup>127</sup> Table [PEN.010.0305]

**28.77** More generally, of the 14 centres included in the table, only two referred to offence being caused and, in both instances, that was by handing leaflets to donors. Some other centres merely made the leaflets available. Usage ranged from 500 leaflets in three months in Cardiff, to Lancaster where an average of 9500 leaflets per month had been used, no doubt because in Lancaster the leaflets were issued when donors were called up. In his evidence, Dr Mitchell referred to complaints from hall-keepers because of the large number of leaflets left on the floor after a donating session.

They [the leaflets] weren't taken away by donors, they were dropped on the floor by donors. That can either mean two things: One, the donor had read and understood; or, two, the donor was very upset and concerned to see such a reference to what he thought or she thought had been a group of well meaning people and of which they hoped to be a member. Certainly, to be confronted with this thing which said, 'Wait a minute, maybe you are not wanted here.' They may have come miles and miles, just for the sake of doing good, to be turned away.<sup>128</sup>

**28.78** Dr McClelland referred in his statement to the fact that some Directors were very concerned about the risk of offending donors by giving too much prominence to the leaflet.<sup>129</sup> In his paper, Dr Gillon highlighted the meeting of the English RTDs on 18 May 1983, where it was minuted that the Directors rejected the option of questioning donors about their private lives.<sup>130</sup> However, Dr McClelland had 'no recollection of having to deal with major donor complaints that reached my level about any version of this leaflet or the subsequent ... questioning process'.<sup>131</sup>

**28.79** It was clear that all those connected with transfusion in 1983 and 1984 were concerned that these new measures should not alienate donors and were conscious of the sensitivity of asking donors about their sexual behaviour, an unprecedented step which there was deep-seated reluctance to take.<sup>132</sup>

**28.80** The scope for differences of opinion (valid or otherwise) about the risks of undermining blood collection was considerable. Commenting on public education leaflets available in England and Wales, warning higher risk individuals against donating, Hugh Barnes said in an article in *Nature* dated 13 December 1984:

Leaflets are, of course, only as effective as their circulation. A receptionist at a NBTS centre was recently asked why no such warning to prospective blood donors was on display. 'We did have them out', she said, 'but they frightened our customers away'. Dr Harold Gunson of NBTS admits to some haphazard distribution in the past, but promises 'efforts will be made to ensure that all donors attending the clinic receive a copy'.<sup>133</sup>

**28.81** 'Haphazard distribution' appears to be an accurate description of the situation in Scotland in 1983 and 1984. Dr Mitchell, and others of a like mind, had the capacity to frustrate the public education programme. On the other hand, Dr McClelland's experience demonstrated that there was no unavoidable problem where there was a predisposition

<sup>128</sup> Day 9, page 177–178. In his statement, Dr Mitchell described a single instance of this: [WIT.003.0033] at 0334.

<sup>129</sup> Statement [WIT.003.0036] at 0041–42

<sup>130</sup> Statement [SNB.014.3125] at 3131. See Minutes [SNB.001.3489] at 3491–92.

<sup>131</sup> Day 12, page 42

<sup>132</sup> Ibid pages 24 and 42

<sup>133</sup> Barnes, 'Paper prophylaxis backfires', *Nature*, 13 December 1984 [PEN.017.0658]

to inform and a sensitive approach was adopted in making information available to prospective donors.

**28.82** A further aspect of the concern for donors was that there appeared to be fear that giving blood carried a risk of contracting AIDS. This concern was demonstrated in the responses to a series of surveys commissioned by the South East Scotland BTS.<sup>134</sup> In a revision of the leaflet in 1984, Dr McClelland introduced into a revision of the leaflet a question and answer about this, making it clear that donating blood carried no such risk.<sup>135</sup>

**28.83** These concerns about the effect on donors had a basis in experience as it evolved. Dr Gillon advised the Inquiry that there was a fall of 5–6% in the number of donations in the first quarter of 1985, necessitating an advertising campaign.<sup>136</sup>

### The donor population

**28.84** Dr McClelland was asked about the AIDS outbreak in Scotland, with particular reference to a report dated March 1993 by a Working Group convened by the CMO. This showed that, from 1984 to 1989 inclusive, among those testing positive for HIV, the largest single group in terms of mode of transmission was the group of intravenous drug users. However, as between Glasgow and Edinburgh (more precisely, Greater Glasgow and Lothian Health Board areas), of 321 people testing positive in the former area, 30% were intravenous drug users; whereas in the latter area, of 913 people testing positive, 53% were intravenous drug users.<sup>137</sup>

**28.85** Dr McClelland said that these figures showed the effect to a very large extent, in the years before testing, of the ‘Muirhouse Outbreak’. Muirhouse is an area in Edinburgh which experienced a major outbreak of HIV/AIDS in people who had a history of injecting drug use. The outbreak had an impact on Scottish statistics generally as well as locally. Dr McClelland said that the figures for HIV infection associated with intravenous drug use in Scotland were heavily biased by this one rather dramatic, highly localised outbreak.<sup>138</sup>

**28.86** The significant question was whether there would have been an overlap between the people in the outbreak described among the drug-using population and the blood donor population. Dr McClelland’s view (ultimately vindicated by scientific investigation) was that it was highly unlikely that there would have been individuals from that outbreak presenting as blood donors.<sup>139</sup>

**28.87** Dr McClelland was also asked about features of individual donors which may have made leaflets less successful, such as illiteracy or lack of fluency in English. His recollection was that such issues were not addressed in 1983.<sup>140</sup> In fact, in the chronology ‘Action Taken in S.E.B.T.S. To Endeavour to Make Blood Transfusion Safe’, one of the steps highlighted as taken with effect from the week beginning 19 November 1984 specifically referred to donors who were unable to read or were blind. In those circumstances, staff

<sup>134</sup> Dr McClelland – Day 12, pages 61-62

<sup>135</sup> Draft leaflet [SGH.001.0499] at 0502

<sup>136</sup> Report – *Donor Selection Policies and Procedures* [SNB.014.3125] at 3131

<sup>137</sup> Report – *Acquired Immune Deficiency Syndrome and HIV-Related Disease in Scotland* [SNF.001.0284] at 0296

<sup>138</sup> Day 12, page 85

<sup>139</sup> *Ibid* page 86. Subsequent genetic analysis of blood samples from the Edinburgh Cohort of haemophilia patients supports Dr McClelland’s view: IVDUs were excluded as sources of the infected donations. Holmes et al, ‘The molecular epidemiology of human immunodeficiency virus type 1 in Edinburgh’, *The Journal of Infectious Diseases* 1995; 171:45–53; [PEN.012.1679] at 1686. See Chapter 10, *Knowledge of the Geographical Spread and Prevalence of HIV/AIDS 2*, paragraphs 10.121–10.124.

<sup>140</sup> Day 12, page 89

had to satisfy themselves that these people understood the declaration and definition of risk groups. This was noted at the time to be 'established practice' anyway for the medical questionnaire.<sup>141</sup> Dr McClelland observed that issues of the presentation of information for those with difficulties in accessing it were less well addressed in the 1980s than they are now.<sup>142</sup> As Dr Hewitt's letter (paragraph 28.71 above) makes clear, some issues were well-recognised in London and shared with Dr McClelland in January 1985.

## Discussion

**28.88** The first questions that arise in relation to this topic are:

1. Whether steps should have been taken in Scotland earlier than May/June 1983 to alert blood donors to the risks of transmitting AIDS via donated blood and to prevent higher risk donors from giving blood.
2. Whether there were other measures which should have been adopted but were not.

**28.89** Any answer to the first question has to take account of the reality that regional autonomy meant that individual RTDs were free to adopt their own policies, an important factor that has arisen frequently throughout this Report. In the Edinburgh and South East Scotland BTS, Dr McClelland responded to the lead from the USA, where the outbreak was more advanced than in the UK, as soon as could have been expected. Advice was issued in the USA in the first months of 1983 and by May of that year Dr McClelland, Dr Anne Smith and Dr MacMillan not only had a leaflet in draft form but had established a liaison group with representatives of the SHRG to revise the advice. Dr McClelland's speed of response, and the effort he dedicated to making progress in preparing leaflets and securing the agreement of the gay community to an acceptable formula, were not universally applauded in Scotland. Dr Mitchell, in particular, did not do so. However, much that happened in Scotland, then and later, was as a result of Dr McClelland's efforts. His views were remarkably prescient and it is appropriate to recognise in this Report that, insofar as progress towards an acceptable solution was made, the credit is due to him.

**28.90** It was to become clear in time that HIV infection had already entered the blood donor population in Scotland. In 1983 blood was collected and pooled that, processed to produce Factor VIII concentrate, led to the infection of the 'Edinburgh Cohort'. As noted in paragraph 28.60, the 'implicated batch' associated with the Cohort, eventually shown to have infected the vast majority of the Cohort, contained plasma from all five Scottish transfusion regions. Sophisticated genetic analysis has shown that the infected donations probably involved were not collected from the intravenous drug using population or from those known to have been infected by heterosexual contact. So far as published, the geographical source of the donations has not been identified: they might have been collected anywhere in Scotland. Earlier cases of transfusion-transmitted infection would in due course be identified, and their sources are no better defined so far as the Inquiry's investigations have discovered.<sup>143</sup>

---

<sup>141</sup> Booklet [SNF.001.3381] at 3387

<sup>142</sup> Day 12, page 90

<sup>143</sup> Details are set out conveniently in Chapter 12 *HIV/AIDS: Response and Clinical Practice*.



**28.91** AIDS cases among coagulation defect patients occurred in all areas except the Dundee and Inverness regions. Whether or not steps taken earlier than May/June 1983 to alert blood donors to the risks of transmitting AIDS via donated blood and to prevent higher risk donors from giving blood might have been effective to prevent transmission of infection, the distribution of the leaflet in the Edinburgh and South East Scotland BTS, as revised following consultation with the SHRG, on 15 June 1983 could not reasonably have been earlier. In that area, the answer to the first question is clearly no.

**28.92** There is more difficulty with the rest of the country, so far as the evidence disclosed what happened. The position in Dundee and Inverness is not known. The problem of AIDS may indeed have been seen as 'minor' in north east Scotland at the time but the objective of the exercise was related to preventing or mitigating future risk. As to that, past experience could not be conclusive. Assessment required to take account of the magnitude of the harm that was targeted: AIDS was already known to be an extremely serious disease. The balance of opinion among transfusionists was moving towards a viral aetiology: HIV was apparently transmitted by blood. A precautionary approach to the possibility of risk required action.

**28.93** Dr Mitchell's observation about Dr McClelland's draft leaflet of 14 June 1983, that in some places in Glasgow 'this kind of leaflet would be met with a certain amount of derision...' by donors, reflects an unconstructive attitude to the use of leaflets aimed at discouraging high-risk donors. If the comment was a true reflection of his opinion of his donor population, as distinct from an observation reflecting on Dr McClelland, it was less than complimentary. One would not have expected the donor population of Glasgow, or any part of the West of Scotland region, to have responded to advice about the transmission of AIDS in that way. If they had, it would have been reasonable to expect Dr Mitchell and his colleagues to have corrected them. On any view, however, the observation disclosed an attitude that might have influenced less senior and less experienced Directors in framing their own policies.

**28.94** Dr Mitchell's own response, putting a stick-on label on his own questionnaire, was inadequate given the AIDS threat to the blood supply. Its wording was inapposite. The first sentence, 'Have you heard of AIDS ...' has no connection with the second, either textually or as a matter of substance. By May 1983 (which seems to be the likely date of adoption of the label) there would have been few people who had not heard of AIDS. That was never the issue to be addressed.

**28.95** The second sentence, 'If you have any doubts about giving a donation consult the doctor ...', was obscure. It left it open whether the prospective donor's doubts related to the risk of acquiring AIDS from the donation procedure (a misconception that was in fact entertained at the time: see paragraph 28.82 above) or the risk of passing on infection. So far as the risk of transmission of infection was concerned, it gave no guidance on who might be expected to have such doubts. It might reasonably be inferred that advice sought from the doctor at the session would relate to giving a donation, if that had been the whole advice, but reference to the prospective donor's own GP clouds that issue also. It is unclear what a GP would know about, or have concern about, in relation to blood donation. The final suggestion that the donor write to the Regional Director offered no assistance at all.

**28.96** The terms of Dr Mitchell's stick-on label gave no specification of the nature of the risk. The notice was lacking in guidance on reasons that might have been relevant to the

prospective donor's decision. In this respect the label was in marked contrast to the rest of Dr Mitchell's leaflet.<sup>144</sup> The leaflet listed, among other things, infectious diseases such as mumps, chickenpox and measles, and serious illnesses such as jaundice, asthma, blood diseases and diabetes, as conditions to be reported for consideration by the session doctor who would decide whether or not the individual would be allowed to donate blood. It was very specific about the factors that might give rise to concern.

**28.97** Dr Mitchell's sensitivity to the interests of donors, as he saw them, was highly developed. It was illustrated in his response to the pressure to discontinue collections in prisons and other penal institutions.<sup>145</sup> In relation to AIDS, and in retrospect, it appears likely that he gave those interests too much weight, given the gravity of the threat.

**28.98** The adoption of the UK-wide leaflet, with the support of the DHSS and the SHHD, put an end to controversy about whether it was appropriate to have such documents in issue. Dr Mitchell's suggestion that few were taken and that premises were strewn with discarded leaflets indicates that making leaflets available for distribution was not a sufficient solution to the problem of communicating the seriousness of the AIDS threat to recipients of blood and blood products. It required action on the part of the blood transfusion service. The resistance of an intransigent Director would have been difficult to overcome.

**28.99** Outside Edinburgh and South East Scotland BTS, an earlier initiative by the SHHD would have been required to give emphasis to the risks of transmission of AIDS by blood donation. As discussed in Chapter 17, *Blood and Blood Products Management*, the Common Services Agency (CSA)<sup>146</sup> and its sub-committees, while nominally having delegated responsibility for the SNBTS, were not proficient in technical transfusion matters. Consequently, any initiative would have had to come from the SHHD, which retained policy control over such matters.

**28.100** The SHHD recognised the regional autonomy of RTDs. Short of a major re-organisation of the service, such as was to take place many years later, there was nothing that could have been done to bring other regions into line with Dr McClelland's pioneering work in Edinburgh. Dr Mitchell was free to apply his own views within his own region in relation to advice to prospective donors.

**28.101** So far as central government action is concerned, it is impossible to avoid the conclusion that, to some extent at least, leaflet preparation and distribution were hampered by the number of interests involved. This is true of the UK revision in the course of 1984 (conceded in memorandums exchanged at the time: see paragraph 28.65 above) and also of the Scottish revision in 1984, though that at least was achieved by August. In both these instances, there were leaflets already in circulation but, to borrow Dr Perry's expression from another topic, there were points where the best was the enemy of the good. Nowhere was this more clearly demonstrated, perhaps, than in the memorandum on the matter circulated to 26 recipients. It is paradoxical that the Scots made faster progress with their leaflet, almost certainly because of the lack of government involvement, particularly when one reads the comments in the minutes of the SNBTS Directors' meeting

<sup>144</sup> Leaflet [PEN.013.1395]

<sup>145</sup> See Chapter 26, *Donor Selection – Higher Risk Donors*

<sup>146</sup> Section 19 of the National Health Service (Scotland) Act 1972 provided for the constitution of the Common Services Agency (CSA) for the Scottish Health Service with effect from 1 April 1974. Amongst its several responsibilities was the operational management of the blood services. See Chapter 17, *Blood and Blood Products Management*, paragraphs 17.23–17.25.

of 14 June 1983 where the Directors were hoping for a close involvement of the SHHD in the process. If they had succeeded, Dr Bell's comments on 15 June 1983 suggest that circulation of the leaflet, which was undoubtedly a good thing, would not have begun when it did. The involvement of government not only increased the number of those involved in an already crowded and unwieldy field, it also threatened to prioritise the wrong issues, as can be seen in the DHSS memorandums about the purpose of the leaflet.

**28.102** In the end, this was an issue which was largely practical and dependent on the knowledge and expertise of the transfusionists. It was probably inevitable that it would be thought best left to them to deal with the issue, with government kept informed, notwithstanding that the agreed approach had to accommodate the very widely differing views of individual Transfusion Directors.

**28.103** As for other participants, notably the representatives of the gay community, it looks remarkable from a current perspective that a body of lay people became so involved in the debate about a health issue. In the light of current medical knowledge, it is clear that their initial reaction to the draft leaflet was based on significant misconceptions. However, without their cooperation it is likely that the leaflet exercise would have been less successful and their involvement was, undoubtedly, to the benefit of all concerned.

**28.104** So far as the second question (whether there were other measures which should have been adopted but were not) is concerned, none of the many groups and individuals involved has suggested what else could have been done but was not done. The isolation of the virus, HIV, and the development of a screening test were investigations pursued with unparalleled vigour, in France, the USA and England in particular. The English researchers were successful in a timescale that, but for the unfortunate loss of priority described in Chapter 29, *The Discovery of HIV and the Development of Screening Tests*, almost certainly could not have been improved on. Any possible alternative approach would have been a temporary expedient, similar to the leaflet campaigns. If there had been an obvious step to take, it is not unreasonable to think that someone among those with the primary interest to make the suggestion would have thought of it.

**28.105** The second question, which was formulated in advance of the oral hearings, was designed to bring out any representations that interest groups or individuals might wish to make. There were comments critical of the lack of leaflets in languages other than English and the lack of attention to those with literacy problems. It is not possible to dismiss these comments but they perhaps reflect values that have developed much more recently than in the early 1980s. Against a background in which preparing and distributing any written advice at all was controversial, they appear to be something of a counsel of perfection. In a practical sense, adopting these suggestions could not have failed to hold up the process of production and distribution of the leaflets that were made available. In the end, in the view of the Inquiry, there was nothing more that could have been done that would have improved the situation.

## CHAPTER 29

### THE DISCOVERY OF HIV AND THE DEVELOPMENT OF SCREENING TESTS

#### Introduction

**29.1** This chapter describes the discovery of the Human Immunodeficiency Virus and the scientific research that led to the development in the UK of screening tests for infection.

**29.2** In 1986, the name 'Human Immunodeficiency Virus' (HIV) was adopted by the Varmus Committee.<sup>1</sup> Until then the virus had been known in French-inspired sources as lymphadenopathy-associated virus or immunodeficiency-associated virus (LAV/IDAV) and in US-inspired sources as human T-lymphotropic virus type III (HTLV-III). It was shown in 1984 that the viruses were the same.<sup>2</sup>

#### *The first human retroviruses*

**29.3** By the 1970s, retroviruses had been found in cats, horses, sheep, goats and other mammals and were well known to veterinary clinicians and pathologists.<sup>3</sup> In 1977, Japanese researchers investigating human diseases identified a retrovirus as the causative agent of an unusual leukaemia. Development work proceeded in the USA and the retrovirus was isolated in 1981 by Dr Robert Gallo (the principal US researcher in the area) and his colleagues at the National Institutes of Health (NIH) in the USA. They called it human T-lymphotropic virus type I, HTLV-I.<sup>4</sup> A second retrovirus was then isolated and called human T-lymphotropic virus type II, HTLV-II.

**29.4** The identification of a human retrovirus in 1977 was a 'slightly revelatory moment' for those researchers who had been expecting such a discovery but it was very much a revelation for those who had not known what retroviruses were and now came to realise that there was a new class of viruses capable of infecting humans and causing disease. Against this background, the concept that a pathogenic retrovirus was a possible disease-causing agent in humans became very prominent and topical amongst specialist virologists interested in AIDS.<sup>5</sup> Professor Andrew Lever, Professor of Infectious Diseases at Addenbrooke's Hospital, Cambridge, said that some virologists and infectious diseases specialists would have speculated, in the immediate aftermath of the first reports of AIDS in haemophilia patients, that a retrovirus similar to HTLV-I might 'fit the bill' for AIDS.<sup>6</sup>

#### *Institut Pasteur and LAV*

**29.5** Scientists at the Institut Pasteur in Paris, led by Professor Luc Montagnier, were among those who pursued that speculation. On 20 May 1983, an article was published in the journal *Science* reporting that researchers at the Institut had isolated a novel retrovirus from cultures of T-lymphocytes (a type of white blood cell which plays a central role in cell-mediated immunity) derived from the lymph nodes of a homosexual patient

<sup>1</sup> The Varmus Committee was convened by Dr Harold Varmus, Chair of the Retrovirus Study Group within the Vertebrate Virus Subcommittee of the International Committee on Taxonomy of Viruses: – last accessed 23 December 2014

<sup>2</sup> Cheingsong-Popov et al, 'Prevalence of antibody to human T-lymphotropic virus type III in AIDS and AIDS-risk patients in Britain', *The Lancet*, 1 September 1984; 477–480 [LIT.001.0417]; Preliminary Report, paragraph 8.92

<sup>3</sup> Professor Lever – Day 26, page 14

<sup>4</sup> Professor Lever's Witness Statement [PEN.015.0517] at 0518

<sup>5</sup> Ibid [PEN.015.0517] at 0518; Professor Lever – Day 26, page 13–14

<sup>6</sup> Professor Lever – Day 26, page 16; Professor Lever's report [PEN.015.0517] at 0518. HIV was thought to belong to the sub-group of retroviruses called 'lentiviruses,' although Professor Lever stated that the most recent research suggested that, while certainly a retrovirus, HIV does not properly belong to the sub-group of lentiviruses: Day 26, page 25.

('Patient 1') with signs and symptoms thought to precede AIDS.<sup>7</sup> The patient had multiple lymphadenopathies (swollen or enlarged lymph nodes). They reported that it appeared to be a member of the HTLV family. It was later recognised as identical to that subsequently isolated by Dr Gallo and his team at the NIH in 1984. Neither of the expressions 'LAV' or 'IDAV' appeared in the *Science* article. Rather, the article dealt with the possible classification of the virus as a member of the HTLV family and the differentiation of the new virus from the known viruses, HTLV-I and HTLV-II.

**29.6** The tentative conclusion of the article was that the virus belonged to a family of T-lymphotropic retroviruses that were horizontally transmitted in humans and might be involved in several pathological syndromes, including AIDS. The conclusion was uncommitted on the issue of whether the new virus was the aetiological agent causing AIDS. The 'antigen overload' alternative<sup>8</sup> was explicitly acknowledged. The article stated:

The role of this virus in the etiology of AIDS remains to be determined. Patient 1 had circulating antibodies against the virus, and some of the latter persisted in lymphocytes of his lymph node (or nodes). The virus-producing lymphocytes seemed to have no increased growth potential in vitro compared to the uninfected cells. Therefore, the multiple lymphadenopathies may represent a host reaction against the persistent viral infection rather than hyperproliferation of virus-infected lymphocytes. Other factors, such as repeated infection by the same virus or other bacterial and viral agents may, in some patients, overload this early defence mechanism and bring about an irreversible depletion of T cells involved in cellular immunity.<sup>9</sup>

**29.7** The full significance of the French discovery was not widely acknowledged in 1983. Later, Professor Montagnier commented:

Our results were still controversial ... and we had difficulty in obtaining the funding needed to better characterize the virus and develop a blood test. The tide only turned in France when Robert Gallo and his group in the United States made a similar discovery. In the spring of 1984, Gallo published more convincing evidence that HIV causes AIDS.<sup>10</sup>

**29.8** Despite the hesitancy expressed by Montagnier, there was growing interest in the scientific community in the hypothesis that transmission of a virus caused AIDS, and for some specialists the Montagnier discovery was significant. After the publication of their paper in *Science*, however, the French scientists struggled to persuade some others in the field that the virus they had isolated was indeed the cause of AIDS.

**29.9** In 2008 the Nobel Prize for Medicine was awarded to Luc Montagnier and Françoise Barré-Sinoussi (co-author of the *Science* article) for their discovery of the virus that causes AIDS. There had been controversy as to whether they or Dr Gallo's group had priority. In the opinion of Professor Robin Weiss,<sup>11</sup> the answer was clear: the French group published

<sup>7</sup> Barré-Sinoussi et al, 'Isolation of a T-lymphotropic retrovirus from a patient at risk for acquired immune deficiency syndrome (AIDS)', *Science*, 1983; 220:868–871 [LIT.001.0058]

<sup>8</sup> Discussed in Chapter 11, *AIDS Aetiology*.

<sup>9</sup> Barré-Sinoussi et al, 'Isolation of a T-lymphotropic retrovirus from a patient at risk for acquired immune deficiency syndrome (AIDS)', *Science*, 1983; 220:868–871 [LIT.001.0058] at 0060

<sup>10</sup> Montagnier, 'A History of HIV Discovery', *Science*, 2002, 298; 1727–1728 [LIT.001.3767]

<sup>11</sup> Professor Weiss was, at the time in question, employed at the Chester Beatty Laboratories, London. He is currently Emeritus Professor of Viral Oncology at UCL Medical School.

first.<sup>12</sup> It is not necessary to examine the merits of the controversy over priority any further in this Report.<sup>13</sup> Inevitably, however, against that background there were mixed reactions among scientists to the French paper. Professor Lever said that some were very convinced by it but that others were convinced only after the Gallo publication.<sup>14</sup>

**29.10** As noted in Chapter 11, *AIDS Aetiology*, some Scottish scientists may have been persuaded by Montagnier. However, the impression given overall is that, leaving aside all national prejudices, internationally there was cautious scepticism among many opinion leaders about the French research, until Gallo's announcement. The Montagnier/Barré-Sinoussi team did not have a long track record of discovering viruses.<sup>15</sup> Their work did not have the international esteem required to spark the scientific research and development that followed the work of the Gallo group.

### National Institutes of Health and HTLV-III

**29.11** Dr Gallo and his group announced their discovery on 23 April 1984.<sup>16</sup> They reported the presence of antibodies to HTLV-III in a majority of patients with AIDS and at the same time announced that they had isolated human T-lymphotropic retroviruses from patients with AIDS. Preliminary details were published in two articles in *Science* on 4 May 1984.<sup>17</sup> It was announced that a retrovirus belonging to the HTLV family and designated HTLV-III had been isolated from a total of 48 subjects, some with AIDS, some with 'pre-AIDS' and some without symptoms but in risk groups. The authors concluded that HTLV-III might be the primary cause of AIDS.

**29.12** Gallo's announcement was a turning point in developing knowledge worldwide. The evidence that people who had AIDS-like symptoms had antibodies against HTLV-III was more compelling circumstantial evidence that the virus was associated with the disease than finding the virus itself in somebody with the illness. In the latter case, the virus could have been a 'passenger', a virus to which the real AIDS virus had made the person more susceptible. Gallo's work was a major contribution to developing knowledge.<sup>18</sup> In time, the isolation and characterisation of the AIDS retrovirus enabled retrospective studies to be carried out on stored frozen blood samples from haemophilia patients, using tests for antibodies to the virus.

**29.13** With the development of HTLV-III testing, following US research leading from Dr Gallo's work, further cases of infection emerged and the discovery laid the basis for the general consensus that has prevailed ever since.

**29.14** There was soon intense research activity and an avalanche of technical papers. The characterisation of the virus as a 'true' member of the HTLV family was discussed.<sup>19</sup> The development of cell systems for the reproduction of HTLV antigen, a necessary step in

<sup>12</sup> Day 48, page 173

<sup>13</sup> The debate is more fully set out in John Crewdson's book *Science Fictions*.

<sup>14</sup> Professor Lever – Day 27, page 30

<sup>15</sup> Professor Lever – Day 26 pages 69–70

<sup>16</sup> Preliminary Report, para 8.84

<sup>17</sup> Gallo et al, 'Frequent detection and isolation of cytopathic retroviruses (HTLV-III) from patients with AIDS and at risk for AIDS', *Science*, 1984; 224: 500–503 [LIT.001.3769]; Popovic et al, 'Detection, Isolation, and Continuous Production of Cytopathic Retroviruses (HTLV-III) from Patients with AIDS and Pre-AIDS', *Science*, 1984; 224 (reprint *Plasma Quarterly* Summer 1984) [SNB.004.9457]

<sup>18</sup> Professor Lever – Day 26, pages 71–72.

<sup>19</sup> Schupbach et al, 'Serological analysis of a subgroup of Human T-Lymphotropic Retroviruses (HTLV-III) Associated with AIDS', *Science*, 1984; 224: 503–505 [LIT.001.0685]

developing antibody tests, was researched in May 1984.<sup>20</sup> The high incidence of antibodies specific to HTLV-III in patients with AIDS and pre-AIDS was identified, supporting the suggestion that HTLV-III was the primary cause of AIDS.<sup>21</sup>

### Scientific response to LAV/HTLV-III in the United Kingdom

**29.15** The work of Dr Gallo's group in isolating the HTLV-I retrovirus responsible for the rare form of leukaemia reported in Japan had led to research in the UK. The work done was important in relation to later research on HIV. Professor Lever said in his report:

[M]uch of the research work that had been undertaken in isolating and characterising HTLV-1 was absolutely critical in facilitating the rapid discovery and identification of HIV. The discovery and usage of certain cell lines for isolating viruses and the discovery of growth factors for human cells were all essential prerequisites for retrovirus isolation. If HTLV-1 had not been identified when it was then the identification of HIV might have been delayed by several years.<sup>22</sup>

**29.16** For present purposes, research collaboration between Professor Robin Weiss at the Chester Beatty Cancer Research Institute and Professor Richard Tedder at the Middlesex Hospital, in a project to develop a serological assay for the detection of antibodies to HTLV-I, became particularly significant.<sup>23</sup> Professor Weiss provided Professor Tedder with infected serum and Professor Tedder's laboratory worked to develop the detection of antibodies to HTLV-I. By late 1983, this work was well advanced. As will be seen later, they subsequently used the expertise they gained in that research to develop anti-HTLV-III tests when it became clear that this virus was associated with AIDS.

**29.17** Earlier in 1983, Professor Tedder and his virology colleague Dr Philip Mortimer of the Public Health Laboratory Service (PHLS) both thought that AIDS looked like a transmissible viral infection. They had a meeting with a Department of Health and Social Security (DHSS) official, early in 1983. They explained their views about AIDS, including its similarity to Hepatitis B in terms of the group affected and the likely means of transmission, in order to see if they could assist by exploring the hypothesis that AIDS was a transmissible viral infection. Their overture was, however, rejected, and they were discouraged from promoting the 'transmissible agent' theory of the cause of AIDS.<sup>24</sup>

**29.18** The official government line at the time was that there was 'no conclusive evidence' that AIDS was transmitted by blood products.<sup>25</sup> The rejection of the scientists' approach had an important bearing on what later transpired. Briefly, development work proceeded in the non-government sector. Through their organisations, Professor Tedder and Professor Weiss obtained the intellectual property rights to their discoveries, initially in respect of HTLV-I, and were able to shape the approach to the development of screening. Progress was to be determined by the scientists, not by the UK Government.

<sup>20</sup> Popovic et al, 'Detection, Isolation and Continuous Production of Cytopathic Retroviruses (HTLV-III) from patients with AIDS and Pre-AIDS', *Science*, 1984; 224 (reprint *Plasma Quarterly* Summer 1984) [SNB.004.9457]

<sup>21</sup> Sarnadharan et al, 'Antibodies reactive with human T-lymphotropic retroviruses (HTLV-III) in the serum of patients with AIDS', *Science*, 1984; 224 [LIT.001.5515]; Gallo et al, 'Frequent Detection and Isolation of Cytopathic Retroviruses (HTLV-III) from patients with AIDS and at risk for AIDS', *Science*, 1984; 234: 500–503 [LIT.001.3769]

<sup>22</sup> Professor Lever's report [PEN.015.0517] at 0518

<sup>23</sup> Professor Tedder – Day 49, pages 3–4; Professor Tedder's Witness Statement [PEN.017.1831]

<sup>24</sup> Professor Tedder – Day 49, pages 97–98. For discussion on the 'transmissible agent' hypothesis concerning the aetiology of HIV/AIDS, and competing hypotheses at the time, see Chapter 11, *AIDS Aetiology*.

<sup>25</sup> Extract from *Hansard*, 14 July 1983 [SGH.002.6720] at 6721. See Chapter 9, *Knowledge of the Geographical Spread and Prevalence of HIV/AIDS 1*, paragraphs 9.108–9.110

**29.19** In France, the Institut Pasteur proceeded to develop an antibody screening test based on the LAV isolated by the work of Montagnier and Barré-Sinoussi. Professor Tedder and Professor Montagnier were in contact and, in the autumn of 1983, a courier brought to London a sample of IDAV, the name given at the time to the current version of the first French isolate. IDAV and LAV-I were both epidemic HIV-1 viruses and were in time to be identified as the same, for practical purposes. A ferry and trains were delayed and the courier left the flask in a security locker at Waterloo Station. When it was collected, the virus had died and could not be resuscitated.<sup>26</sup> Professor Weiss obtained more of the French virus in February 1984 but the London scientists had effectively lost some months of research work.

**29.20** Professor Tedder's comments capture the position:

[W]e would have been six months ahead of where we were in September 1984 in terms of the early epidemiology. We might have had a British isolate, a UK isolate, much earlier. We might have been able to work with commerce much earlier.

As a scientist, it grieves me that we lost six to nine months on the field. Had we been publishing the [Cheingsong-Popov] 1984 September paper in January 1984/February 1984, we would have presaged the entire Gallo and Montagnier disclosure in the *Science* paper of May 4th. We would have not only demonstrated the virus, in reality we would have had the break on epidemiology. And I really – I look back and some things happen and some things don't. This young man carrying a bottle of LAV1 in his hand, nobody to meet him, leaving it in a lock-up on Waterloo Station, such are things fairy stories are written about, you know? Such is life ....

I still weep about it. But, you know, we didn't do badly in the end.<sup>27</sup>

**29.21** For the purposes of this Inquiry, speculation on what might have been is not productive. However, the anecdote illustrates an important aspect of the reality of cutting edge scientific research in areas that attract the attention of several groups of researchers: priority may be determined by chance events. There is no necessary logical progression that allows one to transpose one team's success onto another's failure and reach conclusions about what ought to have happened, as distinct from what might have happened.

**29.22** As events unfolded, Professor Weiss' laboratory was the first in the UK to become involved in investigating HIV when they did eventually receive the French isolate of the virus from Dr Montagnier in February 1984.

### **The propagation medium and the selection of test format**

**29.23** At this point, it is convenient to say something about the science of testing since it has an important bearing on the differences between, and the relative merits of, the test developed by Professors Weiss and Tedder and the tests developed in the USA.<sup>28</sup> In simple terms, and in the context of AIDS, the early tests were looking for the antibody to the virus. An antibody is a protein produced by the body in response to an antigen, which

---

<sup>26</sup> Professor Tedder's Witness Statement [PEN.017.1831]; Professor Tedder – Day 49, pages 6–7

<sup>27</sup> Professor Tedder – Day 49, pages 62–63

<sup>28</sup> Ibid, pages 37–48 and 50–60. Professor Tedder explained to the Inquiry these different features of testing kits and this summary is derived from his evidence.



can be thought of as a 'foreign invader'.<sup>29</sup> The formation of an antibody in response to an antigen is a defining characteristic of an antigen. The human immunodeficiency virus – HIV – is an antigen. It stimulates the human body to form HIV antibodies. The screening systems developed at this early period targeted the HIV antibodies produced rather than the antigen. In most infections, the formation of antibodies signals the eradication of the infection.<sup>30</sup> Unlike antibodies produced against many other infective agents, however, the production of HIV antibodies does not indicate the eradication of the disease.<sup>31</sup> The presence of HIV antibodies was consistent with continuing disease.

**29.24** HIV is an intracellular parasite and can only propagate (grow) by getting into human white blood cells.<sup>32</sup> Once Professor Weiss had received a sample from Professor Montagnier in February 1984, it was necessary to propagate the virus in order to produce antigen for the test. The choice of cell line was important. That required the selection and use of appropriate white blood cells – a specific cell line – as a medium for propagation.

**29.25** When the HIV virus is released from a cell line it may carry with it components of the cells making up the line. These components may themselves cause reactions when introduced into a human recipient, eliciting their own antibodies. The cell line (known as H9)<sup>33</sup> used in the production of virus for the early US enzyme-linked immunosorbent assay (ELISA) tests was very efficient: large volumes of HIV antigens could be grown in it. However, the envelope of the cells making up the cell line (their 'lipid membrane') contained proteins other than HIV that could elicit antibodies when administered to some patients. The HIV antibody test produced using this cell medium was therefore responsive not only to HIV antibodies specifically but also to antibodies found in some normal, healthy people who had received a blood transfusion or an infusion of platelets, for example.<sup>34</sup> The test would register positive for antibodies in the case of these individuals whether or not they were infected with HIV. As a result, the risk of false positive results with tests using reagents produced by the H9 cell line was high: the cell line in which the virus was grown was itself responsible for false positive results.<sup>35</sup> The risk was inherent in the basic technology adopted at this early stage.<sup>36</sup>

**29.26** Professor Weiss' team used a different cell line, the 'CEM' cell line,<sup>37</sup> on the advice of a colleague, Professor Mel Greaves.<sup>38</sup> This avoided problems encountered with some of the tests developed in the USA. They developed the CEM cell line initially for research into HTLV-I. The CEM cell line used (and provided by them to the Institut Pasteur on licence)<sup>39</sup> did not express the antigens (in addition to HIV) typically produced by US technology.<sup>40</sup> As demonstrated by the research reported in the Cheingsong-Popov paper referred to at paragraph 29.14 above, it was less prone to false positive results and in fact yielded almost no false positive results in the 1984 research exercise reported.<sup>41</sup> A factor contributing to its success in that respect may have been that the proportion of infected individuals in

<sup>29</sup> See paper produced by Dr Peter Foster [PEN.013.1309], Glossary at 1310.

<sup>30</sup> Dr Cuthbertson – Day 46, page 5

<sup>31</sup> Ibid page 6

<sup>32</sup> Professor Weiss – Day 48, page 165

<sup>33</sup> A sub-line of the leukaemia tumour line.

<sup>34</sup> In particular, the Class-II Major Histocompatibility Complex (MHC-II) antigens (MHC Class II antigens). These are found also in women if they have had children with DR4 positive partners: Professor Weiss – Day 48, page 167

<sup>35</sup> See discussion of this at paragraph 29.29

<sup>36</sup> Professor Tedder – Day 49, pages 45–46

<sup>37</sup> The CEM cell line is associated with some forms of T-cell leukaemia and Hodgkin's disease, a cancer originating from lymphocytes.

<sup>38</sup> Professor Weiss – Day 48, pages 168–169

<sup>39</sup> Ibid page 170

<sup>40</sup> Professor Weiss' report [PEN.017.1261]

<sup>41</sup> Professor Weiss – Day 48, page 159

the donor population was lower in the UK than in the USA<sup>42</sup> but the technology does appear to have been fundamentally more satisfactory at this early stage than that typically employed by US pharmaceutical companies.

**29.27** The second difference that needs to be noted is the difference between radioimmunoassay (RIA) and ELISA tests. Professor Tedder's research work, once virus-infected material had been provided to him, led to an RIA which was considered to be working by 4 July 1984, at least for laboratory purposes.<sup>43</sup> In RIA systems, radioactive isotopes are used in the detection of the target antibody. By contrast, in an ELISA the detection element is provided chemically by an enzyme. Although this initial RIA turned out to be highly successful in the UK research studies, the Inquiry heard evidence that around this time (1984–85) the general scientific climate was turning against RIA testing because of the use of radioactive materials and the safety of staff involved in testing.<sup>44</sup> In the event, no commercial company developed an RIA for the detection of HIV antibodies<sup>45</sup> and Professor Tedder's RIA was to give way later to an ELISA test.

**29.28** A third, and highly technical, distinction relates to the test format and the difference between a so-called solid phase test and a competitive test. The distinction lies in the functioning of the tests. It is relevant in this Report only to the extent that it came to have a part in assessing the respective merits of the US solid phase tests and the Middlesex Hospital/Chester Beatty competitive radioimmunoassay test developed by Professors Weiss and Tedder (the MH/CB assay) in a competitive market.

**29.29** All of the US tests under development were solid phase ELISA tests. To be fully effective, the virus antigen had to be 'pure'. For practical purposes it was assumed that virus antigen and only virus antigen was adsorbed (condensed on the active portion of the test kit). However, as has been described in relation to the cell line typically used in the USA, the material that is applied in the solid phase test may contain antigens other than those to which the test is directed. As a result, the US model was exposed to the risk of attracting non-relevant antibodies and thereby producing false positive results.

**29.30** The commercial companies involved in developing the US tests used large vessels to propagate the virus and then purified the virus from the 'soup' in which the cells were growing. The virus then had to be further purified, pelleted and further cleaned up physically by processing through a density gradient (a centrifuge used to isolate and purify cells, viruses and sub-cellular particles). A great deal of work was involved and the complexity of the process added to the time required for development of effective test kits.<sup>46</sup>

**29.31** By contrast, the competitive test format used in the MH/CB assay did not require 'pure' antigen. It used relatively high volumes of serum and was inherently more specific in application than the US test format. It attracted criticism in the 1980s, however, on the ground that it was relatively insensitive.<sup>47</sup> For present purposes, the technical distinctions between the two approaches need not be developed further. It is, however, important to note that they were distinct and that the UK developments were able to proceed without challenge from the USA on intellectual property grounds.

<sup>42</sup> Ibid page 159. Professor Weiss suggested that this was probably true, not only in those contributing to commercial blood banks but also among volunteer donors in the USA at this time.

<sup>43</sup> Professor Tedder – Day 49, pages 15–16

<sup>44</sup> Ibid pages 65–67; Dr Dow's Witness Statement [PEN.017.1680] at 1681; Dr Mortimer's Witness Statement [PEN.017.1761]; Professor Cash – Day 48, page 136

<sup>45</sup> Dr Dow's Witness Statement [PEN.017.1680] at 1681

<sup>46</sup> Professor Tedder – Day 49, page 10

<sup>47</sup> 'Sensitivity' is a function of the test's ability to capture all cases of infection with the target pathogen. 'Specificity' is a function of the test's ability to identify only the target pathogen.

## United Kingdom research: the initial phase

**29.32** The research projects of Professors Tedder and Weiss in England, and the Institut Pasteur in France, were making progress over substantially the same period as the US research discussed below. When Professor Weiss obtained LAV from Professor Montagnier in February 1984, his laboratory was concerned to investigate the prevalence of the infection and the risks associated with it.<sup>48</sup> At that time, virological research into the disease was at an early stage of development. LAV/HTLV-III infection was a threatening and dangerous condition and funds were diverted by the two scientists from other areas of their respective institutions' research in order to begin the study. They proceeded without funding from either the Medical Research Council (MRC) or the DHSS.<sup>49</sup> They did not await the development of administrative solutions.

**29.33** Dr Gallo also provided Professor Weiss with isolates of HTLV-I, HTLV-II and, in mid-1984, provided HTLV-III for research purposes.<sup>50</sup> The US and French isolates had both been provided in terms of Material Transfer Agreements, a common format between research laboratories that restricts their use to research, stipulates that the provider accepts no liability and stipulates that the material must not be used for commercial developments.<sup>51</sup> The isolate provided by Dr Gallo was HTLV-III B, the same isolate as was provided to all scientists interested in the investigation. Montagnier provided the current version of LAV-1. Professor Tedder and colleagues started developing antibodies using the Gallo isolate and continued with that source material almost exclusively until, in about November 1984, Professor Weiss' group had produced a British isolate against which Professor Tedder's team could develop antibodies. A British test was trialled in November 1984. They propagated the antigen in CEM cells which produced better quality virus and a very high level of viral antigens trapped in the cells.<sup>52</sup> In this way, they continued to produce antigen until spring 1985. In 1984 there was little to choose between the French and US isolates and the choice of the Gallo material for research seems to have been a matter of chance.<sup>53</sup>

**29.34** The Cheingsong-Popov article of 1 September 1984 set out the first published results of that research.<sup>54</sup> In carrying out the project, the MH/CB RIA assay to detect antibodies to HIV developed by Professor Weiss and Professor Tedder was used.

## The MH/CB assay for anti-HTLV-III

**29.35** There were issues for the Inquiry whether any delay in the provision of funding by the UK government, or the US government's attitude to the use of the Gallo isolate (referred to later at paragraphs 29.41–29.43), hampered progress in developing a British screening test. It appears clear from their evidence to the Inquiry that neither factor prevented or hindered progress by Professor Tedder and Professor Weiss in laboratory-based development of the assay. As noted later, funding for scale-up to industrial production became an issue, however.

<sup>48</sup> Professor Weiss' Statement [PEN.017.1261] at 1263; Professor Tedder – Day 49, page 6

<sup>49</sup> Professor Tedder – Day 49, pages 69–70

<sup>50</sup> Cheingsong-Popov et al, 'Prevalence of antibody to human T-lymphotropic virus type III in AIDS and AIDS-risk patients in Britain', *The Lancet*, 1 September 1984; 477–480 [LIT.001.0417] at 0418 regarding ascertainment of prevalence of the virus in patients with haemophilia.

<sup>51</sup> Professor Weiss – Day 48, pages 5–13, and 171

<sup>52</sup> Professor Tedder – Day 49, pages 11–12

<sup>53</sup> Professor Weiss – Day 48, page 170; Professor Tedder – Day 49, page 14

<sup>54</sup> Cheingsong-Popov et al, 'Prevalence of antibody to human T-lymphotropic virus type III in AIDS and AIDS-risk patients in Britain', *The Lancet*, 1 September 1984; 477–480 [LIT.001.0417]

**29.36** For them, it was an incredibly difficult and busy time, with resources stretched almost to breaking point.<sup>55</sup> In some respects, in attempting to meet the demands on them, Professor Tedder and his colleagues acted in a way that would have been constrained by modern employment practices.<sup>56</sup> Professor Tedder said that Dr Rachanee Cheingsong-Popov on one occasion left the maternity hospital where she was in the early stages of labour to finish a procedure in a radioimmunoassay. She gave birth to her first son two hours after returning.<sup>57</sup> Professor Tedder was to complain in strong terms about the lack of support and funding before the end of the year (1984)<sup>58</sup> but that did not inhibit the progress of their work. The scientists were pursuing their own project not only unsupported but also uninhibited by government oversight.

**29.37** In the event, the prototype MH/CB competitive assay was ready for laboratory application on 4 July 1984. At that stage, they were ready to carry out epidemiological studies.<sup>59</sup> On 16 July 1984, Dr Ian Fraser of the Bristol Blood Transfusion Service wrote to Dr Alison Smithies, DHSS, outlining what was proposed.<sup>60</sup> He reported that a screening test for AIDS was likely to be available within the next eight weeks or so for trial, first at Edgware and then at Bristol and Manchester.

**29.38** At that stage the DHSS did not have an isolate that could be provided to a commercial manufacturer in the UK for the development of a test. The MH/CB test was beginning trials but, from the summer of 1984, Professor Tedder and his colleagues believed that they needed a much larger number of donors to be tested than those dealt with in their paper to ascertain the prevalence of HTLV-III in the donor population. For this, they required to involve a wider range of centres. Widening the project involved risk and would require control. The National Blood Transfusion Service (NBTS) was reluctant to introduce general testing because of the risk of attracting individuals seeking access to 'AIDS tests' for personal purposes.<sup>61</sup> Targeted subsets had proved problematic in other contexts. It was important to avoid attracting 'window donors', individuals who thought they had been recently exposed, who were, as Professor Tedder put it, 'bad news' for the blood component issue but could have been 'devastating' for blood products.<sup>62</sup> There was, however, a clear need to expand the research.

**29.39** It was at this stage that DHSS officials made contact with their US counterparts to ask permission to use Gallo technology for screening in the National Health Service (NHS). The DHSS was aware of the development of the RIA by Professors Weiss and Tedder from isolate supplied by Dr Gallo 'for research purposes only'. Among other aims, the DHSS was keen to commence screening of donated blood for the virus, initially at two or three Regional Transfusion Centres. To do so, as the DHSS saw it, it was necessary to obtain further supplies of the virus from the USA.

**29.40** On 10 August 1984, a DHSS official, probably Dr Walford or Dr Smithies, wrote to the Assistant Secretary for Health in Washington DC. The letter narrated the work of Professor Tedder and Professor Weiss, and the anticipated publication of their research, and stated:

---

<sup>55</sup> Professor Tedder – Day 49, pages 78–79

<sup>56</sup> Ibid page 79

<sup>57</sup> Ibid page 70

<sup>58</sup> Ibid page 79; Letter to Dr A Smithies, DHSS dated 18 December 1984 [DHF.001.8856]

<sup>59</sup> Professor Tedder – Day 49, pages 15–16

<sup>60</sup> Letter [DHF.002.9126]

<sup>61</sup> Professor Tedder – Day 49, pages 71–72; Professor Tedder's report [PEN.017.1831] at 1833.

<sup>62</sup> Professor Tedder – Day 49, pages 72–74

We are anxious to extend the screening test initially to two or three of our Regional Transfusion Centres in order to establish the incidence of carriers amongst donors in a varied donor population. To do this further supplies of antigen are required over and above those that could be regarded as purely for research purposes which was the understanding on which [Dr Weiss] received the isolate from [Dr Gallo] in the first place. I am writing to request your agreement to our using the virus isolate originally provided by Dr Gallo to scale up production of the antigen.<sup>63</sup>

**29.41** It was stressed that the intention was for the isolate to be used mainly for NHS purposes. Permission was refused on 14 November 1984.<sup>64</sup> It was now clear that, outwith the boundaries of the Material Transfer Agreement entered into by Professor Weiss and Professor Tedder, the NHS was denied the Gallo isolate by the US government.

**29.42** The precise date on which the MH/CB assay was ready for routine use is not clear. It was reported to the Advisory Group on AIDS on 27 November 1984 that Professor Weiss had a UK isolate and cell line suitable for assay<sup>65</sup> but the information appears to have lacked clarity. Dr Brian McClelland, Director of the Edinburgh and East of Scotland Blood Transfusion Service, reported that he could get no clear picture of when or how a serviceable assay would be provided. Having regard to the then pending patent application in the names of the Middlesex Hospital and the Chester Beatty Laboratory,<sup>66</sup> it would have been highly unlikely that Professor Weiss and Professor Tedder would have disclosed details of their test. Professor Weiss wrote to the DHSS on 3 December 1984 confirming that he had a local independent isolate of the AIDS retrovirus.<sup>67</sup> An RIA from this isolate was also developed at the Middlesex Hospital.<sup>68</sup> Professor Weiss suggested that the use of US reagents should be stopped and that scaling-up of their methods should be developed independently. He also reported continuing discussions to expedite the development of reagents.

**29.43** The Inquiry was initially concerned to establish whether the unwillingness on the part of the US Department for Health and Human Services to allow the US isolate to be used for blood donor screening in the UK delayed the introduction of screening in this country. In fact, Professor Weiss advised the Inquiry that, by the time the reply was received from the US government, an independent isolate had already been developed by his team. Neither Professor Weiss nor Professor Tedder considered that the refusal by the US government delayed the development of a test for use in screening blood donors in the UK.<sup>69</sup>

**29.44** As regards HTLV-III antibody screening, Professor Tedder advised the Haemophilia Reference Centre Directors on 10 December 1984 that the Gallo cell line was available for research although the US government had made the isolates difficult to obtain. Looking forward, the testing of donors for HTLV-III antibody required either mass commercialisation of a British test or application of a US commercial test when that became available.<sup>70</sup>

<sup>63</sup> Letter [DHF.001.5619]

<sup>64</sup> Crewdson, *Science Fictions*, pages 188–189 [PEN.017.0568] at 0592–0593. See position paper 'Aids and its prevention in the United Kingdom' (undated and without appendices) [DHF.002.0431] at 0432, para 4. Date is probably 31 December 1984 – see [DHF.002.0430]. See also letter from Department of Health & Human Services, Bethesda, Maryland to Chester Beatty Research Institute dated 19 December 1984 [DHF.001.8858]

<sup>65</sup> Dr McClelland made notes of the meeting [PEN.012.1938] at 1939

<sup>66</sup> Referred to in [DHF.001.9036], dated 4 January 1985: see paragraph 29.50.

<sup>67</sup> Letter [DHF.001.8805]

<sup>68</sup> Letter dated 18 December 1984 from Professor Tedder to DHSS [DHF.001.8856]

<sup>69</sup> Professor Weiss – Day 48, page 172; Professor Tedder – Day 49, pages 12–14

<sup>70</sup> Notes of Meeting [SNF.001.3850]

**29.45** The approach of Professor Weiss and Professor Tedder differed from the US approach in a number of significant respects, as already discussed. Their work was now at a critical stage. In order to provide a test for general use, the laboratory-based work had to be scaled-up to industrial levels for commercial manufacture and marketing.

***Scaling-up the MH/CB assay for routine use***

**29.46** On 18 December 1984, Professor Tedder wrote to Dr Smithies:

- i. We urgently need to be able to scale-up ... the Middlesex Hospital/Chester Beatty radioimmunoassay (MH/CB RIA).
- ii. The MH/CB RIA has been designed to be compatible with the current BTS hepatitis testing. Pilot studies are of the utmost priority in selected centres to confirm this is indeed the case.
- iii. Until the MH/CB RIA has been routinely used for a considerable time, it is very important that reactive sera are referred to a designated laboratory for confirmatory testing and that donors and their blood products are followed up.
- iv. There is an initial need to monitor the efficiency with which the MH/CB RIA and the forthcoming commercial kits detect anti-HTLV III.<sup>71</sup>

**29.47** He sought financial support and commented that his Dean (Professor Sir John Pattison) and he, 'must emphasise that we see the necessary UK commitment to this problem increasing over the next few years' but that the hospital would not be able to take up the work without support.<sup>72</sup>

**29.48** On 31 December 1984, Dr Smithies, DHSS, drafted and circulated a position paper on 'AIDS and its prevention in the UK' in response to a request from the Chief Medical Officer (CMO).<sup>73</sup> She commented on the response on 14 November 1984 from the US government to the request for permission to make wider use of the Gallo isolate and noted that, by the time the response had been received, Dr Weiss had succeeded in isolating the virus from a British patient. She noted that negotiations had been opened with Wellcome (Wellcome Diagnostics, a UK pharmaceutical company) to use the UK isolate to develop a UK test, and that Wellcome had sub-contracted CAMR Porton, who had the appropriate containment facilities, to produce the antigen.<sup>74</sup> The advantages of the UK test were noted: with luck, it might be available at about the same time as the US commercial tests; it was suitable for use in RTCs which already had experience of the RIA format; it was also more sensitive and specific than the US tests; and it was likely to be less expensive.

**29.49** In addition, Dr Smithies prepared a draft submission to Ministers seeking approval for the introduction of an AIDS screening test. In sending the paper to Dr Richard Alderslade, DHSS, for consideration by the CMO, she wrote:

---

<sup>71</sup> Letter [DHF.001.8856]

<sup>72</sup> Ibid [DHF.001.8856] at 8857

<sup>73</sup> Covering letter [DHF.002.0430]; position paper [DHF.002.0431]

<sup>74</sup> Formerly the highly secretive MOD technology park DSTL Porton Down, the establishment closed as an MOD facility in 1979 and re-opened in 1980 as the Centre for Applied Microbiology and Research (CAMR) within the Public Health Laboratory Service (PHLS).

The UK test is currently being used at the Middlesex Hospital and at the Central Public Health Laboratory, Colindale to detect antibody carriers among patients thought to have AIDS or the AIDS related complex, haemophiliacs and male homosexuals attending STD clinics.

Scale up of production of the reagent is necessary before the test can be applied more widely.<sup>75</sup>

**29.50** In the event, testing of patients (particularly haemophilia patients) was already widespread by the end of 1984. From the researchers' point of view, that might have been characterised as an extension of the research project. From the clinicians' point of view it was an aspect of patient care. It had revealed that a significant proportion of English and Welsh haemophilia patients and at least 33 Scottish haemophilia patients were positive for the AIDS virus.<sup>76</sup> Professor Tedder's letter of 18 December 1984 had sought funds for development to promote donor screening, not testing of patients.

**29.51** It appears that the distinctions between 'research' testing of assays for HTLV-III by Professor Tedder and subsequent testing of wider groups, for example the haemophilia population, for antibodies to HTLV-III/HIV, may have become blurred by the beginning of 1985 so that 'patients' were beginning to be screened rather than 'research subjects' evaluated. This was probably increasingly the position in relation to the use of the initial tests based on Gallo/Montagnier isolates and subsequently in the evaluation of the test based on the UK isolate from December 1984. By early 1985 the majority of UK haemophilia patients had been tested for HTLV-III in a piecemeal fashion, without a developed protocol having been worked out and promulgated. It seems likely that, because testing arose in this way, many of the issues around informed consent and counselling which were soon to emerge were not dealt with and haemophilia doctors found themselves in possession of important information about their patients with which they were ill-prepared to deal. Practical response on the ground had run beyond official guidance. These issues are dealt with in Chapters 32 and 33.

**29.52** In addition to the two papers referred to at paragraphs 29.48–29.49, Dr Smithies prepared a further paper dated 4 January 1985 for the Research Liaison Group (a joint NBTS/BPL research group).<sup>77</sup> In it she supported Professor Tedder's application for funding.<sup>78</sup> She narrated the work of Professor Tedder and Professor Weiss in developing the MH/CB RIA, its compatibility with the BPL Hepatitis B RIA (then routinely used to screen blood donors for Hepatitis B); and the role of Wellcome, and stated:

There has been a Patent application in the names of the Middlesex Hospital and the Chester Beatty Laboratory ... and commercial exploitation is likely.

The MH/CB RIA is thus a product of the co-operation of British Science and British Industry. There is general agreement that it is the most sensitive RIA for HTLV III presently available.<sup>79</sup>

---

<sup>75</sup> Letter [SGH.002.7303]

<sup>76</sup> The number of seroconversions in Edinburgh among recipients of the implicated batch was 18, as explained in the Preliminary Report, paragraph 8.207. See also Chapter 10, *Knowledge of the Geographical Spread and Prevalence of HIV/AIDS 2*.

<sup>77</sup> BPL, The Blood Products Laboratory, is the manufacturer of NHS blood products in England and Wales.

<sup>78</sup> Covering Letter [DHF.001.9040]; Paper [DHF.001.9036]

<sup>79</sup> Paper [DHF.001.9036]

**29.53** As noted above, the MH/CB RIA was, in fact, the only RIA developed for the HTLV-III antibody.<sup>80</sup> Dr Smithies drew heavily on Professor Tedder's representations in supporting further work, which she said was strongly supported by the Medical Division of the DHSS. In relation to the anticipated arrival of commercial kits, she commented that Middlesex Hospital would be uniquely qualified to assess them when they arrived.

**29.54** The expectation of officials at this stage (January 1985) appears to have been that the joint venture between academic researchers and a drug company<sup>81</sup> would lead to an RIA, developed in the UK, becoming available about the same time as the US ELISA tests would become available.<sup>82</sup>

**29.55** In terms of technology, Professor Tedder commented that Dr Smithies' information was already out of date, possibly encouraged by his letter to her of 18 December 1984. The group had already begun work on an ELISA with Wellcome in October or November 1984. His letter appears to have been drafted in the light of experience of the approach most likely to be productive of funding.<sup>83</sup> On the other hand, protection of intellectual property rights in the MH/CB assay and related work would have been a legitimate reason for caution in disclosing information, given the initial refusal by the DHSS of support for research in response to the threat of AIDS.

**29.56** The scientific research and initial development work necessary to produce a specification for a commercially marketable product had been done. Outstanding was the development work required to scale-up the project for industrial manufacture and general supply.

**29.57** As Dr McClelland explained to the Inquiry, there is a 'huge difference' between an assay which works well in a laboratory in the expert hands of research scientists, and a test which can be used for hundreds of thousands of tests daily in the sort of working environment surrounding the screening of donors.<sup>84</sup> The achievement by Professors Weiss and Tedder of a functioning assay did not mean that there was immediately a test ready for use in screening blood donors in the UK for the AIDS virus. Much further work was needed and that required collaboration with Wellcome and their sub-contractors CAMR Porton.

**29.58** The scaling-up of the project and progress towards commercialisation are discussed in Chapter 30, *Screening of Donated Blood for HIV*.

---

<sup>80</sup> Professor Tedder – Day 49, page 82

<sup>81</sup> There was pride in this cooperation between British science and British industry – see paper of 4 January 1985 [DHF.001.9036] as quoted above.

<sup>82</sup> See draft position paper 'Aids and its prevention in the United Kingdom', 31 December 1984 [DHF.002.0431] at 0432

<sup>83</sup> Professor Tedder – Day 49, pages 81–82

<sup>84</sup> Dr McClelland – Day 50, page 5





## CHAPTER 30

### SCREENING OF DONATED BLOOD FOR HIV

#### Introduction

**30.1** This chapter deals with the general introduction of screening of donated blood in the UK for the AIDS virus, HIV. Although adopted later than many of the events discussed in this chapter, the name HIV is used in the narrative, except where context requires the use of one of the alternative historical names for the virus, since it is now well understood that the various names used historically (such as HTLV-III and LAV) referred to the same virus. The introduction of the screening of donated blood for HIV was dealt with in the Preliminary Report at paragraphs 8.122–8.139. Since the writing of that section, the Inquiry has obtained more information about the process which led to the introduction of screening for HIV and has perused more documents. The account which follows is therefore fuller than the account in the Preliminary Report and varies from it in part.

**30.2** Screening for HIV infection was designated as a topic which required to be considered at the Oral Hearings of the Inquiry. The topic was described as follows:

The decision not to use kits from the United States of America for testing donated blood for the virus as soon as they became available but, instead, to follow a process of evaluation of the kits before any such use.

**30.3** As defined, the topic focused on tests developed in the USA, reflecting a view held by some interested parties that progress there provided criteria against which to measure what happened in the UK in general and Scotland in particular. As the discussion in Chapter 29, *The Discovery of HIV and the Development of Screening Tests*, shows, however, the position was altogether more complex and there had been significant developments in knowledge in France and the UK in 1983 and early in 1984. It is appropriate, nonetheless, to deal with the development of screening in the USA in the first instance, since there was, on the part of some parties, a clear conception that the perceived leadership of the USA in this area was of central importance.

**30.4** While the topic was originally narrowly expressed, the hearings were not, in the event, restricted to decision-making in relation to the evaluation of kits but also examined, so far as practicable, the whole sequence of events leading to the introduction of screening of donors. It was clear from the evidence before the Inquiry that a significant focus in the UK in the second half of 1984 was on developing a British test to screen blood donations for AIDS. Whether that took priority over the introduction of US test kits became a significant question. The Inquiry has not sought direct evidence from US scientists and clinicians involved in research and development of test kits in the mid 1980s but has relied on indirect sources in narrating material events, in particular published material. Where secondary sources are relied upon, the facts have not been independently validated.<sup>1</sup>

**30.5** In summary, the issues covered in this chapter are: the development of HIV test kits in the USA following Dr Robert Gallo's announcement that he had identified the AIDS

---

<sup>1</sup> The Inquiry has drawn on information in John Crewdson's book, *Science Fictions* (2002; London: Little Brown & Co) [PEN.017.0568]. Crewdson was a journalist formerly of the Chicago Tribune. His book was cited extensively by Dr McClelland in his statement [PEN.017.1337] at 1361 and in evidence on Day 50, pages 69–79. Professor Weiss had reservations about some aspects of Crewdson's book, specifically where it attributes emotions to those quoted and discussed after the fact (Day 48, pages 151–2). Those reservations are accepted. Leaving aside Crewdson's comments, his account of events was accepted as generally accurate.

virus in April 1984; the steps taken prior to the introduction of testing in the UK, including evaluation of all available kits; Government involvement in the decision-making process; and, finally, the issue of whether matters could have been handled more expeditiously. Issues related to the identification of the virus, the initial development of the British test and the nature of the tests are discussed in detail in Chapter 29, *The Discovery of HIV and the Development of Screening Tests*, and are referred to in this chapter only where necessary to provide context.

**30.6** The period covered in this chapter runs from early 1984, when it was understood that serological tests for antibodies to HTLV-III were likely to become available imminently, until October 1985, when routine screening of blood donations for antibodies to HIV was introduced throughout the UK. It was a time when many issues regarding the screening of blood for HIV infection were being progressed simultaneously.

## The development of tests in the United States of America

### *Initial reaction to the isolation of HTLV-III*

**30.7** In the USA, reports of Dr Gallo's isolation of HTLV-III<sup>2</sup> immediately acquired a high political profile. On 23 April 1984, a press conference was held in Washington DC, involving Dr Gallo and Margaret Heckler, the US Secretary of State for Health and Human Services. At the press conference, Ms Heckler predicted that a test to screen the blood supply with 100% certainty would become widely available within six months.<sup>3</sup> This was to prove over-optimistic: on the evidence available to the Inquiry, it was to be some time before an acceptable test was developed.

**30.8** A period of intense activity sponsored by the US Federal Government followed the announcement of Dr Gallo's work. A notice in the *Federal Register*, the official journal of the federal government of the USA, dated 3 May 1984, invited proposals for the manufacture of a blood test for HIV.

**30.9** On 14 June 1984, the journal *Nature* reported that the companies selected by the US government to manufacture a blood test for HIV were expected to be announced that week.<sup>4</sup> The chosen companies would be provided with Dr Gallo's method for mass-producing the virus in return for a royalty payment, expected to be 5%.<sup>5</sup> Five companies were chosen by a committee of the Department of Health and Human Services.<sup>6</sup> Of these, Abbott Laboratories, thought by Crewdson to be the most formidable competitor, had links with the Scottish National Blood Transfusion Service (SNBTS) in Glasgow and the West of Scotland and development of the Abbott test was particularly relevant to the course of events in this country. As anticipated, they were given the then-current version of the isolate, HTLV-IIIB, in return for a royalty payment. *Nature* reported that members of the scientific panel said that they had given emphasis to the ability to manufacture the product quickly and in large quantities, as millions of test kits would be required annually.<sup>7</sup> None of the companies, however, achieved the goal set by Ms Heckler: by the end of October 1984, Ms Heckler's deadline, no test to screen the blood supply was widely

<sup>2</sup> See Chapter 29, *The Discovery of HIV and the Development of Screening Tests*, paragraphs 29.11–29.14

<sup>3</sup> See the narrative of events given at the commencement of proceedings on Day 48, pages 6–8. The press conference is also described by Douglas Starr in *Blood* [LIT.001.2936] at 2968.

<sup>4</sup> Budiansky S, 'NIH to License HTLV', *Nature*, 14 June 1984; vol 309 [SGH.002.6605]. This cutting was distributed within the DHSS with a note asking if testing would be done routinely in the UK and, if so, whether US kits would have to be bought for that purpose.

<sup>5</sup> Crewdson, J. *Science Fictions* [PEN.017.0568] at 0572

<sup>6</sup> *Ibid* [PEN.017.0568] at 0572

<sup>7</sup> Budiansky S, 'NIH to License HTLV', *Nature*, 14 June 1984; vol 309 [SGH.002.6605]

available. Abbott and other licensees were still field-testing their screening kits, enzyme-linked immunosorbent assays (ELISAs),<sup>8</sup> in cities where significant numbers of potential blood donors were presumed to be infected with the AIDS virus.<sup>9</sup>

**30.10** In order to understand developments in the USA, it is necessary to have some regard to the structure of the blood services complex in that country. In 1974, the Federal Government had published a National Blood Policy, reflecting the national interest in assuring an adequate and safe supply of blood.<sup>10</sup> The policy set out a broad statement of goals with respect to blood collection and distribution. No legislation was enacted, however. Rather, the Federal Government accepted and partially funded a private sector plan to establish an American Blood Commission to implement most of the objectives of the National Blood Policy. The American Blood Commission had no powers of enforcement and became, rather, a forum for discussion, and in many cases resolution, of blood banking issues among the private sector components of the blood services complex in the USA.<sup>11</sup> The regulation of health and safety, including blood collection and distribution, remained primarily a matter of local concern, as it had been historically.<sup>12</sup>

**30.11** The advent of AIDS prompted a new Federal initiative. In March 1983, the Food and Drug Administration (FDA), in consultation with the major blood banking and plasma derivative organisations, the National Hemophilia Foundation, the National Gay Task Force, the Centers for Disease Control and the National Institutes for Health, issued recommendations to initiate, among other measures, educational programmes to promote self-deferral and expanded medical screening of blood and plasma donors.<sup>13</sup>

*'The psychic costs to donors labelled as suspect': the problem of false positive results*

**30.12** As of May 1984, the FDA Blood Products Advisory Committee was considering whether specific 'surrogate' tests<sup>14</sup> should be instituted for all whole blood and plasma collections.<sup>15</sup> At that stage, such testing had been initiated in some centres, with two types of surrogate tests in use: (i) detection of abnormalities associated with AIDS or the preclinical stages of AIDS and (ii) evidence of past infection with diseases that had a high prevalence in population groups that were at increased risk of AIDS. A high level of false positive results (where the test result for the surrogate marker was positive but the AIDS virus was not, in fact, present: a frequent problem with any surrogate test) had been tolerated with surrogate testing for the AIDS virus. It was commented in January 1985 that:

Current surrogate tests lead to exclusion of far more donors than are ever expected to actually have or develop AIDS, and seem to have been instituted more to allay patients' and physicians' fears rather than in hopes of decreasing exposure to AIDS.<sup>16</sup>

<sup>8</sup> ELISA tests use an enzyme to detect antibodies in a sample and include various reagents which give a colour reaction. Dr Dow – Day 4, pages 85–86; Professor Weiss, Day 48, pages 160–161

<sup>9</sup> Crewdson, J. *Science Fictions*, page 185 [PEN.017.0568] at 0589

<sup>10</sup> See Blood Policy & Technology (Washington, DC; US Congress Office of Technology, OTA-H-260 January 1985) [LIT.001.4558] at 4566. The policy was National Blood Policy: US Dept. of Health, Education and Welfare. Fed Reg 1974; 39(47): part 3.

<sup>11</sup> Ibid [LIT.001.4558] at 4566

<sup>12</sup> Hillsborough County v Automated Medical Labs 471 U.S. 707 (1985)

<sup>13</sup> Blood Policy & Technology (Washington, DC; US Congress Office of Technology, OTA-H-260 January 1985) [LIT.001.4558] at 4576

<sup>14</sup> A surrogate test detects a 'marker', a directly measurable physical entity that has a statistical association (correlates) with a disease where it is not possible to test directly for the disease or where any direct test would be problematic. See Chapter 27, *Surrogate Testing of Donated Blood for non-A, non-B Hepatitis*.

<sup>15</sup> Blood Policy & Technology (Washington, DC; US Congress Office of Technology, OTA-H-260 January 1985) [LIT.001.4558] at 4576

<sup>16</sup> Ibid [LIT.001.4558] at 4579

**30.13** It was recognised that the approach adopted was detrimental to the interests of donors:

[T]he psychic costs to donors labelled as suspect have been subordinated in order to reduce the psychic costs of potential and actual recipients and their physicians.<sup>17</sup>

**30.14** It is against that background that the announcement of Gallo's findings, and the race to produce HIV tests, has to be understood. It was expected that the balancing of interests would be the same with direct laboratory tests for the AIDS virus as with surrogate testing. In the paper published in January 1985 already referred to, it was commented in relation to prevailing practice that:

The criterion used in decisions to institute these programs appears to be whether the added costs can be handled, not whether in fact AIDS will be reduced. *However, these decisions seem entirely compatible with public reaction to the threat of AIDS in the blood supply. The risk is very small, but the fear is great, and the perception that something is being done is important to public confidence.*

*A highly accurate, AIDS-specific test should decrease the perceived need for adopting any of the surrogate tests that have been proposed, but reassuring the public will probably mean that these tests can also be expected to be applied far beyond the application that would be scientifically justifiable.*

....

Thus, it can be expected that the test for HTLV-III will be a requirement for all blood and plasma collections, regardless of the relative degree of risk among blood banks and geographical areas. Even if not required for all, blood banks and plasma collectors will feel compelled to perform the test anyway because of the public confidence factor and the threat of lawsuits.<sup>18</sup>

**30.15** Testing of all blood donors for HIV was expected to become a general requirement, not conditional on scientific proof of its effectiveness. It was concluded that the prudent course was to continue with the cooperative arrangements in-hand and to monitor key developments. Discussion placed emphasis primarily on the safety of the recipient. The paper noted that blood banking and commercial plasmapheresis organisations were 'currently grappling with the social and ethical issues surrounding the imminent availability of the blood test'<sup>19</sup> but there was no explicit recognition of a duty of care towards donors such as underlay the UK approach to blood collection.

**30.16** By 1990, the official position had not changed. The disadvantages to donors in tolerating large numbers of false positives was, however, discussed in an article for the journal *Transfusion* by Dr Merlin Sayers of the Puget Sound Blood Center, Seattle, entitled *Duties to Donors*.<sup>20</sup> He expressed the view that blood bankers had inescapable responsibilities to donors. In respect of the implications for the donor, the article said:

---

<sup>17</sup> Ibid [LIT.001.4558] at 4579

<sup>18</sup> Ibid [LIT.001.4558] at 4579–80 (emph. orig.)

<sup>19</sup> Ibid [LIT.001.4558] at 4605

<sup>20</sup> Sayers, 'Duties to Donors', *Transfusion*, 1992; 32/5:465–466 [PEN.017.0649]. Though published in 1992, the article was originally submitted in January 1990.

What can be done about the 'nonspecificity trap'? In this context, heavy reliance is placed on laboratory testing in pursuit of the risk-free blood transfusion. This emphasis is not surprising, if one bears in mind the extent to which our society has enshrined technology. Though there is a beguiling simplicity in the idea that a test that could even slightly enhance transfusion safety should be implemented, technology-driven donor screening carries a price.

As 100-percent specificity does not exist, at least not side-by-side with 100 percent sensitivity, some donors have had to contend with false-positive results. As more screening tests are introduced, so will their ranks be increased. This does not bode well for anxious donors or for blood bankers trying to explain why, if some test results really are false, donation is still forbidden. Concepts such as test sensitivity, test specificity, and indeterminate results are difficult to translate into lay terms. There is scant enlightenment, let alone consolation, for the donor deferred with a 'false-positive' result ....<sup>21</sup>

**30.17** Sayers' article reflected concern, continuing in 1990, that the interests of the US donor were not taken fully into account. The more-or-less exclusive emphasis in US practice on the interests of the recipient (and of the industry, ever-anxious about exposure to litigation) is relevant to the acceptance of a high incidence of false positive results as HIV tests were rolled out in the USA, first for evaluation and then commercially. The problem in the UK relating to the efficacy of the tests was similar, although the solution was to be different and took time to develop. An issue for the Inquiry was whether the introduction of testing for HIV was unduly delayed and whether the interests of donors came to be a factor in the developing picture.

**30.18** Once testing began in the USA, problems with false positive results were evident. Abbott's product licence application, dated 19 December 1984, disclosed that, of 42 positive tests from 7758 samples, 17 proved to be true positives and 25 proved to be false, a false positive rate of about 60% relative to the initial positive results.<sup>22</sup>

**30.19** On 13 December 1984, *Nature* reported that the 'crash effort' by the Public Health Service to develop a blood test for AIDS had run into difficulties.<sup>23</sup> The article referred to significant variations in the sensitivity and specificity<sup>24</sup> of the tests being developed by the five contractors and to the suspicion that the tests were subject to significant false positive and false negative rates. Scrutiny of the performance of the kits had not been assisted by the fact that each company had received a different set of 6000 samples. Each company had run its own ELISA test and then its own confirmatory test (all using Western blot technology), complicating the interpretation of their findings.<sup>25</sup>

### *The pressure to introduce screening grows*

**30.20** Despite these problems, US government agencies pressed forward with arrangements for the introduction of screening. On 11 January 1985, the *Morbidity and*

<sup>21</sup> Ibid [PEN.017.0649]

<sup>22</sup> Crewdson, J. *Science Fictions*, page 567, footnote 'e' [PEN.017.0568] at 0598

<sup>23</sup> Budiansky S, 'False Test Results Raise Doubts', *Nature*, 13 December 1984; 312:583 [PEN.017.0658]

<sup>24</sup> 'Sensitivity' is a function of a test's ability to capture all cases of infection with the target pathogen. 'Specificity' is a function of a test's ability to identify only the target pathogen.

<sup>25</sup> The article drew on comments by Dr John Petricciani, head of the FDA's division of blood and blood products. Petricciani and colleagues from the public service published a short report of their findings in a letter, 'An analysis of serum samples positive for HTLV-III antibodies', to the *New England Journal of Medicine* vol 313. no 1 47-48, 4 July 1985 [PEN.017.0651]

*Mortality Weekly Report (MMWR)*<sup>26</sup> published Provisional Public Health Service Inter-Agency Recommendations for screening donated blood and plasma for antibody to the virus causing AIDS,<sup>27</sup> anticipating that tests would be licensed and commercially available in the USA 'in the near future'. The recommendations provided that all donors should be told that their blood would be tested for the virus and that they would be notified if the test was positive. The article commented on the efficacy of the US kits expected to be available, stating:

In the early phases of testing a number of false-positive tests may be encountered. Adjustments in interpretation are anticipated as more is learned about the performance of the test in an individual laboratory and about the specific proportion of falsely positive or falsely negative tests in the screening setting where the test is used.<sup>28</sup>

**30.21** The proportion expected to be false positives was not disclosed. However, the article noted:

When the ELISA is used to screen populations in whom the prevalence of HTLV-III infection is low, the proportion of positive results that are falsely positive will be high.

**30.22** Repeat and alternative testing systems were recommended before the donor was notified of a positive result. At the end of January 1985, Ms Heckler said that AIDS test kits would be licensed by the FDA by mid-February.<sup>29</sup> When this did not happen, Ms Heckler explained that the FDA needed more data from the manufacturers.

**30.23** In the article in *Nature* dated 13 December 1984, Dr Peter Page, Director of the American Red Cross, was quoted as having expressed concern that political pressure was rushing the process so much that there was no time to resolve the problems of false positive results that were arising.<sup>30</sup> Dr Page thought that, having regard to improvements in the blood supply brought about by appeals to high-risk groups to abstain from donating, there was no compelling case to rush ahead with blood tests. The conclusion of the article, by Stephen Budiansky, was that the ELISA test might prove to be problematic, a marked contrast to the government's push for the introduction of testing.

### *The introduction of screening in the USA*

**30.24** The Abbott test was licensed on 2 March 1985. Ms Heckler again made the announcement. According to Crewdson, the first blood bank in the world to get the AIDS test was the Red Cross Blood Center on Ohio Street in downtown Chicago. A leaflet with the kits contained a warning that 'false positive test results can be expected with a test kit of this nature'. Crewdson also reports that, at this point, Abbott only had 60,000 ELISA kits on hand, which was not nearly enough to fill the nationwide demand.<sup>31</sup>

<sup>26</sup> The *MMWR* is published by the Centers for Disease Control and Prevention (CDC), a US government public health agency with its headquarters in Atlanta, Georgia.

<sup>27</sup> 'Provisional Public Health Service Inter-Agency Recommendations for Screening Donated Blood and Plasma for Antibody to the Virus Causing Acquired Immunodeficiency Syndrome', *MMWR*, 1985; 34/1:1-5 [SNB.004.9195]

<sup>28</sup> *Ibid* [SNB.004.9195]

<sup>29</sup> Crewdson, J. *Science Fictions* [PEN.017.0568] at 0589

<sup>30</sup> Budiansky S, 'False Test Results Raise Doubts', *Nature*, 13 December 1984; 312:583. [PEN.017.0658]

<sup>31</sup> Crewdson, J. *Science Fictions* [PEN.017.0568] at 0591. The date of the announcement must have been 2 March, the first Saturday in the month, having regard to the timing of the licence granted to Electro Nucleonics Inc.

**30.25** More licenses followed in quick succession. A second US test, the 'Virgo' test manufactured by Electro-Nucleonics Inc, was licensed on 7 March 1985<sup>32</sup> and in May 1985 a US patent was granted to the US National Cancer Institute for their ELISA HIV test. Testing of blood donations was introduced in the USA in April 1985 and by the summer there were six brands available in the USA. Dr Thomas Zuck, a haematologist, was the FDA official in charge of monitoring the performance of the AIDS test. He is reported by Crewdson to have believed that the decision to grant licences had been made in haste.<sup>33</sup> Initial supplies were still not sufficient to meet demand in the domestic market.

### *Difficulties with the first generation of tests*

**30.26** One source of difficulty with the first generation of tests was the cell line, H9, in which the virus had been grown.<sup>34</sup> A more technical explanation is set out in Chapter 29, *The Discovery of HIV and the Development of Screening Tests*. In short, the cultivated virus released from the cell in which it had been growing for the purpose of test manufacture took with it certain human proteins from the membrane of the cell. Those human proteins stimulated an antibody response in some groups of individuals. Thus those individuals tested positive, although the positive result indicated antibodies to foreign proteins *other* than HIV.<sup>35</sup> The problems persisted and ultimately the FDA intervened to require Abbott to improve the specificity of its test.<sup>36</sup> As well as the problem of false positives, the Abbott test also gave false negative results.<sup>37</sup>

**30.27** The 'pure' antigen required for effective operation of the US ELISA tests had proved difficult to achieve with HTLV-IIIb grown in the H9 cell line and some highly unsatisfactory outcomes from the use of the early ELISA tests were reported. Professor Richard Tedder, Professor of Medical Virology at UCL Medical School, London, provided an extreme example from 1985 relating to an epidemiological survey of malaria among Ugandan children. The children were bled and tested for HTLV-III by Dr Carl Saxinger and Dr Gallo. The results purported to show that 85% of the children were HTLV-III antibody positive although none had, in fact, been exposed to the virus. The antigen used was not 'pure' HTLV-III: it included other proteins that were recognised by the test and erroneously characterised as HTLV-III. The children's history of malaria would have caused their plasma to be more 'sticky', resulting in proteins other than the target, HTLV-III, adhering to the antigen on the plastic strip used in the test, resulting in a false positive result.<sup>38</sup>

**38.28** Some of the practical problems caused in the USA by this flaw in the tests are outlined by John Crewdson in his book on the history of AIDS research, *Science Fictions*.<sup>39</sup> For example, the Red Cross blood centre in Springfield, Illinois, had elicited 200 positive results after one round of testing but, when those donors were re-tested with another ELISA, only 86 remained positive. Of those 86, Western Blot testing revealed that only two were true positives.<sup>40</sup> Crewdson provided another extreme example: a group of black

<sup>32</sup> See product material from Electro Nucleonics Inc [DHF.001.9700]

<sup>33</sup> Crewdson, J. *Science Fictions* [PEN.017.0568] at 0605

<sup>34</sup> Ibid [PEN.017.0568] at 0593

<sup>35</sup> Professor Weiss – Day 48, pages 165–169

<sup>36</sup> Crewdson, J. *Science Fictions* [PEN.017.0568] at 0605 and 0606. See also a comment by Jean-Pierre Allain that the specificity of the Abbott test during the first six months to a year was not very good: *Science Fictions* [PEN.017.1057] at 1066

<sup>37</sup> Ibid [PEN.017.1057] at 1063

<sup>38</sup> Professor Tedder – Day 49, page 48

<sup>39</sup> Crewdson, J. *Science Fictions* [PEN.017.0568] at 0600

<sup>40</sup> Further examples of the problems caused by false positive results in the US in the second half of 1985 are set out at *Science Fictions* [PEN.017.0568] at 0605 onwards.



farmers in South Carolina, whose risk for AIDS was virtually zero, exhibited a false positive rate of 300% (that is, there were three false positive for every true positive).<sup>41</sup>

### *Supplies of test kits*

**30.29** According to Crewdson, Ms Heckler reported in mid-April 1985, at an international AIDS conference at the Centers for Disease Control (CDC), that the domestic backlog of supplies had been filled. She said:

As a result ... our manufacturers will now be able to turn their attention to *your* needs – meeting the foreign demand for the test, which has been significant ....<sup>42</sup>

**30.30** As the situation was understood by Crewdson, however, at this stage Abbott still could not make enough tests to satisfy the domestic demand.<sup>43</sup>

### *Lack of supplies for export*

**30.31** An arrangement for cross-approval of test kits between France and the USA (whereby US tests would be approved in France and French tests approved for use in the USA) could not be brought into effect as had been intended in May 1985. At the time, Abbott still did not have enough tests to supply the US market, much less the French. The company intended to meet European demand from a factory in Delkenheim, Germany. In the event, the factory did not begin production until the autumn of 1985.<sup>44</sup>

**30.32** It is noteworthy that, as at 11 March 1985, there were no Abbott kits available in the UK for general use. A small quantity was being imported so that some preliminary examination of the kits and apparatus could occur.<sup>45</sup> With the information now available, the comment in the Preliminary Report (paragraph 8.139) that kits manufactured by US companies were 'available' in March 1985 requires to be qualified by the observation that it appears that these kits were not near to being available in sufficient numbers in the UK to have allowed general screening of donated blood to commence.

**30.33** The capacity of other manufacturers to meet demand is not known. Abbott's capacity was taken generally to be the appropriate reference for discussing these issues. Irrespective of the reasons, if Abbott could not meet an existing contractual commitment to supply kits to France until mid-July 1985, it is most unlikely that there would have been stock available for supply to the UK for general use (as distinct from limited use in test evaluation and research) before that time and likely that there would have been some further delay before adequate supplies could have been made available for routine screening across the UK.

## **Testing in the United Kingdom: background**

### *The pressure to introduce testing in the UK*

**30.34** In the USA, the comments on and after 23 April 1984 of Margaret Heckler made it clear that screening tests, expected to be widely available within six months, would be

<sup>41</sup> Ibid [PEN.017.0568] at 0594. (See also: Professor Weiss – Day 48, page 168.)

<sup>42</sup> Ibid [PEN.017.1057] at 1059

<sup>43</sup> Ibid [PEN.017.1057] at 1061

<sup>44</sup> Dr McClelland – Day 50, page 79

<sup>45</sup> Memorandum dated 11 March 1985 'Introduction of Test to AIDS Related Antibody' [DHF.002.5475] at 5476. Although this is redacted, it is evident from the reference to the 'first US firm to have been given FDA approval' that it refers to Abbott.

applied generally.<sup>46</sup> The prediction proved inaccurate but, in the spring and summer of 1984, UK blood transfusion experts were aware that testing donated blood for the AIDS virus would be introduced generally in the USA. One of the major issues anticipated was that considerable pressure would then be put on the UK Transfusion Services to introduce an HIV test in the UK as in the USA.

**30.35** Although there was relief that the virus had been identified and that tests were being developed, there was also anxiety about the practical problems which testing would involve. In particular, as noted above, there was concern about false positive and false negative results and about how to counsel donors whose blood had tested positive.<sup>47</sup>

**30.36** Against this background, there was a powerful body of opinion in the UK, especially among the scientific community and transfusion practitioners, that all kits, whether produced in the USA or in the UK, should be evaluated locally before being recommended for use by Regional Transfusion Centres. The contrary opinion was expressed by some haemophilia clinicians who were concerned about delay, especially after the FDA had licensed kits for domestic use in the USA.

### *The UK regulatory framework*

**30.37** As noted in paragraph 30.2, the topic discussed in this chapter questioned ‘the decision not to use kits from the USA for testing donated blood for the virus as soon as they became available but, instead, to follow a process of evaluation of the kits before any such use’. Apart from the problem of lack of supplies for export discussed above, ‘availability’ of kits imported from the United States may require definition. Unlike the USA, where kits had to be approved and licensed by the FDA before they could be used for screening, UK authorities had no powers, under the Medicines Act 1968 or otherwise, to regulate the sale of kits imported into this country.<sup>48</sup> The FDA might grant an export licence before approval of a kit for domestic, US, use.<sup>49</sup> Kits might therefore be ‘available’ in the UK despite having no regulatory approval for domestic use in their country of origin.

**30.38** The Department of Health and Social Security (DHSS) responded promptly to the announcement of Abbott’s US licence, congratulating the company three days later in a letter dated 5 March 1985.<sup>50</sup> The letter gave a clear indication of the regulatory context and, notwithstanding the lack of statutory control over the importation and use of test kits, the expectations of the Department regarding the assessment of available test kits before their introduction to the UK:

You will know that we have no legal powers to prevent the sale of these products in the UK. However, an evaluation is needed because we know that would-be purchasers in the NHS will be looking to the Department for objective information which will help them in decision making. Of necessity, it will take a little time to get underway and we appreciate that you will wish to start selling now. In the absence of an evaluation report from the Department, we should be grateful if you would provide inquirers with as much information as you can in response to their questions about performance.<sup>51</sup>

<sup>46</sup> See narrative of events given at the commencement of proceedings on Day 48, pages 6–8. The press conference is also described by Douglas Starr in *Blood* [LIT.001.2936] at 2968.

<sup>47</sup> The atmosphere of the time was described by Dr McClelland – Day 50, pages 7–10

<sup>48</sup> A point made to Abbott in a letter to the company dated 5 March 1985 [DHF.002.6938]

<sup>49</sup> See Chapter 31, *The Introduction of Screening for Hepatitis C Antibodies in the Blood Donor Population in Scotland*, paragraphs 31.169–31.170. Ortho had an export permit for their Hepatitis C ELISA before the test was licensed for routine use within the USA.

<sup>50</sup> DHSS Letter [DHF.002.6938]

<sup>51</sup> *Ibid* [DHF.002.6938]

**30.39** From the outset, it was left to Abbott to decide whether to provide their own performance claims and supporting data and enter the market immediately. The Department's intention, as intimated in the letter, was to devise an evaluation protocol, on which all companies in the field would be given an opportunity to comment. Data in support of performance claims would be required and Abbott were invited to submit data confidentially for early review. Internally, a draft test protocol was prepared on 8 March 1985.<sup>52</sup> The Virus Reference Laboratory, CPHL Colindale, was to be involved in the evaluation and detailed requirements were drafted.

**30.40** As matters had developed in 1984 and early 1985, there were problems with the American ELISAs, including Abbott's kit, other than adequacy of supplies. As noted above, once testing began in the USA, serious problems with false positive results were evident.

### *The evaluation programme debate*

**30.41** As discussed in Chapter 18, *Collection of Blood – General*, the voluntary principle embedded in blood collection, in the UK generally and in Scotland in particular, imposed on the public sector transfusion services obligations of care towards donors, for their safety and general well-being in the course of the management of donation procedures.

**30.42** Regional Transfusion Directors (RTDs) in the UK considered that local evaluation was necessary. In Scotland, the emphasis remained on the use of commercial kits. On 12 February 1985, Professor Cash, National Medical Director of the SNBTS, wrote to Dr John Reid, Chief Medical Officer (CMO) at the Scottish Home and Health Department (SHHD).<sup>53</sup> He set out his concern about the rate of false positive results anticipated with the use of commercial kits and highlighted a number of factors supporting the need for a national kit evaluation programme. On 21 February 1985, Professor Cash and others from the SNBTS and National Blood Transfusion Service (NBTS) sent a letter to *The Lancet*, published on 2 March substantially repeating these views. The letter stated:

We believe that current commercial kits for HTLV-III antibody tests are likely to give a high rate of false-positive results. We would therefore recommend that careful consideration be given before they are introduced for the screening of all voluntary blood donors, for the amount and degree of unnecessary stress and hardship that a fair number of our donors and their families would thus have to undergo is unacceptable. This in turn could lead to a sizeable drop in the supply of blood and blood products. Of no less importance, for the safety of transfused patients, is the need to ensure that the first priority for the introduction of any HTLV-III antibody tests into a community is given to patients attending special (venereal disease) clinics and other members of the general public who wish to have access to these tests. If this is not done, many high-risk people, from a blood transfusion point of view, may present themselves at blood-donation sessions simply to find out their HTLV-III antibody status.

We do support, strongly, the screening of all blood donors for HTLV-III antibody testing, but we would advise that this is delayed until test systems have been appropriately evaluated and efforts have been made to give all members of the public access to HTLV-III antibody testing.<sup>54</sup>

<sup>52</sup> Draft test protocol [DHF.002.6939]

<sup>53</sup> Professor Cash's letter [SNB.013.2233]

<sup>54</sup> Ala et al, 'HTLV-III antibody screening of blood bank donors', *The Lancet*, 2 March 1985, page 524 [LIT.001.0374] at 0375. Consideration of 'alternative testing sites', for non-blood donors who might wish to be tested for HIV, are discussed below at paragraphs 30.156–30.161.

**30.43** The letter was signed by 11 NBTS Directors and seven Directors from Scotland, the five SNBTS Directors, Professor Cash as National Medical Director and Dr Robert Perry, Director of the Protein Fractionation Centre (PFC, the manufacturer of NHS blood products in Scotland). The emphasis on the interests of donors and their families highlighted the policy differences between the USA and the UK. The US policy of subordinating the 'psychic costs' of false positives to donors was not acceptable in the NHS environment.

**30.44** The letter was published on 2 March 1985. A different point of view was expressed in the same edition by Dr James Carlson and others of California, who advocated using a test with high sensitivity followed by confirmatory testing.<sup>55</sup> They concluded that, with proper procedures, the use of the most sensitive ELISA would not result in a major disruption in the procurement of blood or in the significant loss of future blood donors. However, the view of the UK transfusion specialists was strongly expressed and it is unlikely that a US view would have prevailed given the differing policy background circumstances.

**30.45** The need for local evaluation was acknowledged by others. For example, a widely attended international conference on AIDS, sponsored by the US Department for Health and Human Services and the World Health Organization (WHO), was held in Atlanta, Georgia (USA), from 15–17 April 1985. The conclusions and recommendations for member states included:

- Each country should assess the risk that AIDS poses to its population and establish methods of diagnosis through surveillance and laboratory testing, including specific tests for LAV/HTLV-III.
- Where feasible, potential donors of blood and plasma should be screened for antibody to LAV/HTLV-III....<sup>56</sup>

**30.46** In addition to the need to evaluate the tests' effectiveness in local populations, it was necessary, as with any new test system, to develop the practical, technological and procedural aspects of the introduction of HIV tests in Scottish laboratories, and laboratories elsewhere in the UK, to ensure that the kits adopted could be used rapidly and reliably for diagnostic and for screening purposes. A DHSS draft protocol of 8 March 1985 anticipated an evaluation report on each product submitted which would cover, among other practical issues, the compatibility of the assay with the needs of diagnostic, blood transfusion and research laboratories.<sup>57</sup>

**30.47** Any evaluation exercise had to be carried out on the actual assays proposed for introduction. As will appear later, there were significant differences in experience between different versions of fully developed commercial products marketed for general use. Starting some time after March 1985, when the US kits became available for research purposes, a UK evaluation would have taken some months. It was, however, a necessary step: Professor Tedder spoke of the general experience of assays, in transfusion and diagnostic settings, which had not been tried on the target population, giving rise to devastatingly high levels of false positivity. His view, which is accepted, was that:

You conduct a field trial to make sure that assays are giving you useful and as accurate as possible results and, of course, without having your repeat reactive

<sup>55</sup> Carlson et al, 'HTLV-III antibody screening of blood bank donors', *The Lancet*, 2 March 1985, [LIT.001.0374] at 0374–75

<sup>56</sup> Acquired Immune Deficiency Syndrome (AIDS) – WHO Consultation [DHF.001.7253] at 7253–54

<sup>57</sup> Draft Test Protocol for the Evaluation of Commercial Kits for AIDS – Related Virus Antibody Screening [DHF.002.6939] at 6942

panel from your donors, you do not know what form of confirmatory testing you need. So, until you have got the substrate for your confirmatory testing, which is your repeat reactive donors, you can't define what's going to be the best algorithm or the best protocol for confirmation. You really don't want to be screening donors and developing a large panel of repeat reactors without knowing how to deal with them. That would be very damaging to transfusion practice.<sup>58</sup>

### ***Development of a United Kingdom HIV test***

**30.48** The background to the development of scientific tests for HIV infection in the UK is described in Chapter 29, *The Discovery of HIV and the Development of Screening Tests*. In short, Professor Tedder and Professor Robin Weiss,<sup>59</sup> following rebuff by the DHSS<sup>60</sup> initiated research and developed an effective serological assay on a commercial basis on behalf of their institutes, the Chester Beatty Cancer Research Institute and the Middlesex Hospital, and in due course established unchallenged right to the intellectual property developed. As matters transpired, all of the test kits that became relevant to progress towards screening had one thing in common: research institutes, pharmaceutical companies and individuals had intellectual property rights in the science underlying the tests. In the USA, Dr Gallo's know-how was licensed to pharmaceutical companies for development.

**30.49** The work of Professors Weiss and Tedder was known, in general terms, to the UK government but, throughout the development stages and, in particular, until 4 July 1984, when the prototype assay was ready for laboratory application, it was funded by their institutions.<sup>61</sup> As commented in Chapter 29, *The Discovery of HIV and the Development of Screening Tests*, paragraph 29.42, it would have been highly unlikely that Professor Weiss and Professor Tedder would have disclosed details before publication of the patent specification: until that stage, the validity of the patent could have been undermined.

**30.50** Professor Tedder sought UK government funding for the scale-up of the Middlesex Hospital/Chester Beatty Cancer Research Institute test (MH/CB test) for industrial production in a letter to Dr Alison Smithies, DoH, dated 18 December 1984.<sup>62</sup> At the end of the year and early in 1985, Dr Smithies prepared draft submissions to Ministers supporting the application and seeking approval for the introduction of the screening test.<sup>63</sup> Her advocacy in support of the project marked the beginning of a new phase in the progress towards routine screening for anti-HIV in the UK as a whole. As she presented the project, it was 'a product of the co-operation of British Science and British Industry', implicitly acknowledging the non-governmental character of the test.<sup>64</sup>

**30.51** In following the history of events in 1984 and 1985 relating to the development of a UK test for HIV below, it has to be borne in mind that institutions which had sought intellectual property rights, in common with all manufacturers of test kits, had interests which depended in part on maintaining the confidentiality of their work.

<sup>58</sup> Professor Tedder – Day 49, page 77

<sup>59</sup> Currently Emeritus Professor of Viral Oncology at UCL Medical School, London.

<sup>60</sup> Professor Tedder and Dr Philip Mortimer (PHLS) attended a meeting at the DHSS early in 1983. See Chapter 29, *The Discovery of HIV and the Development of Screening Tests*, paragraph 29.17.

<sup>61</sup> See Chapter 29, *The Discovery of HIV and the Development of Screening Tests*.

<sup>62</sup> Professor Tedder's letter [DHF.001.8856]

<sup>63</sup> See Chapter 29, *The Discovery of HIV and the Development of Screening Tests*.

<sup>64</sup> Dr Smithies' Paper 'Further Development and Establishment for Routine Use In the Blood Transfusion Service of a Screening Test for Acquired Immunodeficiency Syndrome (AIDS)' [DHF.001.9036]

## The progress of introducing a test to the United Kingdom

### *Establishment of expert groups*

**30.52** At a meeting of the UK Central Blood Laboratories Authority (CBLA) Central Committee for Research and Development in Blood Transfusion in June 1983, a Working Group on AIDS in relation to Blood Transfusion was set up and first met on 14 October 1983.<sup>65</sup> By that stage, the Medical Research Council (MRC) had set up a similar committee which had its initial meeting on 10 October 1983.<sup>66</sup> The MRC committee noted that, while the laboratory markers for AIDS were well established, their relevance in screening and in a possible 'precursor state' was not. As reported, screening was not among the topics discussed in detail by the working group on 14 October. Although it appears that there was nothing of importance to note at that point specifically relating to the development of serological assays for HIV identification other than uncertainty, the interest of two important UK advisory bodies had been engaged.

**30.53** In Scotland, a special meeting of the Co-ordinating Group of the SNBTS took place on 7 February 1984.<sup>67</sup> It was agreed that Professor John Cash, Medical Director of the SNBTS, should write to Dr Harold Gunson, Director of the Manchester RTC and Chairman of the Regional Directors of the National Blood Transfusion Service for England and Wales (NBTS), recommending that there should be a single UK Working Group on AIDS with Scottish representation. Instead of writing to Dr Gunson directly, Professor Cash wrote to Dr Albert Bell, SHHD, reporting the recommendation on 15 February 1984 and suggesting that the group should be responsible to the health departments (DoH and SHHD) for coordinating research covering the interface between blood transfusion and AIDS.<sup>68</sup> He included in the major areas requiring attention a prospective clinical study to determine the value of existing AIDS tests.

**30.54** Professor Cash's hopes of a UK-wide advisory group, including Scottish representatives with the wide remit he proposed and a direct relationship with the health departments, were not realised. Professor Cash would later write, on 24 January 1985, that he did not know whether the SNBTS Directors' views, communicated to Dr Bell on 15 February 1984, had been transmitted to the DHSS.<sup>69</sup> It appears from his letter that he, and other officials in the transfusion service in Scotland, were frustrated by the arrangements made in England. Professor Cash complained that they were left 'completely in the dark' about developments.

**30.55** Professor Cash's protestation was not wholly justified. Dr Gunson met with Dr David Tyrrell, Chairman of the MRC Committee on AIDS, Professor Tedder and two NBTS Directors, Dr Tim Wallington and Dr Marcella Contreras, on 28 June 1984 to discuss issues surrounding the introduction of tests. Dr Wallington was Consultant Clinical Immunologist at NHS Blood and Transplant and the North Bristol NHS Trust. Dr Contreras was Director at the Regional Transfusion Centre at Edgware, London, and that centre was believed to be most likely to show early evidence of the virus entering the donor population.<sup>70</sup> Dr Brian McClelland, Director of the Edinburgh BTS, had been invited but was prevented from attending the meeting by travel problems.<sup>71</sup>

<sup>65</sup> Minutes of CBLA meeting [DHF.002.4834]

<sup>66</sup> Minutes of MRC meeting [SNF.001.3759]

<sup>67</sup> Minutes of SNBTS co-ordinating group [SNB.011.1393]

<sup>68</sup> Professor Cash's letter to Dr Bell [SNB.004.8639]

<sup>69</sup> Professor Cash's letter [SNB.005.7304]

<sup>70</sup> Dr McClelland – Day 50, pages 2–3

<sup>71</sup> *Ibid* pages 2 and 7

**30.56** Dr Gunson sent a letter, dated 3 July 1984 and copied to Dr McClelland among others, recording the discussions which had taken place at the meeting on 28 June.<sup>72</sup> He narrated that Dr Tyrrell had taken the initiative by proposing that the MRC could help in setting up a research project on blood donors using the detection of anti-HTLV-III as a possible marker of donors at high risk of transmitting infection. The development of a viable test for anti-HTLV-III by Professors Weiss and Tedder was identified as promising. The stages in the evaluation project then envisaged included testing at the Middlesex Hospital, North West Thames RTC and Bristol and Manchester RTCs. Dr McClelland thought that, if he had attended the meeting, he would have suggested that it would have been useful for the evaluation to be extended to include a Scottish centre: the West of Scotland centre was very experienced in evaluation and it would have been a valuable learning experience to get in 'at the ground floor'.<sup>73</sup> That did not happen, however.

**30.57** Dr Gunson's letter stated:

[We] all agreed that at the present time this test should be regarded as a research project and that it should not be introduced as a routine screening test on blood donations without proper appraisal. It is important, however, that a study should be started as soon as possible so that it would be possible from a practical point of view to answer questions on the use of the test in the U.K.<sup>74</sup>

**30.58** Dr McClelland sent a copy of the letter to Professor Cash on 7 August 1984. In the covering note, he wrote:

I will be keeping in touch with Richard Tedder about the development of assay reagents and I feel this is something we should discuss in the near future.

....

I imagine there is likely to be a breathing space of many months before a test is available and relevant trials come forward to put us under pressure to introduce screening. Nevertheless ... it would seem very important indeed that we do whatever is necessary to retain participation in this development.<sup>75</sup>

**30.59** It appears unlikely that Dr McClelland was fully informed of developments at this stage. The first results of research using the MH/CB assay developed by Professor Weiss and Professor Tedder were published in an article by Dr Rachanee Cheingsong-Popov and others on 1 September 1984.<sup>76</sup>

### *The practicalities of introducing screening*

**30.60** In the autumn of 1984, the emphasis turned to the practical implementation of screening. A working group was proposed by the DHSS to provide guidance about the consequences for the NBTS of the introduction of a screening test for HIV.<sup>77</sup> The initial list of proposed members did not include any from Scotland but, as a result of the intervention of the SHHD, Dr McClelland was allowed to join the group.<sup>78</sup>

<sup>72</sup> Dr Gunson's letter to Dr McClelland [SNB.006.5978]

<sup>73</sup> Dr McClelland – Day 50, pages 6–7

<sup>74</sup> Dr Gunson's letter [SNB.006.5978]

<sup>75</sup> Covering note [SNB.006.5977]

<sup>76</sup> Cheingsong-Popov et al, 'Prevalence of antibody to human T-Lymphotropic virus type III in AIDS and AIDS-risk patients in Britain', *The Lancet*, 1 September 1984 [LIT.001.0417]

<sup>77</sup> Memorandum dated 13 August 1984 [DHF.002.5897]

<sup>78</sup> Letter dated 26 September 1984 [SGF.001.0929]

**30.61** The working group held its first meeting on 27 November 1984.<sup>79</sup> Although the DHSS view was that the meeting had gone reasonably well,<sup>80</sup> Dr McClelland reported back to his fellow Directors in Scotland on 11 December 1984 that he had found the outcome of the meeting ‘disappointing’.<sup>81</sup> He recorded, however, that it had been agreed to test all donors once an antibody test for HIV was available. The minute of the Regional Directors’ meeting on 23 January 1985 described the November meeting as ‘unproductive’.<sup>82</sup> Professor Cash’s reaction to the report in his letter to Dr Bell of 24 January 1985, describing the meeting as ‘wholly inadequate’ and ‘a waste of public money’,<sup>83</sup> was perhaps extreme but may reflect a view still held by some Scottish transfusion experts that they were not fully engaged with developments in England.

**30.62** There was an attempt to engage directly with Professor Tedder’s team. On 20 December 1984, Dr Robert Crawford of the West of Scotland BTS visited Professor Tedder at the Middlesex Hospital, apparently to obtain information about the tests being developed and, possibly, to assess whether there might be potential for the development of tests in Scotland.<sup>84</sup> Dr Crawford reported that he had been told of the Weiss/Tedder test in radioimmunoassay (RIA) format (though, as discussed below, that had already been superseded by work on an ELISA format) and had a description of the US tests. He knew of the different cell lines employed to propagate the virus antigens. He told Professor Tedder that, given the cells and virus and his support, Scotland might ‘go it alone’ and discussed the capacity of Glasgow to do the work. Dr Mitchell explained that the West of Scotland had 100,000 specimens that could be tested and could help the development programme.<sup>85</sup> By this stage West of Scotland BTS staff were experienced in investigating the Hepatitis B virus.<sup>86</sup> The proposal did not find support, however. Dr Mitchell thought (probably correctly, even at this late stage) that there were difficulties in sharing information. As commented already, the MH/CB assay was a proprietary test. Wellcome Diagnostics had entered into a commercial contract for development of the MH/CB test. It appears that there was no reasonable prospect of scientists in Scotland becoming involved in the English programme.

**30.63** The development of the English evaluation programme to the end of 1984 had not involved the Scottish scientific service to any material extent. Work carried out in Scotland included collaboration with French and US colleagues and that continued into 1985. Encouraged by Professor Cash, Dr Perry wrote to Dr Luc Montagnier on 8 February 1985, discussing a number of projects and, in particular, attempted to obtain supplies of LAV (that is, HIV) test kits from the Institut Pasteur, in order that these kits could also feature in a Scottish evaluation.<sup>87</sup> Professor Cash said that the initiative with the Institut Pasteur failed after ‘the lawyers moved in’.<sup>88</sup> It appears, however, that scientists working in Scotland would not have been able to carry out an independent virological evaluation of

<sup>79</sup> Agenda [DHF.001.6026]

<sup>80</sup> Memorandum dated 27 November 1984 [DHF.001.6037]

<sup>81</sup> Minutes of SNBTS Directors’ meeting of 11 December 1984 [SGF.001.0137] at 0139

<sup>82</sup> Minutes of the Regional Directors’ meeting of 23 January 1985 [SNB.011.1971]

<sup>83</sup> Professor Cash’s letter to Dr Bell, dated 24 January 1985 [SNB.005.7304]

<sup>84</sup> Dr Mitchell – Day 51, page 3; Report on visit [SNB.004.8803]. Dr Mitchell did not remember this event when questioned about it.

<sup>85</sup> Dr Mitchell – Day 51, page 10

<sup>86</sup> *Ibid* page 11

<sup>87</sup> Letter [SNB.007.4920]. Dr Perry could not recall ever receiving a response to this letter – see his Witness Statement [PEN.019.0860]

<sup>88</sup> Professor Cash – Day 48, page 49: it is not clear what aspect of Dr Perry’s proposals failed in this respect, but there appears to have been no progress on any part of it.



the kits available: what they were engaged in was a practical assessment of the mechanics of introducing US test kits.<sup>89</sup>

## Scottish concerns at lack of progress

### *A perceived lack of effective coordination*

**30.64** Professor Cash's frustration at a perceived lack of progress is reflected in documents recovered by the Inquiry: he was clearly concerned about what he saw as the lack of effective coordination of the UK approach to transfusion and AIDS. In his letter to Dr Bell dated 24 January 1985, he said:

[I]t is with dismay that I must conclude that there are just no mechanisms in the UK for these crucially important topics to be discussed, openly and confidentially, and for clear, co-ordinated policies to emerge. The biggest anxiety of the NBTS Directors with regard to this problem is the Scots: that they will unilaterally move to come in line with the American proposals. They're right: we are in detailed discussion with commercial (kit) companies, our technical staff are already looking at ways of introducing the technology within existing staff establishments, we have the Western Blot technique (HQ and SE labs). We are already liaising with local (Communicable Disease) physicians with a view to securing care for our positive donors and we are currently arranging our financial planning accordingly. I advised the NBTS Directors that we would do everything possible to avoid such a development. They were not impressed ... I had much sympathy with them ....<sup>90</sup>

**30.65** The threat in Professor Cash's letter, that the SNBTS would proceed unilaterally to introduce US test technology, had some basis. At the time, commercial companies were approaching Regional Transfusion Directors (RTDs) in Scotland with ELISA tests. In his witness statement, Professor Cash said that the SNBTS had evidence that the FDA was by then well-advanced in its assessment of HIV donation screening kits, which was later published.<sup>91</sup> As far as the SNBTS could judge, there was no evidence that their pleas for interdepartmental collaboration were succeeding.<sup>92</sup>

**30.66** Professor Cash said, with reference to the national blood transfusion services generally:

We, the people responsible, were not in control of actually, urgently getting together, looking at these tests, to actually determine: is it 1 per cent or 0.5 per cent or 10 per cent? What are we dealing with here? For me, as a manager, it's a madness when the whole thing is drifting away here, and there are very serious matters that, in my view, were not being properly addressed.<sup>93</sup>

**30.67** Professor Cash was not alone in expressing concern about progress. Dr McClelland was also concerned, though the focus for his frustration was different. On 8 January 1985, he wrote to Wellcome on behalf of the RTDs in Scotland expressing continuing concern about the lack of a screening test for blood donations:

<sup>89</sup> On 25 November 1985, Dr Perry wrote to Professor Weiss [SNB.007.5427]. He noted that progress on earlier proposals had been interrupted by Health and Safety problems. The PFC had not been technically equipped to handle live virus.

<sup>90</sup> Letter [SNB.005.7304]

<sup>91</sup> Witness Statement [PEN.017.1038] at 1040; Patricciani et al, 'An analysis of serum samples positive for HTLV-III antibodies', *New England Journal of Medicine*, 4 July 1985 [PEN.017.0651]

<sup>92</sup> Witness Statement [PEN.017.1038] at 1040

<sup>93</sup> Professor Cash – Day 48, page 43

I am not reassured by the information available to me at present.

....

I am concerned at the apparent lack of progress and I sincerely hope that you can reassure me that Wellcome will shortly be in a position to make some form of antibody detection system available. I feel certain that I am speaking not only for my Scottish colleagues but for other Regional Transfusion Directors in the UK if I say that it would be a tremendous step forward if even a limited supply of materials for HTLVIII antibody testing were to be made available in the near future ....

I really cannot over emphasise the urgency of this situation. I am sure that from the recent press coverage, you can be under no doubt of the extreme pressure being placed on the transfusion services to ensure that no 'high risk donors' donate blood – a task which is essentially quite impossible unless some form of screening test is available.<sup>94</sup>

**30.68** He was looking for a positive proposal from Wellcome. He explained the background to his letter in evidence to the Inquiry – he was frustrated that 'we weren't getting on with it'.<sup>95</sup> Wellcome did not respond. Dr McClelland thought they were 'up to their ears in trying to make the test'.<sup>96</sup>

**30.69** Against this background, Professor Cash took steps to progress matters, at least insofar as Scotland was concerned. He was keen that a Scottish centre should be involved in any evaluation exercise and attempted to promote such an exercise involving the west of Scotland centre.<sup>97</sup>

**30.70** Professor Cash's frustration is clear, particularly because he and his Scottish colleagues were not more closely involved. It is less clear what Scotland could have done alone, however. If Scotland had followed an individual path at this time there would still have been a need for a prior assessment of local data on the specificity of each proposed test.<sup>98</sup> That would have required the growth and propagation of HTLV-III. While that could be done at CAMR Porton,<sup>99</sup> Dr McClelland thought it highly unlikely that there was a facility in Scotland that could undertake the virology involved.<sup>100</sup> The containment facilities required to handle live virus were not available.

### *The proposal to commence test kit assessment in Scotland*

**30.71** On 21 January 1985, Dr Mitchell wrote to Professor Cash, advising that Abbott had visited 'with a view to starting some evaluation of the Abbott ELISA test system'.<sup>101</sup> Abbott were frequent visitors to check on Glasgow's progress with the testing of other products.<sup>102</sup> Professor Cash was also visited by Abbott.<sup>103</sup> Dr Mitchell noted that some

<sup>94</sup> Dr McClelland's letter of 8 January 1985 [SNB.005.9501]

<sup>95</sup> Dr McClelland – Day 50, page 20

<sup>96</sup> Ibid page 20

<sup>97</sup> Professor Cash – Day 48, pages 54 and 77

<sup>98</sup> Ibid page 130

<sup>99</sup> Formerly the highly secretive MOD technology park DSTL Porton Down, the establishment closed as an MOD facility in 1979 and re-opened in 1980 as the Centre for Applied Microbiology and Research (CAMR) within the Public Health Laboratory Service (PHLS).

<sup>100</sup> Letter dated 7 August 1984 [SNB.006.5977]

<sup>101</sup> Dr Mitchell's letter to Professor Cash [SNB.005.9715]

<sup>102</sup> Dr Mitchell – Day 51, page 16

<sup>103</sup> Day 48, page 74

problems had arisen from FDA requirements for blind testing and ethics review board approval.<sup>104</sup> He thought that these problems could be overcome and he had been asked to write a letter to Abbott setting out the position in terms advised by the company.

**30.72** In a minute to Mr Alexander Murray, SHHD, coincidentally also dated 21 January 1985, Dr Bell said that '[t]he RTC at Law [Hospital, Glasgow] is testing the Abbott (USA) screening test'.<sup>105</sup> In the light of Dr Mitchell's letter to Professor Cash, Dr Bell's understanding that testing was already in hand was incorrect: it was about March or April 1985 that an Abbott HIV test kit was first available for initial evaluation, at Ruchill Hospital.<sup>106</sup> However, the SHHD understood the intentions of the SNBTS at the time. It appears that Professor Cash, Dr Ewa Brookes (Director of the Dundee RTC), Dr William Whitrow (Director of the Inverness RTC), Dr McClelland and Dr Mitchell had discussed the issue when they were at Trinity Park House in Edinburgh in the week beginning 14 January 1985.<sup>107</sup> According to Professor Cash, the outcome of those discussions was a decision that the Scottish Directors had to take action themselves.<sup>108</sup>

**30.73** Meanwhile, and in response to Dr Mitchell's letter, Professor Cash developed his proposals:

1. That the [West of Scotland BTS] should undertake, on behalf of the SNBTS, initial evaluation studies of commercial HTLV-III antibody kits, but that the current pressure from commercial organizations to meet their deadlines should be resisted and priority given to SNBTS interests – particularly in terms of confidentiality and ethical clearance.
2. That retrospective studies (on donor samples) currently in store should be used provided:
  - (a) Steps are taken to ensure that no one can identify the donors.
  - (b) That the selection of donor samples is representative and random (not exclusively high risk donors and does not deliberately exclude high risk donors by virtue of previous tests).
  - (c) That the donors associated with factor VIII batch 023110090<sup>109</sup> are not used for these evaluation studies.
  - (d) That the donor samples would come exclusively from the WBTS donor panel.
3. That initial donor samples should be of sufficient volume to enable the following:
  - (i) Initial test
  - (ii) Repeat test if necessary
  - (iii) Reference test (? Western Blot) if necessary
  - (iv) As many residual 1 ml aliquots (at least 2) so that the same samples can be tested with other emerging kits and the results compared.<sup>110</sup>

<sup>104</sup> Dr Mitchell – Day 51, pages 17–18

<sup>105</sup> Minute [SGH.002.7301]

<sup>106</sup> Dr Dow's Witness Statement [PEN.017.1680]

<sup>107</sup> Professor Cash – Day 48, pages 75–76

<sup>108</sup> *Ibid* pages 75–76

<sup>109</sup> That is, the 'implicated batch' thought to be responsible for the infection of 'The Edinburgh Cohort' of haemophilia patients with HIV in 1984. See Chapter 10, *Knowledge of the Geographical Spread and Prevalence of HIV/AIDS 2*.

<sup>110</sup> Professor Cash's letter to Dr Mitchell [SNB.005.9713]

**30.74** He also discussed ethics approval and offered his assistance to secure that if necessary. He reported that the manufacturers had readily agreed to supply the kits necessary for evaluation free of charge.<sup>111</sup> He copied his letter to all the RTDs in Scotland and also to Dr Bell at the SHHD. At that stage, there were no commercial tests available for donor exclusion purposes but it was envisaged that initial evaluation studies would not be restricted to Abbott.<sup>112</sup>

**30.75** In his oral evidence, Dr Mitchell thought that the proposal would not have been practicable. He said:

I think the difficulty would have been to pursue this idea would be – firstly, the availability of samples, availability of commercial tests. I think there would be a difficulty in any manufacturer at that level, at this time, supplying sufficient tests for us to have a look at and – I think they were busy as it were, in their own backyard, trying to develop the tests. I think what Abbott might have been saying was, ‘In the event that we were willing to do this, we would ask you to do the following things’, or insist on the following things.

I always said to all companies that ever approached us about any test, ‘We will look at your test, we will analyse it, quite unknown to you, we will look at the results, we will publish the results, fear or favour.’ We believe in telling what exactly we find. We will not be stampeded into making allowances for this, making allowances for that. We had to be sure that the test was fit for purpose. That was for mass screening, day in, day out. Same test today, same test tomorrow, the same expected results, the same expected performance.

....

I think the reason that we couldn’t pursue this was just because the materials were not available, weren’t readily available.<sup>113</sup>

**30.76** As he saw it, 1000 kits might have enabled an exercise that was worth doing but he did not think that a manufacturer would have been prepared to supply such a number of kits.<sup>114</sup> Further, he did not think that access would have been allowed to the MH/CB material necessary for evaluation of that assay.<sup>115</sup>

### ***SHHD opposition to the SNBTS undertaking its own kit evaluation***

**30.77** The proposal was not put to the test, however. Professor Cash advised the Inquiry that, some days after this letter was sent, he was invited to discuss the situation with Dr McIntyre who ‘made it clear that SHHD was strongly opposed to the prospect of SNBTS undertaking its own kit evaluation’.<sup>116</sup> Dr McIntyre also advised Professor Cash that the SHHD had assured the DHSS that they were content with the evaluation of the kits being managed by the DHSS and that ‘the commencement of routine HIV donation testing in Scotland would be determined by Ministers, on the advice of DHSS and that this date would apply across the UK’.<sup>117</sup> On that approach, the question was answered conclusively

---

<sup>111</sup> Professor Cash’s Witness Statement [PEN.017.1038] at 1040

<sup>112</sup> Dr Mitchell – Day 51, page 23

<sup>113</sup> Ibid pages 26–27

<sup>114</sup> Ibid page 29

<sup>115</sup> Ibid page 35

<sup>116</sup> Professor Cash’s Witness Statement [PEN.017.1038] at 1040

<sup>117</sup> Ibid [PEN.017.1038] at 1040

by policy decisions made by the SHHD, which Professor Cash described as 'hostile' to the initiative.

**30.78** Dr Mitchell and his colleagues were disappointed at being excluded from the overall UK process: it hurt their sense of pride.<sup>118</sup> While he was less than certain, the general tenor of Dr Mitchell's recollection was that the proposal did not proceed because there had by this time been agreement between the DHSS and the SNBTS that the Tedder/Weiss process should have priority.<sup>119</sup> Professor Cash's approach was different: he was not willing to accept that the SHHD and the DHSS might have a legitimate interest in avoiding duplication of costs. He thought that responsibility lay with the SNBTS and that they should have been allowed their investigation.<sup>120</sup>

**30.79** From the sequence of events, it appears that decisions taken by the Expert Advisory Group on AIDS (EAGA, a non-departmental body established to provide the UK Health Departments with Expert advice on AIDS) contributed to the discontinuation of the Scottish initiative.<sup>121</sup>

**30.80** Professor Cash maintained that the SNBTS initiative had to be stood down 'in view of the hostile reaction of SHHD'.<sup>122</sup> The Inquiry sought comments from Dr McIntyre on this account of events and his response came in an e-mail from the Scottish Government.<sup>123</sup> Dr McIntyre took issue with the proposition that he ever spoke to Professor Cash in a hostile manner. He commented that 'SHHD treated Dr Cash and his colleagues in a professional manner and did all they could to help as this was a major health problem'.<sup>124</sup>

**30.81** Professor Cash thought that he had discussed the matter with Dr Mitchell and Dr McClelland. In a further attempt to shed light on this episode, both Dr McClelland and Dr Mitchell were asked for their recollections. Dr McClelland had 'no recollection of this whatsoever'.<sup>125</sup> Dr Mitchell had no recollection of actual discussions on the subject in 1985, although he could remember it being said that the SNBTS were not going to do the evaluations.<sup>126</sup> Professor Cash's account of the Department's 'hostility' to an SNBTS *initiative* was not disputed, including by Dr McIntyre, however, and it is appropriate to conclude that the SHHD did indeed express strong opposition to an independent Scottish evaluation.

**30.82** The question of an independent Scottish evaluation was effectively settled at this point by the EAGA. The EAGA was set up around the turn of 1984–85<sup>127</sup> with the purpose of providing 'advice on such matters relating to HIV/AIDS as may be referred to it by the Chief Medical Officers of the Health Departments of the United Kingdom' and first met on 29 January 1985.<sup>128</sup> The membership of the group was announced in the House of Commons on 20 February 1985.<sup>129</sup> The Group had a wide range of specialist interests: Genito-Urinary; Blood Transfusion; Epidemiology; Physicians and Nurses; Virology;

<sup>118</sup> Day 51, pages 37–39

<sup>119</sup> Ibid pages 30–34; Dr Mitchell's Witness Statement [PEN.017.1002] at 1003

<sup>120</sup> Day 48, page 86

<sup>121</sup> See paragraphs 30.82 *et seq* below.

<sup>122</sup> Professor Cash's Witness Statement [PEN.017.1038] at 1040

<sup>123</sup> Email dated 26 September 2011 [PEN.017.1836]

<sup>124</sup> Ibid [PEN.017.1836]. It is unfortunate that this response did not deal in detail with the substance of Professor Cash's observation.

<sup>125</sup> Dr McClelland – Day 50, page 41

<sup>126</sup> Dr Mitchell – Day 51, page 34

<sup>127</sup> The group continues to exist at the time of writing this report: <https://www.gov.uk/government/groups/expert-advisory-group-on-aids> (last accessed 30 December 2014)

<sup>128</sup> Minutes of meeting [SNB.001.0002]

<sup>129</sup> Extract from *Hansard* [SNF.001.3323]

Immunology; and Microbiology were all represented.<sup>130</sup> Professor Cash and Dr McClelland both attended the first meeting.

**30.83** At that meeting it was agreed that a screening test for all UK blood donors should be made available as soon as practicable and a sub-group on implementation was set up to consider screening tests for AIDS and, in particular, the best way of introducing the service when the tests became available.<sup>131</sup> The sub-group comprised Dr Gunson, Dr McClelland, Dr Philip Mortimer (Consultant Virologist), Dr Tony Pinching and Dr Philip Rodin (GUM specialists) and Professor Tedder, under Dr Smithies as Chair. It was not the specialist UK advisory group envisaged by Professor Cash, although Scottish interests were now fully represented at the national level. At a meeting of the SNBTS Co-ordinating Group held on 19 February 1985, the evaluation programme (monitored by an EAGA sub-group) was noted and it was agreed, after full discussion, that the proposals for a west of Scotland study should not be pursued at that time.<sup>132</sup> Professor Cash reported to Dr Bell that the SNBTS directors had agreed to hold off from validation of kits until protocols had been agreed through EAGA.<sup>133</sup> Dr Bell welcomed the news on 6 March.

**30.84** The decision to await the completion of the tests arranged by EAGA was reinforced on 20 June 1985, when the SNBTS Directors again considered the introduction of testing for HIV.<sup>134</sup> It was noted that the SHHD had undertaken to provide funds for testing kits once it had been agreed to commence routinely.<sup>135</sup> On 27 June 1985, Professor Cash wrote to Mr Davies, SHHD, giving advance notice of a need for additional resources for screening.<sup>136</sup>

**30.85** In his evidence to the Inquiry, Professor Cash commented that it was his view that, if the SNBTS had been allowed to 'go it alone', testing of donated blood for HIV in Scotland with commercial kits could have been introduced around the same time as such screening commenced in the Netherlands and Australia.<sup>137</sup> In round terms, that would have involved a saving of about four months.

**30.86** Dr Scott was asked to comment on Professor Cash's position but, apart from noting generally that Professor Cash's views were not always entirely favourable to the SHHD, felt he could not comment on the impression Professor Cash gave, that the SHHD were holding him back.<sup>138</sup> He deferred to Dr McIntyre on the sequence of events that led to the abandonment of the proposal for a Scottish evaluation but Dr McIntyre was not able to assist.<sup>139</sup>

**30.87** It should be borne in mind that the first meaningful supplies of Abbott kits for evaluation did not arrive in Glasgow until April and scientists in the West of Scotland BTS did not have access to the MH/CB assay. There was, on the balance of evidence, no real prospect of Scotland being able to introduce screening four months before 14 October 1985.

<sup>130</sup> The members and representatives of government departments are listed in the notes of the first meeting [SNB.001.0002]

<sup>131</sup> Ibid [SNB.001.0002] at 0005. Dr Covell also prepared a note of the meeting [SGH.002.7296]

<sup>132</sup> Minutes of Meeting [SNB.003.9171] at 9177

<sup>133</sup> Letter of acknowledgment from Dr Bell to Professor Cash [SGH.002.7260]

<sup>134</sup> Minutes of Meeting [SGF.001.0203]

<sup>135</sup> Ibid [SGF.001.0203] at 0205

<sup>136</sup> Professor Cash's letter to Mr Davies [SNB.005.7915]

<sup>137</sup> Professor Cash – Day 48, pages 185–187. According to a DHSS memo of 20 May 1985 [DHF.001.7323], screening had already begun by that date in Australia and in the USA. Other countries are discussed in the Appendix at 7325. An earlier version of the document, [DHF.001.7239] at 7240, refers to the Netherlands, where it is said that '[b]y mid June all except 2 blood collecting centres will be screening blood donations for antibody'.

<sup>138</sup> Dr Scott – Day 49, Pages 133–135

<sup>139</sup> Ibid pages 139–140

## Development of an HIV test in the United Kingdom

### *Choosing the test format: radioimmunoassay or enzyme-linked immunosorbent assay*

**30.88** The need to scale up testing from an assay working in the laboratory to kits which could be used for hundreds of thousands of tests in the blood transfusion services raised questions as to the nature of the test to be taken forward as well as to the selection of a manufacturer. The characteristics of the two test formats considered are discussed in Chapter 29, *The Discovery of HIV and the Development of Screening Tests*, at paragraph 29.27.<sup>140</sup> Professor Tedder's test was initially developed as a radioimmunoassay (RIA), in which radioactive isotopes are used in the detection of the target antibody.<sup>141</sup> Within the NBTS in England and Wales in 1984, there was a preference for RIA testing<sup>142</sup> and Professor Tedder's initial work reflected the reality of that preference. In his letter of 3 July 1984 to Dr Smithies, Dr Gunson expressed the view that '[i]t would be an advantage for the NBTS if [the new test] was in the format of the Blood Products Laboratory (BPL) RIA test for [the Hepatitis B surface antigen]'.<sup>143</sup> The BPL were familiar with RIA testing and that was an obvious attraction. On 23 January 1985, at the meeting of the RTDs in England, the position was still that '[t]he preference within the NBTS [was] for an RIA'.<sup>144</sup>

**30.89** Within the public service in England and Wales, it was also hoped that the CBLA might become involved in the preparation of the test kits.<sup>145</sup> At official level, there was interest in involving other public sector institutions in the development work, in particular CAMR Porton, who were thought to have the necessary equipment and expertise.<sup>146</sup>

**30.90** Initially, official support for the principle of a UK test reflected the BPL's preference. For example at the 16th meeting of the CBLA on 1 February 1985, the subject was discussed. The minutes record:

The Director [of BPL] advised that if given the antibody BPL could produce a test as an alternative to the Chester Beatty's work in association with industry, at a much lower cost. Dr Gunson confirmed the necessity for the test and referred to a Departmental working party considering the matter. It was noted that the CBLA role in this matter was not yet established but there would be a related capital requirement for equipment for RIA tests.<sup>147</sup>

**30.91** Throughout the industry, however, RIA technology was being superseded in routine testing because the radioisotopes employed in such assays were potentially dangerous.<sup>148</sup> It was increasingly recognised that radioactivity involved risk and, while the risk could be contained in the laboratory, it was considered undesirable to have a 'widespread proselytization' of RIAs into the community.<sup>149</sup> Once Professor Tedder and Professor Weiss had decided to work with the diagnostic industry it would have been difficult to resist

<sup>140</sup> See also: Professor Tedder – Day 49, pages 65–67

<sup>141</sup> Ibid pages 65–67

<sup>142</sup> The preference within the NBTS in England and Wales for RIA testing did not appear to be replicated in the SNBTS: Dr McClelland's Witness Statement [PEN.017.1337] at 1358

<sup>143</sup> Dr Gunson's letter to Dr Smithies [SNB.006.5978] at 5979

<sup>144</sup> Minutes of RTDs meeting [SNB.011.1971] at 1974

<sup>145</sup> Letter from Dr Gunson, NBTS, to Dr A Smithies, DHSS dated 3 July 1984 [SNB.006.5978] at 5979

<sup>146</sup> Note: 'Aids Immune Deficiency Syndrome AIDS – Current Developments' [DHF.001.5555] at 5557 Date of 27 July 1984 is given on the covering memo [DHF.001.5554]

<sup>147</sup> Minutes of CBLA meeting [DHF.003.0219] at 0224

<sup>148</sup> Professor Cash – Day 48, page 136

<sup>149</sup> Professor Tedder – Day 49, page 66

the global move towards ELISAs and away from RIAs.<sup>150</sup> ELISA technology carried no biological hazard and Wellcome had scientists highly skilled in producing the enzyme ligands used in such assays.<sup>151</sup>

**30.92** Professor Tedder remembered attempts being made to involve the BPL and meetings being held with Dr Lane, the CBLA and the BPL. Eventually, however, it became necessary 'to let them down and say, "We don't want to do a radioimmunoassay, we are going to run with Wellcome"'.<sup>152</sup> Wellcome Diagnostics was engaged to carry out the research and development necessary to achieve the ELISA-based test kit and CAMR Porton were enlisted to help with the scaling up as sub-contractors to Wellcome.<sup>153</sup> Engagement with Wellcome led to the abandonment of Professor Tedder's RIA in favour of ELISA technology.

**30.93** Although in the end Wellcome was selected, the choice of a manufacturer for the MH/CB test was not straightforward. Professor Tedder told the Inquiry that he made contact with the five diagnostic companies licensed in the US to develop tests and a number of British companies. None of the US companies would work with the British scientists, although they were discarding large quantities of the antigen required for the British test.<sup>154</sup> Professor Tedder thought that the reason for rejection was twofold: (i) the terms of the contracts to which the US companies were party and (ii) scepticism about the effectiveness of the competitive assay which he and Professor Weiss had developed.<sup>155</sup> In order to work with companies outside the National Cancer Institute franchise it was necessary to have an independent UK-based isolate, such as the isolate he and Professor Weiss were developing. Wellcome were 'the most enthusiastic and the quickest off the mark'.<sup>156</sup>

**30.94** The question of scale-up of the test reagents, including quantities of the virus, had been moving forward since the previous summer, with implications for the type of test which would eventually be manufactured. As Professor Tedder commented, references in the DHSS minutes around this period to the development in the UK of an RIA for screening were inaccurate because, at that time, the test which he was developing with Wellcome was already an enzyme-based test, not an RIA, though that does not seem to have been understood by officials.<sup>157</sup> The research group had already begun work on the ELISA with Wellcome in October or November 1984.

**30.95** Failure to appreciate that there had been a decision to adopt the ELISA format appears to have continued. At the meeting of EAGA on 29 January 1985 Dr Gunson reported that BTS were in overwhelming favour of an RIA test on the view that it was more accurate than an ELISA test on which all the US tests were based and suited the equipment which they already had for Hepatitis B testing. Professor Arie Zuckerman (Professor of Microbiology, Royal Free Hospital School of Medicine, London) was in favour of the evaluation of the US test before an RIA test was adopted.<sup>158</sup> A note prepared by Dr Covell, SHHD, of the meeting of EAGA on 29 January 1985 reported that Professor Weiss

<sup>150</sup> Ibid pages 65–66

<sup>151</sup> Ibid pages 67–69. (In this context, ligands are 'enzyme labels' that create a coloured substrate, through binding to a receptor, in the presence of a positive sample.)

<sup>152</sup> Ibid page 69

<sup>153</sup> 'Aids and its prevention in the United Kingdom – a position paper' [DHF.002.0431] at 0432

<sup>154</sup> Letter dated 26 September 2011 from Professor Tedder to the Inquiry [PEN.017.1831] at 1832

<sup>155</sup> Professor Tedder – Day 49, pages 63–64

<sup>156</sup> DHSS paper dated 28 January 1984, which almost certainly should read 1985 [DHF.002.2267]

<sup>157</sup> Professor Tedder – Day 49, pages 81–82, in relation to [DHF.001.9036] dated 4 January 1985

<sup>158</sup> Minutes of EAGA meeting on 29 January 1985 [SNB.001.0002] at 0005, paragraph 21



was negotiating with Wellcome Diagnostics to develop a test for BTS.<sup>159</sup> The note did not reflect an understanding that there had been a move to adopt an ELISA format. The assumption that the MH/CB test would have an RIA format appears to have continued.

**30.96** While it is necessary to be aware of this issue, having regard to the extensive references to it in the evidence already noted and noted later in historical context, in the end it did not impact on progress. In this, as in other areas, Professor Tedder and his industrial collaborators got on with the work necessary to develop their assay, adopting the test format thought best to suit market demand.

### *Progress with scale-up*

**30.97** As already noted, CAMR Porton were enlisted to help with the scaling-up as sub-contractors to Wellcome.<sup>160</sup> CAMR initially did not provide antigen appropriate for use in the assay, however, as they did not follow the exact protocol Professor Tedder and his colleagues had developed for engendering maximal antigen retention in the cell component. Professor Tedder acknowledged the difficulties CAMR had in scaling up for industrial production: the conditions of the culture they used encouraged antigen to come out of the cell into the supernatant, whereas it was necessary for the assay under development that the virus remained in the cells.<sup>161</sup> It was not until late spring 1985 that the CAMR antigen came on-line.<sup>162</sup> That did not affect the progress of research or cause delay, however, since enough high-quality antigen was produced by Professor Tedder's laboratory-scale equipment to enable the research programme to continue.<sup>163</sup> When it was decided that Wellcome should develop a test based on the MH/CB patent-protected competitive technique, Professor Tedder and Professor Weiss supplied their own British isolate.<sup>164</sup>

**30.98** Reports of work in hand at the first meeting of EAGA on 29 January 1985 indicate that research was continuing.<sup>165</sup> The availability of screening tests was discussed and Professor Weiss reported on the work with Wellcome Diagnostics. There were still problems to be solved.<sup>166</sup> There was still intent among the RTCs to proceed uniformly across the transfusion services, a point stressed at a meeting of the RTDs on 17 April 1985: their interest was in having 'uniformity of action'.<sup>167</sup>

**30.99** Dr Covell, SHHD, prepared a note of the meeting of 29 January 1985 that indicated that the choice of test systems was still open. He reported:

Prof Weiss said that he was negotiating with Wellcome Diagnostics to develop a test for BTS which would be as reliable as other tests and would detect serum antibodies specific to HTLV III. Negotiations were just beginning and he could not give a date when it would be available. It may turn out that overseas tests may be produced quicker and could be more reliable.

Prof Zuckerman said that three United States firms, Travenol, Dupont and ? [third firm not named in the text] have tests ready which he hopes to evaluate

<sup>159</sup> Note of meeting [SGH.002.7296] at 7299

<sup>160</sup> 'Aids and its prevention in the United Kingdom – a position paper' [DHF.002.0431] at 0432

<sup>161</sup> Professor Tedder – Day 49, pages 64–65

<sup>162</sup> Professor Tedder's Witness Statement [PEN.017.1831] at 1832

<sup>163</sup> Professor Tedder – Day 49, pages 11–12

<sup>164</sup> Memorandum [DHF.002.0431] at 0432

<sup>165</sup> Minutes of EAGA meeting [SNB.001.0002]

<sup>166</sup> Ibid [SNB.001.0002] at 0005

<sup>167</sup> Minutes of RTDs meeting [SNB.001.3172] at 3174

within the next three months and to compare with Dr Tedder's test. He hoped they would not only be available for BTS, indeed even if there was a delay they should wait until others could also be supplied.

Dr Whitehead said there were technical difficulties in the scaling up of the test. He also mentioned the possibility of patent restrictions on the viral strain involved.<sup>168</sup>

**30.100** Dr Covell's note disclosed a significant move from the earlier concentration on the interests of the blood transfusion services in discussing the approach to the development and introduction of HIV assays. Professor Tedder commented that a test would have to be made available to all who wanted it, reflecting his understanding that many individuals attending genito-urinary medicine (GUM) clinics, haemophilia patients and those who encountered needle stick injuries in the course of their work wanted access to the test, even though doctors could not tell them its full significance. Appropriate resources had to be provided for that demand.<sup>169</sup>

### The evaluation project

**30.101** As noted above, unlike the USA, where kits had to be approved by the FDA before they could be used for screening, the UK did not have a requirement for test kits to be licensed under the Medicines Act 1968 or otherwise.<sup>170</sup> The DHSS had no statutory authority to force manufacturers to have their products evaluated before sale to the NHS was permitted.<sup>171</sup> There was thus no legal impediment to sale of such kits in the UK. Abbott were informed of that position on 5 March 1985.<sup>172</sup>

**30.102** The DHSS had decided that an evaluation of all the competing kits (including any developed in the UK) was necessary, however: it was seen as important that the most suitable tests were chosen for NHS use and that there was uniform introduction throughout the transfusion services.<sup>173</sup> As already noted in paragraph 30.50, Professor Tedder wrote to Dr Smithies on 18 December 1984, seeking funding for monitoring the efficiency with which the MH/CB test and the forthcoming commercial kits detected antibody to HIV.<sup>174</sup> It appears that by this stage the need for an evaluation of test kits in the specific context of the UK population had been recognised, although a specific date for a decision to that effect has not been identified. The intention behind the assessment was described as being to 'inform the NHS through suitable media of those products which were worthy of consideration. Thereafter the would-be purchasers could make a decision based on price and the results of appraisal with local circumstances in mind'.<sup>175</sup>

**30.103** On 16 January 1985, a draft of the evaluation programme was sent to Dr Smithies in the form of a letter to be sent to the producers of test kits.<sup>176</sup> The formulation of plans to conduct a detailed evaluation of test kits may have occurred in part during telephone conversations of which the Inquiry has no formal record. For example, the minute to Dr

<sup>168</sup> Note of SHHD meeting [SGH.002.7296] at 7299

<sup>169</sup> Ibid [SGH.002.7296] at 7299

<sup>170</sup> See letter from Travenol Laboratories Ltd to DHSS dated 19 December 1984 [DHF.001.8859] and (undated) form of certificate [DHF.001.8860]

<sup>171</sup> Minute of DHSS meeting 30 January 1985 DHF.002.7016]

<sup>172</sup> Letter to Abbott [DHF.002.6938]

<sup>173</sup> Draft Submission to Ministers [DHF.002.2250] at 2251

<sup>174</sup> Professor Tedder's letter Dr Smithies [DHF.001.8856]

<sup>175</sup> Notes of DHSS meeting [DHF.001.9250]

<sup>176</sup> Draft evaluation programme [DHF.001.9098] and minute [DHF.001.9097]. Compare the more developed protocol of 8 March 1985 [DHF.002.6939]

Smithies dated 16 January 1985 refers to 'our telephone conversation about setting up an evaluation programme'. What is evident is that a letter was sent by the DHSS to all those known to be developing tests, including Wellcome, around 21 January 1985.<sup>177</sup>

**30.104** The draft was discussed within the department and there was some consideration of whether only kits approved by the FDA should be 'accepted' in the UK. On 21 January 1985 Dr Smithies commented:

We also discussed whether or not any reference should be made to tests not being accepted in the UK unless they had FDA approval and decided that such stipulation might not act in Wellcomes best interests in the short term.<sup>178</sup>

**30.105** Professor Tedder commented:

There is little difference in having an American manufacturer or the FDA pontificating on the performance of a test and then accepting matters as gospel in this country. That would run completely counter to everything that we had ever done in the transfusion service in the UK and anything that we do nowadays. And indeed, if we had been tied to FDA ... we would have been locked into an antediluvian regulatory system.<sup>179</sup>

**30.106** The letter sent to manufacturers on 21 January 1985 made clear that the results of the evaluation exercise would form the basis of 'firm advice' to the NHS on which materials might be used and that it was likely that the NHS would also be advised not to use materials not tested in the programme.<sup>180</sup> The programme was to comprise a systematic study of each candidate material's performance against a panel of patients' samples, both positive and negative; investigation of the controls provided; and the convenience and time required to carry out each test. Information to substantiate claims made for each product would be required.

**30.107** All those manufacturing tests agreed to participate.<sup>181</sup> Wellcome responded almost immediately, replying on 29 January 1985 and agreeing to submit their product to evaluation but noting that their main priority was to make a kit available to the blood transfusion services as quickly as possible.<sup>182</sup> Professor Tedder interpreted the letter as indicating that, while Wellcome were willing to participate in the evaluation programme, they would not have prepared the usual, fully detailed portfolio of manufacturers' claims for its product and the data normally submitted for evaluation: there was not time to do that.<sup>183</sup>

**30.108** In Scotland, the SHHD were kept informed of developments. The DHSS submission to Ministers regarding the need to introduce screening into the NBTS was sent on 17 January 1985.<sup>184</sup> Dr Bell acknowledged receipt of these documents from Mr Murray by minute dated 21 January 1985.<sup>185</sup>

<sup>177</sup> Copy of DHSS letter to manufacturers [DHF.001.9140]

<sup>178</sup> Memorandum [DHF.002.7101]

<sup>179</sup> Day 49, page 91

<sup>180</sup> Copy of DHSS letter to manufacturers [DHF.001.9140]

<sup>181</sup> Wellcome's confirmation of 29 January 1985 [DHF.002.7106]

<sup>182</sup> Ibid [DHF.002.7106]

<sup>183</sup> Professor Tedder – Day 49, page 84

<sup>184</sup> Hand-written letter [SGH.002.7302] with enclosed Minute [SGH.002.7303] and Submission [SGH.002.7304]

<sup>185</sup> Minute [SGH.002.7301]

### *A potential conflict of interests*

**30.109** Initially, it was considered that Professor Tedder's laboratory might provide the evaluation service. The proposal that Professor Tedder and Professor Weiss should be funded to do this work was quickly dropped, however, when it was recognised that there was a potential conflict of interests in this approach.<sup>186</sup> As matters had developed, Professor Weiss and Professor Tedder had independent interests in promoting their distinctive technology in collaboration with Wellcome Diagnostics. On 11 February 1985, the DHSS wrote to Wellcome noting that commercialisation was a separate issue from the evaluation programme that was being set up.<sup>187</sup>

**30.110** The potential for a conflict of interests if Professor Tedder had been selected to do the evaluation was acknowledged in a DHSS memorandum dated 13 February 1985.<sup>188</sup> When he had sought funding, Professor Tedder had wanted to be able to look at the performance of the various kits in order to define the best algorithm for use, but that did not require extensive access to assays.<sup>189</sup> The full evaluation process would require much more access to assays while Professors Tedder and Weiss were, at the same time, working on their own test. Professor Tedder commented:

You know, I tore my hair out with our colleagues in DHSS over these early years. I think it's actually correct to have some form of Chinese walls because otherwise there is a conflict of interest, and I can't see how you can have a commercialisation of a test being carried out under the same umbrella as the evaluation programme. I think you do need to separate them because they are different issues.<sup>190</sup>

**30.111** Professor Tedder was anxious to avoid potential conflicts of interests. He was particularly concerned that no favours should be shown to his assay; his institution had financial interests in benefiting from its own intellectual property. He said that there had been no intention to delay the evaluation process to favour Wellcome and agreed with the refutation by Dr Barbara and Dr Hewitt that there had ever been any such idea.<sup>191</sup> Professor Tedder said:

Looking back I'm relieved that we were not asked to undertake such an evaluation, it would have been a massive deflection. It would also have constituted ammunition for the comment of conflicts of interest. I see ... the potential for a conflict of interest had we been asked to conduct an evaluation of commercially available assays while working with an industrial collaborator at the same time. To be in such a position would have rendered it extremely difficult for us to have meaningful conversations with the diagnostic firms concerned.<sup>192</sup>

<sup>186</sup> See paragraph 8.127 of the Preliminary Report for further details.

<sup>187</sup> DHSS letter [DHF.001.9175]

<sup>188</sup> Memorandum [DHF.001.9212]

<sup>189</sup> Professor Tedder – Day 49, pages 86–87

<sup>190</sup> Ibid pages 85-86

<sup>191</sup> Barbara and Hewitt, 'Delayed AIDS testing', *New Scientist*, 29 August 1985 [DHF.001.7755].

<sup>192</sup> Letter from Professor Tedder to the Inquiry dated 26 September 2011 [PEN.017.1831] at 1834

### *Preparatory work*

**30.112** On 13 February 1985 there was an internal DHSS meeting at which it was noted that Dr Mortimer had expressed a willingness to carry out an evaluation for the department and it was agreed that he would be acceptable to the DHSS.<sup>193</sup> At the time, Dr Mortimer was Director of the Central Public Health Virus Reference Laboratory of the Public Health Laboratory Service (PHLS). Dr Mortimer was selected to do the work<sup>194</sup> and an ad hoc Expert Working Group would be set up to help in the management of the evaluation.

**30.113** Professor Tedder said that there was a multiplicity of groups with different interests involved in monitoring the evaluation exercise.<sup>195</sup> There was a screening test sub-group of EAGA, which was to look at broader issues than the DHSS technical group, and the RTDs had a working party. By the time of the meeting on 13 February 1985, Dr Mortimer was drafting a protocol for the exercise.<sup>196</sup> The report of the evaluation exercise, dated September 1985, refers to the protocol having been drafted by an ad hoc Expert Working Group set up by the DHSS.<sup>197</sup>

**30.114** Dr McClelland said that, in his view, the ad hoc Expert Working Group established by the DHSS and the Screening Test Sub-Group of EAGA had ‘two completely different tasks’. The first group was ‘to design and possibly oversee the technical evaluation’, whereas the second was ‘to look at the broader group of issues for the transfusion service that had to be addressed in preparing to introduce large-scale screening testing of blood donors’.<sup>198</sup> Both groups played useful, timely and important roles as matters developed in 1985.

**30.115** On 15 February 1985, the screening test sub-group of EAGA met.<sup>199</sup> Dr McClelland had tabled a paper, dated 11 January 1985 and prepared by the Division of Biometrics of the FDA’s Department of Health and Human Services, reporting on phase 1 of the Public Health Service evaluation of US kits.<sup>200</sup> It was reported that the kits had not been tested by the participating companies on the same serum samples (a point made in the *Nature* article of 13 December 1984)<sup>201</sup> and it was agreed that it was essential to repeat the process in the UK using the same samples for each test. It was also agreed that the evaluation would have to embody confirmatory procedures and the requirements for field trials were discussed and agreed. The evaluation exercise would consist of initial testing by PHLS against a panel of sera with a follow-up evaluation in RTCs and in laboratories serving sexually transmitted diseases (STD) clinics also undertaken. Dr Gunson and Dr McClelland were asked to consider the feasibility of collecting samples and preparing aliquots from them at transfusion centres while Dr Pinching was to deal with STD clinics. It was noted that:

Regional Transfusion Directors had been unanimous in wanting a common date for the introduction of a test into the NBTS. The group considered that

<sup>193</sup> Note of DHSS meeting [DHF.001.9250]

<sup>194</sup> Professor Tedder – Day 49, page 88

<sup>195</sup> Day 49, pages 93–95

<sup>196</sup> Note of meeting [DHF.001.9250]

<sup>197</sup> Public Health Laboratory Service and Department of Health and Social Security – Evaluation of Five Commercial Anti-HTLV III/LAV Assay Kits [SNB.004.8847] at 8850. The members of the ad hoc working group are listed in [SNB.001.0264] and included Dr Eddie Follett of Ruchill Hospital, Glasgow, and Dr Mortimer.

<sup>198</sup> Dr McClelland – Day 50, page 35

<sup>199</sup> Note of EAGA sub-group meeting [SNB.001.0170]

<sup>200</sup> Memorandum dated 11 January 1985 from Division of Biometrics entitled ‘Evaluation of Reactivity to HTLV-III Antibody Observed in Phase 1 of PHS Study’ [SNB.001.0141] (See also note of meeting of 15 February 1985 [SNB.001.0170] at 0171)

<sup>201</sup> Budiansky, ‘False Test Results Raise Doubts’, *Nature*, 13 December 1984; 312:583 [PEN.017.0658].

individual RTCs should be dissuaded from implementing tests on a local basis. In fact it was agreed by the sub group that tests should better be made available for the clinical setting first.<sup>202</sup>

**30.116** The reference to 'NBTS' was intended to apply to the UK as a whole.<sup>203</sup>

### Development of the evaluation programme

**30.117** The EAGA sub-group met next on 1 March 1985.<sup>204</sup> Dr Gunson and Dr McClelland tabled a paper outlining a proposal for the second phase of evaluation, a BTS field trial using 10,000 specimens collected routinely from blood donors, to follow on completion of the PHLS evaluation coordinated by Dr Mortimer. Dr Pinching confirmed that he could collect the required specimens from STD clinics. There was general discussion of the technical problems involved and of the counselling and other services thought to be required.

**30.118** Dr McClelland described the plan to have a laboratory assessment of the kits using a smaller number of samples and then a field assessment as 'a fairly conventional sequence of events'.<sup>205</sup> Later, he said that the first stage, carried out by the PHLS and funded by the DHSS for the UK transfusion services, was a 'perfectly reasonable position for the first part of the evaluation'.<sup>206</sup> The second part of the evaluation then had to involve the transfusion services directly because 'that was the operating environment in which the test would have to be proven'.<sup>207</sup>

**30.119** An internal DHSS memorandum dated 11 March 1985 set out the anticipated arrangements for the introduction of screening tests.<sup>208</sup> All manufacturers known to be making diagnostic reagents had been informed that the DHSS intended to evaluate their kits and five had agreed to cooperate. The steps envisaged were:

- An initial evaluation against 300 to 500 serum samples by the Virus Reference laboratory at the PHLS Colindale.
- A field evaluation of the kits prompted by the experiences of the FDA as disclosed to the DHSS. This could not be started until completion of the initial evaluation. The required sera were already being collected and stored.
- The PHLS laboratories were to provide panels of standard sera and would provide a reference service.
- Kits satisfying the evaluation, including the UK test if produced on a large enough scale, would be listed.
- The Regional Transfusion Directors had agreed to commence testing at the same time and had indicated a wish to use the same test.

**30.120** On 15 March 1985, the DHSS wrote to the RTDs describing the two-phase programme then envisaged.<sup>209</sup> The letter commented that it was the intention of the Department to evaluate any commercially produced tests which were marketed and to

<sup>202</sup> Note of meeting of 15 February 1985 [SNB.001.0170] at 0171

<sup>203</sup> Dr McClelland – Day 50, page 37

<sup>204</sup> Note of EAGA sub-group meeting [SNB.001.0172]

<sup>205</sup> Day 50, page 38

<sup>206</sup> Ibid page 42

<sup>207</sup> Ibid page 42

<sup>208</sup> DHSS memorandum [DHF.002.5475]

<sup>209</sup> See letter to Chairmen of RTDs, 15 March 1985 – DoH copy is to Bristol [DHF.001.9430]

give advice to the NHS on the suitability of the tests. It noted the view of the RTDs that there was an imperative need for a coordinated introduction of screening tests into all centres simultaneously, and EAGA's endorsement of that view, and that the view had been endorsed by Regional Medical Officers in discussion with the Department the previous day. The RTDs' interest in having a cohesive position was stressed at their meeting on 17 April 1985.<sup>210</sup> The DHSS was anxious that all blood transfusion authorities should wait until the results of the evaluation process were available and coordinated arrangements had been made to use the tests at all centres.

**30.121** It was considered very important that testing begin simultaneously throughout the UK. Dr Mitchell said that it was very clear that 'we were all to sing from the same hymn sheet' and he agreed with that approach.<sup>211</sup> Arrangements were in hand for the preparation of protocols for the evaluations and other procedural matters. Abbott's kit was to be tested and a small quantity was to be imported for that purpose. As the DHSS understood it, there were no kits in the UK at that point. Professor Cash observed that Dr Mitchell had not envisaged any problem in obtaining kits.<sup>212</sup> However, it is not clear that Professor Cash was well-informed about the availability of kits at the time.<sup>213</sup>

**30.122** 'Singing from the same hymn sheet' would not be easy: not all relevant agencies were up-to-date. The minutes of the meeting of the CBLA Central Committee for Research and Development in Blood Transfusion held on 2 April 1985 indicate that, until that date, the Chairman was not aware that UK evaluation studies of the tests had been set up or that a protocol for the evaluation had been sent to manufacturers.<sup>214</sup> However, in light of the information provided:

The importance of evaluation of the tests was emphasised and it was agreed that an adequate confirmatory laboratory service was required, especially in view of the high incidence of false positive results.

In answer to a question raised by the Chairman about testing in the haemophilic population in the UK, [Dr Rizza] and Professor Luzzatto informed the Committee of tests they had carried out in Oxford and at the Middlesex Hospital and the results of these had confirmed the importance of evaluation.<sup>215</sup>

**30.123** In Scotland, Dr McClelland prepared a paper dated 15 May 1985 for the RTDs, outlining some of the practical issues that would arise from the evaluation programme.<sup>216</sup> He emphasised the need for the evaluation of test systems in the light of evidence that some tests gave significantly lower false positive rates than others. He outlined the practical problems for Transfusion Directors in interpreting screening test results and in dealing with donors who were 'screen positive' on initial testing but unconfirmed and the need for confirmatory tests. He commented on the need for documentation and for communication with donors and donors' GPs, for the purposes of monitoring and counselling, among other matters. Dr McClelland's paper would have informed any Director who had been less than fully involved in the preparations for the evaluation programme of the range and

<sup>210</sup> Minutes of RTDs meeting [SNB.001.3172] at 3174

<sup>211</sup> Day 51, page 49

<sup>212</sup> Professor Cash – Day 48, pages 88–89

<sup>213</sup> Ibid page 43: 'There is a view that I see here, that there weren't many tests available, that this was a major problem. That never struck me'. See paragraph 30.232 below.

<sup>214</sup> Minutes of CBLA Meeting [DHF.001.9652] at 9654

<sup>215</sup> Ibid [DHF.001.9652] at 9655

<sup>216</sup> Dr McClelland's paper [SNB.005.9600]

complexity of the preparations required, as well as providing a valuable check-list for all Directors.

**30.124** The views of Ministers were communicated to the PHLS on 31 May 1985.<sup>217</sup> It was intended to review the position on 7 June and the PHLS was asked to prepare a flow chart projecting dates for completion of the evaluation and for countywide introduction of testing, with take-up facilities for confirmatory testing. The PHLS prepared a flow chart and explanatory paper in June.<sup>218</sup>

**30.125** From the terms of the PHLS paper it appears that the initial evaluation process was not limited to Professor Tedder's work on the MH/CB test at the Middlesex Hospital and Dr Mortimer's wider exercise at the PHLS Virus Reference Laboratory, Colindale. Four other public health laboratories, at Newcastle, Leeds, Oxford and Birmingham, were testing for antibody to HIV.<sup>219</sup> Wellcome was developing the competitive MH/CB assay and Abbott, Electro-Nucleonics Inc, Organon, Litton/Ortho, Travenol and Production Pasteur were developing indirect assays. Abbott and Electro-Nucleonics Inc had said that they could supply the British transfusion and clinical markets immediately but both had withdrawn the kits originally delivered to the PHLS Colindale and supplied replacements, raising doubts about the claims. At Colindale, the first stage evaluation of Abbott, Electro-Nucleonics Inc and Wellcome test kits had begun with each company demonstrating their products. Colindale and Middlesex Hospital were proceeding to test the available assays. The summary of the paper suggested that the ideal position would be to have one UK kit (Wellcome) and one US kit available for use.<sup>220</sup>

***Concerns about perceived delay revisited: should US kits be introduced before evaluation is complete?***

**30.126** Among some haemophilia clinicians in the UK, including Professor Arthur Bloom,<sup>221</sup> there was still a degree of anxiety about delay. At the meeting of EAGA in May 1985, Professor Bloom expressed concern at delaying the introduction of a screening test in the blood transfusion service.<sup>222</sup> On 31 May 1985 he wrote to the chairman of the group to reinforce his views.<sup>223</sup> He was concerned for people with haemophilia, patients undergoing surgery, leukaemia patients and others needing blood and blood products, given the rising prevalence of HIV positivity. He thought that one or more of the FDA-approved tests should be introduced immediately for testing donations, leaving over re-testing, confirmatory testing and donor counselling to be dealt with as separate issues.

**30.127** At the meeting of the screening test sub-group of EAGA on 10 June 1985, there was a proposal to allow the three commercial kits due to have been evaluated by the end of June to proceed to the field test stage. However, the counter view – that it was better to wait until the PHLS had evaluated more tests, including that of Wellcome – appears to have prevailed.<sup>224</sup>

<sup>217</sup> Memorandum dated 31 May 1985 [DHF.002.0119], confirmed by letter the same day [DHF.002.7010]

<sup>218</sup> PHLS paper dated June 1985 [DHF.002.6785] at 6786

<sup>219</sup> Ibid [DHF.002.6785] at 6786

<sup>220</sup> Ibid [DHF.002.6785] at 6785

<sup>221</sup> Director of the Cardiff RTC, Chairman of the UK Haemophilia Centre Directors Organisation and a member of the CBLA.

<sup>222</sup> Minutes of EAGA Meeting [SNB.001.0365] at 0367 paragraph 5.4

<sup>223</sup> Professor Bloom's letter to the Chairman of EAGA [DHF.002.5510]

<sup>224</sup> See note of meeting of 10 June 1985 [DHF.002.7538] at 7539



**30.128** Professor Bloom continued to advance his similar suggestion. With Dr Forbes and Dr Charles Rizza (Director of the Oxford RTC), he wrote to the *British Medical Journal* (*BMJ*), his letter being published on 22 June 1985.<sup>225</sup> By this time, three commercial HIV screening kits had been approved by the FDA. The authors wrote:

[People receiving] whole blood, platelet transfusions, cryoprecipitate or other blood derivatives from 50 or more donors in a short space of time [may be exposed to the risk of HTLV-III infection]. The risk of HTLV-III infection in such patients could now be as high as one in 20 in certain areas of Britain.

All these considerations underline the need rapidly to introduce screening for HTLV-III antibody for all blood donations. Three commercial test kits have now been approved by the American Food and Drug Administration and, although there may be a small number of false positives, it is unreasonable to delay testing until this possibility is eliminated.<sup>226</sup>

**30.129** Professor Cash was angered by the letter. He drafted and distributed to Professor Bloom, Dr Forbes and Dr Rizza a severely critical response, but did not submit the letter for publication. He criticised them for publishing matters more appropriately discussed in established professional forums and speculated that they had done so in the hope of causing a media and public reaction (as, he said, had happened). He challenged as unfounded on any evidence the statement that the risk of HTLV-III infection in such patients could now be as high as one in 20 in certain areas of Britain and characterised as ‘an extraordinary and cruel distortion’ of the evaluation process the notion that it was concerned merely with logistical problems that could be dealt with after testing was introduced.<sup>227</sup> Though not noted by Professor Cash, Dr Rizza had been present at the meeting of the CBLA Central Committee for Research and Development in Blood Transfusion on 2 April 1985 when it was agreed that evaluation was necessary.

**30.130** Professor Cash sought to explain his position in oral evidence. He believed that there was a ‘major error of fact’ by Professor Bloom and his fellow authors in their letter relating to the assessment of the risk of false positives. Beyond that:

At the time I thought this is a direct attack on the UK transfusion services. And here we were battling away with our colleagues in DHSS to get the kits evaluated quickly, to get them into use. But Arthur [Bloom] didn’t seem to follow that, nor did Charles Forbes, so I reacted pretty angrily ....<sup>228</sup>

**30.131** The position of Professor Bloom and his co-authors was surprisingly close to the policy applied in the USA and at odds with the ethos of the UK blood transfusion services’ voluntary donor system. Professor Cash’s response is at least understandable, albeit expressed in particularly strong terms.

**30.132** The competing advice and representations of interest groups required discussion: the issue of whether US test kits should have been introduced as they became available was real. These exchanges illustrate deep divisions of opinion among those on whom official agencies would normally depend for independent advice.

<sup>225</sup> Bloom et al, ‘HTLV-III Haemophilia and Blood Transfusion’, *British Medical Journal*, 1985; 290:1901 LIT.001.0333]

<sup>226</sup> Ibid [LIT.001.0333]

<sup>227</sup> Professor Cash’s letter [SNB.013.2252]

<sup>228</sup> Professor Cash – Day 48, pages 113–114

**30.133** The factors that were most relevant to the issue whether to introduce US tests were clear:

- The anxiety of Professor Bloom and others to limit the risk of HIV transmission.
- The reliability of foreign (US) validations of test systems in the UK.
- The implication of a high rate of false positive results arising from use of the US kits.

**30.134** The DHSS was anxious that all blood transfusion authorities should wait until the results of the evaluation process were available,<sup>229</sup> although the CMO was concerned to monitor what was happening in other countries.<sup>230</sup> Not only was there monitoring of developments elsewhere, there was also pressure being brought to bear concerning the completion of the evaluation exercise.<sup>231</sup> It is also apparent that, during the process, two of the companies whose kits were involved in the evaluation withdrew material in order to replace one or other of the agents originally supplied.<sup>232</sup>

**30.135** At a meeting of the Central Committee for Research and Development in Blood Transfusion on 9 July 1985,<sup>233</sup> Professor Bloom said that, while he appreciated the need for a proper evaluation of the tests, his immediate priority, as a representative of ‘users’, was the protection of recipients of Factor VIII. He therefore considered that any undue delay in introduction of the tests would be unreasonable. That had been his consistent position. Since by July 1985 all Factor VIII used in the UK was heat-treated to exclude transmission of HIV, the specific risk he mentioned had been reduced, although risk remained at the same level for recipients of Factor IX. Recipients of blood transfusions also remained at risk. At the meeting, the state of play was described as follows under the heading ‘Anti-HTLV III Testing in the NBTS’:

The Chairman confirmed that ... [it] was his view ... that until a proper evaluation of the tests had been carried out within PHLS and the BTS the introduction of the tests should not be used for routine screening of blood donations. By not knowing the prevalence of antibodies in the donor population, the BTS was [as] yet unaware of the most effective test especially as far as false positive results were concerned. It was noted that 6000 donor samples were due to be tested at Edgware and Manchester and results would be analysed as the studies continued. Six PHLS laboratories in addition to PHLS Colindale were being set up as reference laboratories.

....

[Name redacted] informed the committee that excess plasma products released onto the market from BPL were likely to require licensing by FDA and, in addition, any intermediates shipped to other manufacturers could also precipitate inspection of BPL’s facilities and the plasma collection centres by FDA in due course. He said that part of the FDA requirement would be routine screening of donations by an FDA approved test for HTLV-III antibody. The Chairman said that it was possible that an FDA approved test was not necessarily the most appropriate for the BTS.<sup>234</sup>

<sup>229</sup> See letter to chairmen of RTDs, 15 March 1985 – DoH copy is to Bristol DHF.001.9430]

<sup>230</sup> Memorandum dated 20 May 1985 [DHF.001.7323] – Screening already introduced in Australia and USA. Compare the earlier (fuller) version at [DHF.001.7239]

<sup>231</sup> Memorandum 31 May 1985 [DHF.002.0119], confirmed by letter the same day [DHF.002.7010]

<sup>232</sup> Memorandum [DHF.002.6784]

<sup>233</sup> Minutes of meeting [DHF.001.7386]

<sup>234</sup> Ibid [DHF.001.7386] at 7389 (name redacted in original)

*Political interest continues*

**30.136** The preference for having a British test evaluated as a possible candidate was referred to in a briefing note for the private office of the Minister of State on 30 May 1985.<sup>235</sup> In a further background note, 'Screening blood donations for HTLV III antibody', the CMO explained the need to evaluate the screening tests:

More than two million blood donations are collected each year and it is clearly essential to ensure that any tests introduced on this scale must be known to give consistent results and be specific and sensitive. Specificity in this context means that a test which does not give rise to an unacceptable number of false positives each of which would require extensive further investigation and would waste the blood donations involved. Sensitivity is also of paramount importance in order that no genuine positives should be missed.

While the commercial products already on sale have been evaluated elsewhere on an individual basis no comparative evaluation is available. This requires that their performance should be compared against a single carefully chosen panel of sera and that the tests should be conducted under controlled conditions. The PHLS are currently conducting such an evaluation. A field trial designed to explore both the specificity of the test and the operational aspects of its routine use throughout the country is also essential. Ease of use and consistency in large scale screening are prime requirements in selecting a suitable product for use in screening blood donations. Laboratory and field evaluations, both undertaken on a large scale, will enable an informed choice to be made and will promote confidence in those kits which are subsequently chosen .... It has been suggested that testing should be introduced immediately, before the reliability of the tests available has been evaluated. Early experience of other countries and the considerations outlined in this note have led Ministers to decide that it would be wrong to introduce a screening test until the further evaluations mentioned above have been carried out.<sup>236</sup>

**30.137** The need to introduce testing was also raised in the House of Commons when, on 27 June 1985, Kenneth Clarke, Minister of State for Health, gave a written reply to a parliamentary question. He stated:

[A] test will be introduced within the next few months to screen all blood given by blood donors for antibodies to the virus which causes AIDS ....

I understand and share the concern to get these tests in use as soon as possible. However, we must have tests which are accurate and can be trusted. A number of test kits are already available and in use abroad, but reports from those countries suggest that the tests are not entirely reliable. We believe that no test should be introduced in the United Kingdom until its reliability has been established. There is no point in introducing a test which often fails to detect antibodies in blood or detects antibodies where there are none. An evaluation programme is being undertaken by the Public Health Laboratory Service and National Blood Transfusion Service experts as a matter of urgency.... Contrary to reports in today's press, no decisions on choice of test kits have yet been made. We hope that we will be able to introduce a test within four to five months.<sup>237</sup>

<sup>235</sup> Briefing note [DHF.002.2283]

<sup>236</sup> Ibid [DHF.001.7376]

<sup>237</sup> Extract from *Hansard* [SGH.002.6798]

**Progress in the summer of 1985**

**30.138** Scottish officials knew of progress over the summer of 1985 as the evaluation process continued. On 8 July 1985, Dr Scott wrote to all Chief Administrative Medical Officers (CAMOs):

As you know the various tests for HTLV III antibodies are being evaluated; in due course routine screening and confirmatory tests will be recommended. It is probable that routine screening of blood donors will begin before the end of this year. Experience elsewhere has shown that in order to prevent people from presenting as blood donors solely to establish their antibody status the provision of alternative screening facilities is essential.

It would be helpful if you would inform the Department of how you propose to provide this facility.<sup>238</sup>

**30.139** On 11 July 1985, the working party of the Regional Transfusion Directors' Committee produced a report on the first phase of the evaluation exercise, entitled 'Screening of blood donations for anti-HTLV-III in regional blood transfusion centres'.<sup>239</sup> It narrated the agreement of the Regional Transfusion Directors' Committee of the NBTS and the SNBTS Directors' committee that routine screening tests for HIV should not be introduced until the following had taken place:

3.1 The proposed evaluation in the N.B.T.S. of different test kits has enabled satisfactory system(s) to be selected.

3.2 The establishment of Reference Centres for the purpose of carrying out nationally agreed confirmatory tests on sera giving positive results upon screening.

3.3 The establishment of alternative venues for anti-HTLV-III tests on members of the General Public who are not blood donors.<sup>240</sup>

**30.140** An amended report on the first phase of the evaluation programme (presented as paper EAGA (5) 6) was tabled by Dr Gunson at the fifth meeting of EAGA held on 30 July 1985, with an amendment to item 3.<sup>241</sup> Paragraphs 3.2 and 3.3 remained unaltered. The preamble, that routine screening tests for HIV should not be introduced until items 3.1 to 3.3 had taken place, was deleted and item 3.1 was amended to read:

3.1 That an evaluation in the N.B.T.S. of different test kits should be performed to enable satisfactory system(s) to be selected.<sup>242</sup>

**30.141** Dr Gunson explained that the working party recognised the pressure to introduce routine screening in the BTS as soon as possible.<sup>243</sup>

**30.142** The revised form of the report, probably reflecting growing concern about the time taken to complete the evaluation, recognised that there was a degree of urgency for the introduction of routine anti-HTLV-III screening of blood donations which precluded the

<sup>238</sup> Dr Scott's letter [PEN.017.0567]

<sup>239</sup> Report [SNB.001.0357]. See also a discussion of the report in Mortimer et al, 'Which anti-HTLV-III/LAV assays for screening and confirmatory testing?', *The Lancet*, October 19 1985; 873-877 [PEN.017.0653]

<sup>240</sup> RTDC Report [SNB.001.0357]

<sup>241</sup> Meeting minutes [SNB.001.0432] at 0435

<sup>242</sup> Revised Report [SNB.004.9046]

<sup>243</sup> Meeting minutes [SNB.001.0432] at 0435

completion of the NBTS second phase evaluation prior to arrangements being undertaken for the introduction of routine screening. The RTDs were being advised, therefore, to make arrangements with their respective Regional Health Authorities for the introduction of routine screening whilst the NBTS evaluation was proceeding, the selection of kits for use being made on the recommendations from the PHLS study. They were advised that long-term contracts with a particular manufacturer should be avoided until the results of the NBTS evaluation were available.<sup>244</sup> It was thought that by this means it might be possible to commence screening of blood donations by October 1985 and it was agreed that the introduction of the tests should take place throughout the UK over the shortest period practicable.<sup>245</sup>

**30.143** Professor Cash thought that the RTDs were concurring with the message that Dr Smithies had brought them.<sup>246</sup> However, there was more substance to the change than that implies. It appears to be reasonably clear that the discussion at the CBLA research committee meeting on 9 July was reflected in the change of emphasis within the report. Following the revised version of the report, the procedure was truncated. The NBTS would continue to evaluate tests but it would be local Directors who would carry out local evaluations and proceed to make arrangements to obtain kits for their regions. The full stage two evaluation was not completed.<sup>247</sup>

### Evaluation first round completed

**30.144** On 30 July 1985, it was announced, by way of a DHSS circular, that the first round of the evaluation was complete.<sup>248</sup> The fifth meeting of EAGA was also held that day and the Group considered the circular (tabled as paper EAGA(5)11) which would be issued to health authorities as a report on the evaluation of the kits.<sup>249</sup> The circular was sent to regional and district managers, scientific officers and medical officers among others. The recommendations from the exercise were attached. A more detailed account of the evaluation was to become available later. It was noted that the NBTS was undertaking its own second stage evaluation covering the aspects of use of the kits particular to the context of blood screening. Confirmatory testing was to take place at PHLS laboratories funded by the Department.<sup>250</sup>

**30.145** The kits had been tested against a panel of sera from unselected blood donors, from groups of patients with AIDS or AIDS-related diseases and from groups of patients in whom false positive results were a possibility. The kits recommended as most suitable for use in diagnostic laboratories were again Vironostika anti-HTLVIII (Organon Teknika Ltd), Wellcozyme anti-HTLVIII (Wellcome Diagnostics) and HTLVIII BioEnza Bead (Ortho Diagnostic Systems Ltd). These kits had provided a clear distinction between positive and negative results, had a low rate of false positives and gave reliable results with heat-treated sera. The later report of the first phase of the evaluation revealed that 220 samples from blood donors were used, as well as samples from those in high risk groups and those thought likely to give rise to false positive results.<sup>251</sup> Wellcozyme anti-HTLVIII

<sup>244</sup> Revised Report [SNB.004.9046]

<sup>245</sup> Ibid [SNB.004.9046] at 9047

<sup>246</sup> Professor Cash – Day 48, pages 140–141

<sup>247</sup> Ibid page 139

<sup>248</sup> Circular letter from DHSS with attached summary of results [SGH.002.6953]

<sup>249</sup> Minutes of meeting [SNB.001.0432] at 0434

<sup>250</sup> Letter dated 1 August 1985 [SGH.002.6967]

<sup>251</sup> Public Health Laboratory Service and Department of Health and Social Security – Evaluation of Five Commercial Anti-HTLV III/LAV Assay Kits [SNB.004.8847] at 8852

and Vironostika anti-HTLVIII were considered to be particularly suitable for use in blood transfusion centres, being easy to use. These kits would be the first to be investigated in the second stage of the evaluation which was designed to investigate performance in large-scale screening of blood donors.

**30.146** The only documentation the Inquiry has in relation to the second part of the evaluation is a draft report about the second phase.<sup>252</sup> It is not clear when this draft was prepared, other than that it post-dates 5 September 1985 (a date referred to in the text). The second phase study at the Manchester and Edgware RTCs covered 6160 samples, using the two kits which had emerged as the leaders after the first phase of the evaluation. Not all of the 6160 samples were actually tested: the breakdown of samples tested at each centre is shown in a table.<sup>253</sup> Given that the document is described as a 'first draft', that it was written in September 1985 at the earliest and that there is no reference to it in the detail of the other information about testing from that time, it does not appear that this material was disseminated to assist Directors in their choice of kit before testing began in October 1985. In essence, the second phase of the evaluation exercise appears to have been truncated and information about it appears not to have been communicated before decisions about purchasing kits were made in the late summer of 1985. This was probably because, in Dr McClelland's words, 'additional delay was not acceptable'.<sup>254</sup>

**30.147** It was clear from Dr McClelland's evidence that, at least in retrospect, he found the evaluation process to have been less rigorous as a result of departure from the full two-phase plan.<sup>255</sup> Although it was not simply a matter of numbers, the quantity of blood donor samples that were included in the first phase was very small, particularly as a basis for conclusions on false positivity. A more robust estimate of false positives would have been provided by the second phase of the evaluation, though it would not have provided information about false negatives. Dr McClelland contrasted the use of tests in a hospital diagnostic context with their use in blood transfusion. The evaluation of a test for use where a patient is ill and there is a need to find out what is wrong was a different exercise from the evaluation of a test for the more problematic matter of scanning a very large part of the population, most of whom could be assumed to be healthy, for the purpose of picking out the very few who were not suitable as blood donors. Evaluation for blood transfusion purposes had been the focus for the second phase and Dr McClelland clearly thought it necessary for a valid decision, although he thought the decision to choose Wellcome was probably right. In the event, the report of the first phase of the evaluation process would prove to be the principal basis on which the candidate tests were identified as suitable for blood donors.

**30.148** Professor Cash was also concerned about the process. He thought that the rate of progress changed with the publication of Professor Bloom's letter to the *BMJ* of 22 June 1985. He expressed reservations about the appropriateness of the evaluations and opined that HIV screening was introduced in the UK without according the priority that he considered proper to the welfare of blood donors.<sup>256</sup>

---

<sup>252</sup> Phase Two Draft Report [DHF.002.9428]

<sup>253</sup> Ibid [DHF.002.9428] at 9442

<sup>254</sup> Dr McClelland's Witness Statement [PEN.017.1337] at 1353

<sup>255</sup> Dr McClelland – Day 50, pages 47–49

<sup>256</sup> Professor Cash's statement [PEN.017.1038] at 1041

### *Media controversy*

**30.149** On the other hand, there was some controversy in the media at that time as to whether the evaluation process had been delayed deliberately in order to allow Wellcome to catch up with the US companies. On 8 August 1985 the *New Scientist* reported the facts noted above: that the UK government had recently approved three AIDS virus test kits for use in diagnostic laboratories and that two, made by Organon and Wellcome Diagnostics, had been chosen to enter the second phase of assessment for daily use at blood transfusion centres in Edgware and Manchester.<sup>257</sup> According to the *New Scientist*, Abbott Laboratories accused the government of delaying approval until a British test was available.

**30.150** Abbott wrote to the editor on the same day to deny that they had made any such accusation.<sup>258</sup> The immediate response of the DHSS was sent out in a briefing note for Ministers dated 16 August.<sup>259</sup> On 22 August 1985 the *New Scientist* published a letter by Dr Tony Napier, Medical Director, Cardiff BTS, defending the policy in respect of the introduction of testing.<sup>260</sup> It was a spirited defence of the official position. As noted at paragraph 30.111 above, Dr Barbara and Dr Hewitt of the BTS at Edgware also wrote to the *New Scientist* on 29 August 1985, to similar effect.<sup>261</sup> A DHSS press release of 23 August 1985 intimated the introduction of testing by mid-October and the availability of new facilities for testing elsewhere.<sup>262</sup>

### **Local evaluation in Scotland**

**30.151** Organon and Wellcome kits became available in Scotland in about July or August 1985 for the purpose of evaluation and choice of kit for routine application and local evaluations followed.<sup>263</sup> In his written statement, Dr Dow explained the technical evaluation by the West of Scotland Blood Transfusion Centre: it performed a 'mini-evaluation' of the two kits recommended after the first phase of the evaluation, the Wellcome Diagnostics Wellcozyme assay and the Organon Diagnostics Vironostika assay.

**30.152** Dr Mitchell's views on the exercise were similar to those of Dr McClelland. He noted that the second phase of the evaluation was on 'a much smaller scale because ... the test materials were not available'. He said:

[A]t that time I think a number of people were saying, 'Look, hallelujah, let's get on, we have got something, let's look at it.' But remember... that the Mortimer study looked at 360-odd samples, which were selected. Some of them were pretty obviously going to be positive, they were known cases of the disease, whereas when you had to scale that up to the point of technical know-how – Mortimer's group was a group of very eminent virologists, who didn't run a blood transfusion centre, didn't run anything to do with blood transfusion.

<sup>257</sup> 'Ministers delayed launch of AIDS test', *New Scientist*, 8 August 1985 [DHF.001.7660]. At the Conference on AIDS in Newcastle in February 1986, it was stated that the evaluation at Edgware and Manchester had revealed several interesting findings but was still to be finalised. [DHF.002.0816] at 0822

<sup>258</sup> Letter dated 8 August 1985 [DHF.001.7659]

<sup>259</sup> Memorandum dated 16 August [DHF.002.0479]. See Preliminary Report paragraph 8.135 for further background material.

<sup>260</sup> Napier, 'Delayed AIDS testing', *New Scientist*, 1985; 55 [DHF.001.7781]

<sup>261</sup> Barbara and Hewitt, 'Delayed AIDS testing', *New Scientist*, 29 August 1985 [DHF.001.7755].

<sup>262</sup> DHSS Press Release [DHF.001.7729]

<sup>263</sup> Dr Mitchell – Day 51, page 40

What they said was good, their evaluation was very thorough, and I don't think we could have done it at that level of virology, molecular virology. But at the same time 300-odd samples did not really add up to mass screening.

And we had to evaluate – they were telling us what to do but we knew how to do it, if you know what I mean.

....

But, in the knowing how to do it, there was a considerable amount of work still needed to be done. We had to do all sorts of things about sample identification, computerisation, all sorts of things. My centre was the first one in the world to have a computer on line to ... test the system.<sup>264</sup>

**30.153** The results of the mini-evaluation favoured the Wellcome kit and it was therefore chosen for use in the west of Scotland. In the event, after the commencement of screening, as explained by Dr Dow, staff in the west experienced 'horrendous problems with plate validation failures'. The test kit was less sensitive than the original (developmental) version which they had evaluated in July 1985.<sup>265</sup> Dr Mitchell commented:

I think, if I remember rightly, the early samples that we got were good, they were fine, and we could detect known positives and known negatives and so on with the small amount we got, but when that was scaled up, then we ran into all sorts of difficulties ... [and] that's an example of where what looks good suddenly goes bad in your hand when you scale it up. You see, a virology department has all the time in the world – I don't mean that literally, but lots of time to look at a thing: Two hours, two days, four days, next week .... That's fine.

....

Blood transfusion has to get this stuff on the shelves this afternoon .... When you start scaling it up and you discover that you have got to repeat your tests over and over and over again on the same day to get any sense out of it – that is that the manufacturer's own controls are working okay as against the samples, to be sure the results are genuine – then you begin to see, 'My goodness, this isn't really fit for purpose at the moment'.<sup>266</sup>

**30.154** In the first few months of testing, the West of Scotland centre also used some Abbott kits, which were provided by Abbott free of charge in the hope that the poor specificity found in earlier studies (and during use for diagnostic purposes in Ruchill Hospital around March/April 1985) had been resolved.<sup>267</sup> In Dr Dow's laboratory, however, the Abbott kit proved less specific than the Wellcome kit and it was not considered suitable as a replacement.<sup>268</sup>

---

<sup>264</sup> Ibid pages 41–2

<sup>265</sup> Dr Dow's Statement [PEN.017.1680] at 1683

<sup>266</sup> Dr Mitchell – Day 51, pages 44–45

<sup>267</sup> Dr Dow's Statement [PEN.017.1680]. There is contemporaneous correspondence referring to evaluation/use at Ruchill: letter dated 11 February 1985 from Abbott Diagnostic Products GmbH to DHSS [DHF.001.9169]. See also confirmation that this was infectious diseases testing: Professor Cash – Day 48, page 95

<sup>268</sup> Dr Dow's Statement [PEN.017.1680] at 1684



**30.155** The third meeting of the EAGA ad hoc working group on evaluation took place on 25 September 1985. The conclusion then, after the further evaluation at Manchester and Edgware, was that both recommended kits were suitable for the routine screening of blood donations<sup>269</sup> although some reservations were expressed about the operation of each.<sup>270</sup>

### Other necessary steps: the ‘magnet effect’ and confirmatory testing

#### *The ‘magnet effect’ and alternative testing sites*

**30.156** There was, as previously noted, some concern about a possible ‘magnet effect’ once screening of blood donors for HIV was introduced. The concern was that individuals who feared that they might have become infected would donate blood simply in order to be tested for HIV. The solution to that anticipated difficulty was to ensure that there were alternative testing sites, where worried individuals could access testing in as straightforward a manner as possible.

**30.157** Dr McClelland described the reasoning behind the requirement for alternative testing facilities:

Our concern was that a lot of individuals would be extremely reluctant to go to the GP.... [W]e had good reason for that concern, and equally other people, you know, might also be reluctant to go to what would then have been called the ‘VD clinic’. It didn’t have a fantastically good image amongst some people.

....

So we wanted to have this completely neutral [facility]. And we wanted to be able to actually publicise it, and ... to disseminate information as widely as possible that this facility was available.<sup>271</sup>

**30.158** He commented further that ‘it was one of our absolute objectives that this should be operating and open for business before we started our donor testing’.<sup>272</sup>

**30.159** Professor Cash had written to Mr John Mutch of the CSA on 26 February 1985, urging him to liaise with his counterparts in Area Health Boards on this issue.<sup>273</sup> This point was discussed at the meeting of EAGA on 30 July 1985.<sup>274</sup> Dr Graham Scott, Deputy Chief Medical Officer (DCMO) in Scotland, had written to the CAMOs on 8 July 1985, asking for details of the arrangements they had made to secure alternative testing sites.<sup>275</sup> That letter referred to an earlier letter of 16 April 1985, copied to all CAMOs, mentioning that ‘Health Boards should consider what facilities should be made available for testing persons other than bona fide blood donors’.<sup>276</sup> Further information about the need for alternative sites and for counselling of those found to be positive was communicated in a letter from Dr Scott to the CAMOs dated 14 August 1985; it was ‘essential’ that the

<sup>269</sup> Organon’s Vironostika indirect ELISA; and Wellcome’s Welcozyme competitive ELISA.

<sup>270</sup> Note of the Third Meeting of the ad hoc Group in the Evaluation of Anti-HTLV III Kits [DHF.002.3976]

<sup>271</sup> Dr McClelland – Day 50, page 57

<sup>272</sup> Ibid page 58

<sup>273</sup> Letter [SGH.002.7266] and enclosure [SGH.002.7267]

<sup>274</sup> Minutes of meeting [SNB.001.0432]. See also: letter of 22 August 1985 from Professor Cash to DHSS [SNB.001.0430]

<sup>275</sup> Letter [PEN.017.0567]

<sup>276</sup> It has not been possible to locate a copy of this letter, although its content can be deduced from the later letter. Details of the research conducted by the Scottish Government on this topic are set out in a letter dated 18 August 2011 from the Scottish Government to the Inquiry [PEN.017.0565]; evidence on the matter was also given by Dr Scott – Day 49, pages 117–124

arrangements made by each Health Board were finalised and publicised before the end of September.<sup>277</sup>

**30.160** The Inquiry also obtained information from Dr Ray Brettle, a retired Consultant Physician at the City Hospital in Edinburgh. Dr Brettle confirmed that his recollection was of the City Hospital Screening Clinic for HIV starting operation in October 1985.<sup>278</sup> The Inquiry asked Dr Mitchell what equivalent facilities existed in Glasgow but Dr Mitchell's recollection was that individuals seeking a test for AIDS at that time would have required to go either to their GP or to one of the specialist clinics (a drug users' or genito-urinary medicine clinic).<sup>279</sup>

**30.161** There was no evidence that the need to establish alternative testing sites delayed the introduction of screening of blood donors. There was some evidence obtained after the commencement of screening that blood donation would indeed have been used by some worried individuals to obtain a test, had there not been other facilities available.<sup>280</sup>

### *Confirmatory testing*

**30.162** Another factor that had the potential to disrupt progress, but was resolved, was the selection of a laboratory for confirmatory testing.

**30.163** Dr McClelland was asked whether it would have been possible to introduce screening without confirmatory testing being available, with the result that donations testing positive on initial screening would be discarded and that there would be no further use of donations from that donor. Dr McClelland explained that, at the time, the view was taken that donors should not be tested without being told and that positive results should be communicated to them. Donors should not, however, be informed that their result was positive unless it was beyond reasonable doubt that a result was a true positive rather than a false positive.<sup>281</sup> In his view, it was necessary to be 'completely upfront and open' with donors about testing<sup>282</sup> and confirmatory testing therefore had to be in place before screening started. That view was common.<sup>283</sup>

### **Adoption of the United Kingdom decision in Scotland and Ministerial approval**

**30.164** This section deals with the process by which Scotland came to follow the UK model in and after January 1985.

**30.165** As noted already, the DHSS had decided that an evaluation of the competing kits for screening of donated blood for AIDS (including any developed in the UK) was necessary, so that the blood transfusion services could be advised as to which tests were most suitable for them.<sup>284</sup> The DHSS submission to Ministers in England and Wales was copied to the SHHD in January 1985. On 7 February 1985, Mr Davies sent a minute dealing with the issue to Dr Scott, DCMO, and copied it to Mr Macpherson, Mr Robertson and Dr McIntyre, colleagues at the SHHD. He wrote:

<sup>277</sup> Letter [SNB.004.9017]

<sup>278</sup> Letter from Dr Ray Brettle to CLO re: City Hospital Screening Clinic for HIV [PEN.017.0682]

<sup>279</sup> Dr Mitchell – Day 51, page 53

<sup>280</sup> Brettle et al, 'HTLV-III antibodies in an Edinburgh clinic', *The Lancet*, 10 May 1986; 1099 [PEN.012.1968]

<sup>281</sup> Dr McClelland's Witness Statement [PEN.017.1337] at 1363

<sup>282</sup> Dr McClelland – Day 50, page 82

<sup>283</sup> See, for example, a DHSS letter to Health Service Managers in England and Wales dated 1 August 1985 [SGH.002.6967] and the DHSS/SHHD booklets published in October 1985, discussed at paragraph 30.196 below.

<sup>284</sup> See letter to all kit manufacturers dated 21 January 85 – an example is [DHF.001.9140]; see also a briefing note dated 21 February 1985 by Professor Cash for the Chairman of EAGA [SNB.001.0162]

DHSS Ministers have now agreed (apparently with great reluctance) that all donations of blood in England should be tested for the presence of antibodies to HTLV-III. We now have to decide whether we have any alternative to advising our Ministers that it is necessary to follow suit in Scotland.<sup>285</sup>

**30.166** He referred to experience to date and outlined the safety procedures already in place. He suggested that donor selection measures being implemented should reduce the number of infected donations, which he said was already 'vanishingly small'. He correctly concluded that people with haemophilia were not at risk, due to heat-treatment of Factor VIII, but perpetuated the misconception – then widely prevalent – that only a small proportion of those with antibodies would develop AIDS, from 10% down to one in several hundred. He proceeded:

Also, as you yourself have said, there is a considerable danger that people considering themselves at risk may attend blood donor sessions specifically for the purpose of having their blood tested.

....

It seems to me that the balance of rational argument would be heavily against introducing a test on all donations. I accept, however, that there is little rationality to be seen where AIDS is concerned .... I should be grateful for your guidance as to what we should tell Ministers.<sup>286</sup>

**30.167** The next day, Dr Scott sent a reply to Mr Davies' minute. He commented:

Testing for HTLV III antibodies is technically different from testing for hepatitis B antigen. In addition, the test is much more expensive as well as being seriously unreliable. Until a test which identifies the virus itself is available matters will remain unsatisfactory.

From a cold objective scientific viewpoint the case for the introduction of a test for HTLV III antibodies in the present state of development and without being properly validated is not clear cut .... It is most unfortunate that a policy decision on this matter was not made at a UK level, though understandable given the degree of public and media hysteria.

It would be helpful if we could have an office meeting to discuss our advice to Ministers. It is for consideration whether Dr Cash ... might also be invited to the office meeting; if he strongly advocated introducing the test despite its limitations the Minister would be open to criticism if he did not agree to the introduction of the test.<sup>287</sup>

**30.168** Mr Macpherson also replied to Mr Davies' minute.<sup>288</sup> He took a more pragmatic line: if England introduced the test, it would be difficult for Scotland not to introduce screening. Although he accepted the validity of Mr Davies's comments, he thought that the pressure to follow the English example and introduce testing would be irresistible.

---

<sup>285</sup> Minute [SGH.002.7295]

<sup>286</sup> Ibid [SGH.002.7295]

<sup>287</sup> Minute [SGH.002.7294]

<sup>288</sup> Minute [SGH.002.7293]

**30.169** On 21 January 1985, Dr Bell of the SHHD gave his response to the DHSS submission. Although the matter was for the SNBTS, Dr Bell apparently envisaged that Scotland would follow the same approach as the rest of the UK.<sup>289</sup> Dr Bell was well informed of developments in England and it is implicit in his letter that the real issue for Scotland, although the matter was for the SNBTS, was which test method would be adopted in Scotland.

**30.170** In oral evidence, Dr Scott agreed with the suggestion that the tone of Mr Davies' minute suggested that he was not terribly sympathetic to the idea of introducing screening. He commented, however, that if it were to go ahead, finance was not going to be a problem: that had been cleared.<sup>290</sup> At the Inquiry's Oral Hearings it was noted that, at the date of the letter, Factor IX was not heat-treated and that, therefore, Haemophilia B patients remained at risk. Dr Scott was unable to comment on Mr Davies' state of knowledge at the time.<sup>291</sup>

**30.171** The Regional Transfusion Directors met on 23 January and 18 February 1985. Dr Smithies and Mr Williams attended after the close of business at the reconvened meeting on 18 February and provided unspecified information on testing.<sup>292</sup>

### *Scottish evaluation*

**30.172** Within the SNBTS, it was agreed at a meeting of the Co-ordinating Group on 19 February 1985 that no Transfusion Centre in Scotland would commence routine donation testing for HIV unilaterally under any circumstances, whatever pressures might be applied. It was hoped that there would be a Ministerial statement to the effect that testing would not be introduced for blood donations until the tests were likely to yield more accurate results.<sup>293</sup> The decision was noted at the meeting of SNBTS Directors which followed on 27 February 1985.<sup>294</sup>

**30.173** Abbott kits were available for evaluation in March 1985. At a meeting between the SNBTS Directors, Haemophilia Directors and the SHHD on 7 March 1985 dealing with AIDS, including heat treatment, Dr McClelland reported on plans for the new US screening tests for HIV antibodies to be evaluated on a UK basis.<sup>295</sup> He reported that, at that stage, there was deep concern about reports indicating a high proportion of false positive tests in the trials carried out in the US. The Inquiry has not found evidence of marketing of test kits as early as March 1985: rather, test kits were available in small numbers for evaluation purposes only. Abbott kits were used, and evaluated in use, in virology laboratories in Glasgow and Edinburgh as a start to providing an HIV testing service, not as a blood donor screening service.

**30.174** The concern in Scotland, and the rest of the UK, about the high incidence of false positive results was in marked contrast to the position in the USA, already noted, which was tolerant of false positive results in those early US test systems.

<sup>289</sup> Minute [SGH.002.7301]

<sup>290</sup> Dr Scott – Day 49, page 132

<sup>291</sup> Ibid pages 132–133

<sup>292</sup> Minutes of meeting [SNB.011.1971] at 1976–78

<sup>293</sup> Ibid [SNB.003.9171] at 9177

<sup>294</sup> Minutes of meeting [SNB.002.3507] at 3509

<sup>295</sup> Minutes of meeting [SNF.001.0241] at 0242

**30.175** Some in the SHHD continued to have reservations as to the necessity for blood donor screening: a draft memorandum of 21 February 1985<sup>296</sup> suggesting that policy in Scotland should avoid the early introduction of testing became a final recommendation to that effect on 21 March 1985, when the office meeting proposed on 8 February 1985 took place. In respect of tests, the revised memorandum noted:

Tests are becoming commercially available for the screening of blood donations for the presence of HTLV III antibodies. The first of these tests, from the USA, was marketed in the UK at the beginning of March. DHSS Ministers have agreed in principle that, in England, all blood donations should be screened and that Regional Health Authorities should meet the cost of this. Regional Blood Transfusion Directors throughout the UK have written to the *Lancet* ... strongly supporting the screening of all blood donors, but advising that such a screening programme should be delayed until the available test systems have been evaluated and until alternative testing facilities are made available to individuals who may be at high risk of transmitting AIDS.

We consider these views of the Transfusion Directors to be sensible and responsible, and support them, particularly in the Scottish context ....

The tests becoming available from United States companies are likely to give a high rate of false positive results – maybe 4%. On that basis about 10,000 ... Scottish blood donors could be identified as having antibodies to HTLV III who are in fact quite free of them. The implications for the individuals concerned, and for the resources required for further testing and counselling, would be profound and substantial. The tests also have an unpredictable false negative rate, so that an infected person might not be identified; and since the test is for antibody and not antigen it will not in any case identify a person who has been infected with the antigen but not yet developed antibodies.<sup>297</sup>

**30.176** The submission, which discussed the possibility of making AIDS a notifiable disease as well as the introduction of screening of blood donations, went to Scottish Ministers on 21 March 1985. A copy of the Transfusion Directors' letter in *The Lancet* was attached and their recommendation of an evaluation process and the establishment of alternative testing facilities as pre-conditions for the introduction of screening was highlighted and supported. The perceived drawbacks of testing were mentioned: false positive results, with consequent effects on donors and needless loss of donations, false negative results, cost and the 'magnet effect' (discussed at paragraphs 30.156–30.161 above and paragraph 30.194 below). The recommendation was that a phased policy leading to routine screening should be pursued, taking into account the results of the evaluation, the need for alternative testing facilities and the requirement for additional testing and counselling of donors.

**30.177** Mr John Mackay's private secretary responded by telex on 22 March 1985.<sup>298</sup> Mr Mackay, at that time the Scottish Health Minister,<sup>299</sup> fully appreciated the logic of the advice, especially that 'at risk' men might use the transfusion service as a screen. The recommendation of alternative testing sites was 'essential'. He observed that Scotland had to keep in line with, or ahead of, England to avoid severe criticism.

<sup>296</sup> Draft memorandum [SGH.002.7282]

<sup>297</sup> Revised memorandum [SGH.002.7226] at 7227–78

<sup>298</sup> Telex of 22 March 1985 [SGH.002.7225]

<sup>299</sup> Under-Secretary of State for Scotland with responsibility for Health and Social Work.

**30.178** The views of George Younger, Secretary of State for Scotland, followed on 26 March 1985: the Secretary of State also 'agreed the recommendation'<sup>300</sup> and a decision in principle to proceed with screening had been reached by this point, in March 1985.<sup>301</sup>

**30.179** In Oral Hearings, it was suggested to Dr Scott that the advice to Ministers reflected a lack of urgency regarding the introduction of screening on the part of the SHHD at this time. Dr Scott did not accept that proposition.<sup>302</sup> Scottish Ministers took the view that screening should be introduced as Mr Mackay's telex had indicated.

**30.180** At this stage, the CMO for Scotland was, in Dr Scott's term, an 'absentee landlord', often away from Scotland on business for the World Health Organization at which times Dr Scott acted on his behalf. It therefore fell to Dr Scott to follow up the Ministers' decisions. It was Dr Scott's view that it would not have been correct to introduce a screening test before it had been evaluated, because of the risk of false results among other things.<sup>303</sup> As noted above, on 16 April 1985 he wrote to all CAMOs commenting that health boards should consider what facilities should be made available for testing persons 'other than bona fide blood donors'.<sup>304</sup> Implementation, as in England, was seen as a matter for the local health authorities.

**30.181** On 28 June 1985, the SNBTS Directors again discussed the introduction of testing for HTLV-III antibody.<sup>305</sup> Dr Gunson had been invited to attend the meeting and he described the operation of the UK trial of FDA-licensed kits in his own Centre and at Edgware.<sup>306</sup> The kits to be made available for routine screening would be selected from those currently on trial. Dr Gunson agreed to notify Professor Cash in due course which were the likely tests and the Scottish Directors could choose, if they wished, to evaluate them in their own Centres. The Directors acknowledged the need to choose a screening methodology suited to each Centre. It was agreed that the reference centres for confirmatory testing for Scotland would be the laboratories of Professor Morag Timbury (Glasgow) and Professor Gerald Collee (Edinburgh).<sup>307</sup>

**30.182** Dr Gunson explained the work of EAGA, which had established working parties on the counselling of donors and on HTLV-III antibody testing.<sup>308</sup> It had been concluded that a test could be considered positive if it was still so after initial screening, re-testing by the same technique, a test of a sample from the donation itself<sup>309</sup> and after further testing by the reference laboratories.

**30.183** There was discussion of the issue of informing donors. It was agreed that:

[D]onors should be informed that their donations would be HTLV-III [antibody] tested and should indicate by signing they had understood this.

[T]he first contact (counselling) of all confirmed antibody positive donors would be the BTS medical staff.

<sup>300</sup> Telex of 26 March 1985 [SGH.002.7224]

<sup>301</sup> Dr Scott – Day 49, page 117

<sup>302</sup> Ibid page 143

<sup>303</sup> Dr Scott's Witness Statement [PEN.017.0513] at 0514

<sup>304</sup> The Inquiry has not recovered this letter. See a letter from Dr Scott to Chief Administrative Medical Officers in which he refers to his earlier letter dated 16 April 1985 [PEN.017.0567]

<sup>305</sup> Minutes of meeting [SGF.001.0203]

<sup>306</sup> Ibid Item 3 (d) ii. [SGF.001.0203] at 0205

<sup>307</sup> Ibid Item 3 (d) v. [SGF.001.0203] at 0206

<sup>308</sup> Ibid Item 3 (d) vi. [SGF.001.0203] at 0206

<sup>309</sup> Presumably a fresh sample from the donation to exclude the risk that there may have been contamination of the test sample.

That BTS doctors would use their best efforts to encourage donors to agree that their GPs/ dentists be informed by BTS of their positive [antibody] status.

That BTS medical staff would ensure the establishment of appropriate counselling and medical follow up of [positive] donors.

The BTS would take steps to track the recipients of [antibody] positive blood products produced at RTC's by informing the consultant responsible for the care of the patient. All subsequent actions would be determined by the clinician.<sup>310</sup>

**30.184** Dr Gunson wished to see an agreed SNBTS approach so that he could table it for discussion at the next meeting of the NBTS Directors.

**30.185** It was agreed that the ideal would be to retain donor samples as long as possible. Professor Cash was investigating the matter of a central library of samples for Scotland; meantime, all samples would be retained pending the introduction of testing.<sup>311</sup>

**30.186** Finally, a system for Scotland for laboratory reporting of HTLV-III positive antibody tests would be agreed with the Communicable Disease (Scotland) Unit.

**30.187** Practical arrangements to introduce screening and to deal with the associated issues were then made.<sup>312</sup> On 2 August 1985, Professor Cash sent a letter to all Directors, setting out a very detailed summary of the issues and a 'countdown' to testing.<sup>313</sup> The detail of arrangements was canvassed in evidence with Dr McClelland, who described Professor Cash's letter of 2 August 1985 as 'very good briefing'.<sup>314</sup>

**30.188** Professor Cash noted the need to plan for the introduction of screening and advised that the target should be to introduce testing slowly, on a selective basis and at a low level of activity in the later weeks of September, so that the move to full screening in early October would be an operationally smooth exercise.<sup>315</sup> He advised that initial contracts for supplies of kits should be short-term, in order to give flexibility to change suppliers if that should prove necessary. He also encouraged the use of both available kits with a view to obtaining advantage in price negotiations and set out a range of practical guidance for implementing testing. It was a comprehensive briefing, while leaving decisions open for individual Directors in respect of their own regions. On 7 August 1985, Dr McClelland assigned tasks to staff; there was a staff meeting on 19 August 1985 to discuss implementation; and there was a decision to commence routine testing on 23 September 1985.<sup>316</sup>

**30.189** Meantime, Dr Scott had received copies of the DHSS documents and distributed them to the CAMOs and to Professor Cash on 6 August 1985.<sup>317</sup> For confirmatory testing in Scotland, Dr John Peutherer in Edinburgh would handle Southeast (Edinburgh), East (Dundee) and Northeast Scotland (Aberdeen), and Dr Edward Follett in Ruchill would handle Glasgow and Inverness.<sup>318</sup>

<sup>310</sup> Minutes of Meeting: Item 3 (d) vi. [SGF.001.0203] at 0206

<sup>311</sup> Ibid Item 3 (d) vii. [SGF.001.0203] at 0207

<sup>312</sup> As reported in the minute to Mr MacKay dated 20 September 1985 [SGF.001.0831]

<sup>313</sup> Professor Cash's letter to Directors [SGH.002.6977] This is a letter to Dr Whitrow, Director of the Inverness BTS, but Dr McClelland said in his statement [PEN.017.1337] at 1354 and in evidence that Professor Cash had written in these terms to all Directors.

<sup>314</sup> Dr McClelland – Day 50, page 53

<sup>315</sup> Letter [SGH.002.6977]

<sup>316</sup> Witness Statement of Dr McClelland [PEN.017.1337] at 1354; HTLV III Testing – Countdown – List of responsibilities [PEN.012.1949]; Preparation for introduction of HTLV-III AB screening meeting [PEN.012.1950].

<sup>317</sup> Letter [SGH.002.6982]

<sup>318</sup> Dr McClelland – Day 50, page 68

**30.190** On 14 August 1985, Dr Scott again wrote to CAMOs and to Community Medicine Specialists with an up-to-date report on progress.<sup>319</sup> To achieve screening of blood donations from mid-October, it was said to be essential that alternative testing facilities should be in place by the end of September. The letter noted that genito-urinary/STD clinics had relevant experience and would be suitable facilities but that there was also a need to provide for those who did not regard themselves as appropriate clients for such clinics. He advised that GPs had to know the local arrangements and that courses were available for training at St Mary's Hospital in London. Attached to the letter were copies of the guidelines produced by the DHSS Expert Advisory Group on AIDS. There was also reference to further advice yet to be circulated. Dr Scott commented that there would be an opportunity for general discussion at the meeting of the CAMOs and the CMO to be held on 4 September 1985.

**30.191** A scoping exercise was carried out on 19 and 20 August 1985 by a group from Edinburgh and by the Transfusion Directors' Co-ordinating Group.<sup>320</sup> There was to be an evaluation of the Organon and Wellcome kits before selection; the NBTS information on false positive results would be reviewed; and it was noted that there was no commitment to having a single kit for use by the SNBTS. After completion of the evaluation, the SNBTS would move directly to testing incoming donation samples. The practical start date of 23 September 1985, before the official start date in October, was confirmed.<sup>321</sup>

**30.192** In the South-East BTS region, proposals for the study of alternative venues for screening were submitted for grant on 18 September 1985, as a pilot for other health boards.<sup>322</sup> It appears that the work was already well advanced, since the clinic required was in operation at the Infectious Diseases Unit at the City Hospital, Edinburgh before the commencement of routine screening by South East BTS.<sup>323</sup>

**30.193** On 20 September 1985 Mr Liddle of the SHHD distributed a minute on AIDS to Scottish Ministers and to senior colleagues, including the CMO, the Director of the Prison Service and the Director of the Scottish Information Office. The purpose of the minute was to provide an update on Mr Macpherson's minute of 21 March and Mr Davies' minute of 28 June. It noted:

The testing of blood for the detection of HTLV-III antibody, whether by the NHS or by the Blood Transfusion Service is to commence in mid-October and we have impressed on Health Boards the importance of adequate publicity being given to the facilities available outside the Blood Transfusion Service. However, there is a likelihood of a Ministerial Statement ....<sup>324</sup>

**30.194** The decision had been taken. The commercially available test kits had been evaluated by a panel of experts from the PHLS and a summary of the results had been made available to health boards. Confirmatory testing of positive donations was in hand. A start date of mid-October had been fixed.<sup>325</sup> In addition:

<sup>319</sup> Letter [SNB.004.9017]

<sup>320</sup> Minutes of meeting: preparation for introduction of HTLV-III AB screening [PEN.012.1950]

<sup>321</sup> Dr McClelland's Witness Statement [PEN.017.1337] at 1353. The SNBTS sought to ensure that all stocks of blood and blood products had been tested before the official start date – see paragraph 30.191 above and 30.204 below.

<sup>322</sup> Proposal for self referral facility for HTLV-III testing – letter from Dr DBL McClelland to Dr A McIntyre [PEN.012.1956]

<sup>323</sup> Letter from Dr Ray Brettle to CLO re: City Hospital Screening Clinic for HIV [PEN.017.0682]; Dr McClelland's Witness Statement [PEN.017.1337] at 1357 paragraph 29

<sup>324</sup> Minute to Mr MacKay [SGF.001.0831] at 0832–3

<sup>325</sup> Ibid [SGF.001.0831]; 'Countering the Spread of AIDS in Scotland' [SGH.002.7072]



- The cost of confirmatory testing was being met through the Advisory Group on New Developments in Health care; health boards were to absorb the cost of screening facilities but the 1985–86 revenue allocation for the SNBTS had been increased by £322,000 to provide for the purchase of screening test kits.
- Steps were to be taken to provide NHS facilities to protect the SNBTS from the ‘magnet effect’.
- Counselling was to be provided.

**30.195** Wellcome were in a position to provide kits to allow routine donor testing at Ruchill in mid-September 1985. The West of Scotland BTS had problems with plate validation failures, as already noted at paragraph 30.153. It was apparent that the production kit was less sensitive than the original (developmental) batch tested in July 1985. The report of the results of field tests of the kits in England and Wales also produced mixed results.<sup>326</sup> Scottish scientists managed to overcome these validation difficulties, for which Wellcome were grateful.<sup>327</sup>

### *Final preparations*

**30.196** A press release on 1 October 1985 announced the screening of all UK blood donations from mid-October 1985 and emphasised how important it was that those who believed themselves at risk refrain from donating blood simply in order to be tested.<sup>328</sup> The DHSS published a booklet, distributed on 1 October 1985, containing information for doctors concerning the introduction of the HIV antibody test.<sup>329</sup>

**30.197** The covering letter, signed by Dr Donald Acheson, CMO, emphasised the continuing need for exclusion of high risk donors, noting that even a reliable test could not detect early infections to which antibodies had not yet been generated.<sup>330</sup> The booklet stated that the tests were being introduced routinely to screen all blood donations. Donors were to be informed that the test was being done and would be asked to agree before blood was taken. It was explained that the tests introduced had been the subject of careful evaluation by the PHLS and the NBTS.<sup>331</sup>

**30.198** Blood testing positive would not be used for transfusion. The blood was to be re-tested and a sample sent to a Reference Laboratory for testing by ‘another test method’. On confirmation by this procedure, the donor was to be contacted and called in for discussion and counselling. The booklet emphasised that counselling had to be careful: it was still thought that not all those who seroconverted would progress to AIDS and that there would be less serious outcomes for many, although all who seroconverted had to be considered capable of transmitting the disease through sexual contact or through transfusion or inoculation of blood. A further blood sample would be taken for confirmatory testing. The risks of false positives and false negatives were highlighted but fully confirmed positive tests were to be followed by an offer of full clinical evaluation. Doctors were told of possible clinical signs and symptoms.<sup>332</sup>

<sup>326</sup> ‘An Evaluation of Anti-HTLV III Test Kits in the National Blood Transfusion Service’ – Report of the Results on the First and Second Test Kits [DHF.002.9428]

<sup>327</sup> Dr Dow’s Witness Statement [PEN.017.1680] at 1683; Professor Cash – Day 48, page 68

<sup>328</sup> Press release [SGH.002.7099]

<sup>329</sup> Covering letter dated 1 October 1985 and a copy of the booklet [SGH.002.7091]

<sup>330</sup> Ibid [SGH.002.7091] at 7092

<sup>331</sup> Ibid [SGH.002.7091] at 7093

<sup>332</sup> Ibid [SGH.002.7091] at 7093-94

**30.199** The booklet reflected the general perception of the disease at the time: seropositive patients were likely to react badly to confirmation that they were infected with HIV. Quite apart from longer-term prognoses, life patterns would be affected immediately and the risk of adverse reactions from the public and employers was also anticipated. The booklet prescribed procedures for the collection and laboratory testing of samples and for the protection of health workers. It also dealt with confidentiality:

The strictest confidentiality must be maintained when an HTLV III antibody positive individual is identified. Where a person is tested for HTLV III infection or for its complications and it is thought to have been sexually transmitted, health authorities have an obligation to maintain confidentiality of information under the terms of the National Health Service (Venereal Diseases) Regulations 1974 (SI 1974.9). Unless the patient has given his consent, personal health data relating to him must not be disclosed to anyone for any purpose other than the health care of that patient, except where the disclosure is necessary to prevent the spread of infection. Disclosure of this information for purposes other than medical or public health reasons could lead to serious consequences for the informant. Adequate safeguards to protect individuals against unauthorised disclosure must be adopted.<sup>333</sup>

**30.200** Appendix 1 of the booklet dealt with 'Laboratory Investigations'. Appendix 2 dealt with 'Guidance to individuals on measures to control the spread of HTLV III'.

**30.201** The booklet was adapted for use in Scotland.<sup>334</sup> It noted the arrangements made by the SNBTS for screening and the alternative testing facilities available through GUM and STD clinics. As in the case of the English booklet, it outlined the procedures to be followed with positive donations and advised caution in the light of the risk of false positive results. The importance of alternative facilities to prevent people donating blood simply to determine their antibody status was set out. There was a warning of the risk of false negative results arising from the 'window-period' phenomenon of HIV infection. The need for counselling was emphasised.

**30.202** Copies of the booklet, and a 'dear doctor' letter to accompany it, were sent to CAMOs on 1 October 1985 for distribution.<sup>335</sup> The 'dear doctor' letter emphasised the essential elements in the proposals, the need for synchronous provision of alternative arrangements, the need for counselling and the need for very strict confidentiality.<sup>336</sup>

**30.203** The two booklets provided reasonably comprehensive information for GPs and other doctors likely to have to deal with the problems of AIDS.

### *Screening begins*

**30.204** Testing was introduced officially on 14 October 1985, although the SNBTS began testing donations before the official date. In the South East Scotland region testing began on 23 September 1985. There and throughout Scotland, all blood in stock (both the SNBTS stock and that already distributed throughout the NHS) was tested before the official start date.<sup>337</sup> McClelland explained to the Inquiry that testing began slightly early

<sup>333</sup> Ibid [SGH.002.7091] at 7095

<sup>334</sup> Scottish booklet – 'Acquired Immune Deficiency Syndrome – AIDS – Booklet 2 – Information For Doctors Concerning the Introduction of the HTLV III Antibody Test' [SGH.002.7081]

<sup>335</sup> Covering Letter [SGH.002.7079]

<sup>336</sup> Letter [SGH.002.7080]

<sup>337</sup> Dr McClelland – Day 50, pages 51–52; Letter from Professor Cash to Dr McIntyre, SHHD, dated 28 October 1985 [SNB.005.8091]

in this manner, in order that all blood in stock could be said to have been tested by 14 October 1985.<sup>338</sup>

**30.205** On 2 October 1985, the SNBTS Directors, with the exception of Dr Mitchell, who was ill, met.<sup>339</sup> All four regions represented had chosen the Wellcome test; the minutes do not record which test had been chosen in the West area.<sup>340</sup> It was noted that the Wellcome test might be subject to substantial variations between batches. Dr Mitchell was to evaluate the Abbott test in the West, subject to Dr Gunson supplying the material and DHSS authority being obtained. The BTS staff had attended counselling courses. At the PFC, all finished product and plasma was being screened.<sup>341</sup>

### *Post-screening surveillance*

**30.206** On 7 February 1986 there was a meeting at NIBSC on the Virological Aspects of the Safety of Blood Products.<sup>342</sup> The various test kits available and their performance were discussed, as was the experience of screening blood donations so far.<sup>343</sup> Thirteen donations out of more than 600,000 tested had been confirmed to be positive, an incidence of one in 46,000 donations, which was very low in international terms.<sup>344</sup>

**30.207** In a Parliamentary answer on 12 December 1986, Tony Newton, a junior Minister in the DHSS, said:

No cases of HIV transmission through blood transfusion have been reported since testing was introduced. Although there is as yet no corresponding test for new strains, there is no evidence from preliminary monitoring to suggest that these are prevalent in the United Kingdom. Thus there is no reason to believe that blood supplies are at risk from this source although we are keeping the matter under close review.<sup>345</sup>

**30.208** Mr Newton explained that the safety of the blood supply in the UK was maintained by (i) those who may have been exposed to known particular risks of infection being asked not to donate blood and (ii) testing of all donations.<sup>346</sup>

**30.209** The effectiveness of screening came into focus again in January 1987. On 5 January 1987 Miss P A Cox of the SHHD sent a note to the Minister of State and others including Dr Covell, commenting on press coverage of a leukaemia patient in Glasgow who was found to have HIV following a blood transfusion in August 1986.<sup>347</sup> Miss Cox said that the DHSS had been informed of the infected donation, that no Ministerial statement was recommended and that any further information should come from Professor Cash. The incident resulted from viral transmission from an HIV infected patient in the 'window' between infection and the appearance of antibodies in his blood.

<sup>338</sup> Dr McClelland – Day 50, pages 51–52

<sup>339</sup> Minutes [SGH.001.6412]

<sup>340</sup> As reflected in paragraph 30.210 below, the west area would select the Wellcome test also.

<sup>341</sup> Minutes [SGH.001.6412] at 6413–14

<sup>342</sup> Minutes [SNB.005.1495]

<sup>343</sup> *Ibid* [SNB.005.1495] at 1505

<sup>344</sup> AIDS Conference Newcastle – 11th–13th February 1986 [DHF.002.0816] at 0826

<sup>345</sup> *Hansard* extract [SGH.002.7370]

<sup>346</sup> *Ibid* [SGH.002.7370]

<sup>347</sup> Note [SGF.001.1246]

**30.210** Although the data extend beyond the current period, it is worth noting at this stage that the Wellcome HIV test became very effective after its initial teething troubles.<sup>348</sup> In the period from October 1985 to about the end of 1986, 176,149 tests were carried out by West of Scotland BTS on donations in their area using the Wellcome test. The results were:

**Table 30.1: Donations referred for confirmation by West of Scotland BTS**

Number of Donations Tested	176,149	Oct 1985-end 1986
Initial Screen Positive (Manufacturer's Protocol)	73	0.040%
Repeat Reactive	31	0.017%
Confirmed HIV-positive	6	0.003%

**30.211** Twenty-five of the 31 repeat reactive results were false positives. Data on use of the HIV tests on blood donors since 1986 showed that around 99% of repeat reactivities were false positives. During the first few months of testing, the Abbott HIV test was used sporadically (with fewer than 5000 tests used). In the West of Scotland, the Abbott test proved less specific than the Wellcome test: around 30 repeat reactive samples (all false) were referred after testing for a short period of time.<sup>349</sup>

## Discussion

### *The need for local evaluation of US pharmaceutical companies test systems*

**30.212** As noted above, concern grew in 1985 that the UK evaluation exercise was delaying progress and some haemophilia experts proposed that at least one US test system should be introduced without full evaluation having been completed. In the event, however, no witness at the Inquiry's Oral Hearings or in providing a written statement disputed the necessity of an evaluation exercise. Professor Cash,<sup>350</sup> Dr McClelland,<sup>351</sup> Dr Mitchell,<sup>352</sup> Dr Scott<sup>353</sup> and Dr Iain Macdonald<sup>354</sup> (DCMOs for Scotland) and Dr Archibald McIntyre (SHHD)<sup>355</sup> all considered that it was necessary to assess how kits, developed in another part of the world, functioned when used to test donors in the UK. As set out in paragraph 30.45, it was recognised internationally that it was for each country to assess the risk AIDS posed to its population and to establish, among other things, appropriate testing systems. Local evaluation was clearly justified.

**30.213** There was contemporaneous material illustrating the commitment to evaluation. Professor Zuckerman in January 1985 supported the introduction of US tests as soon as practicable but not before his own studies were complete: a clear practical demonstration of the principle that there should be local evaluation before the use of the tests in practice. Similarly, Professor Bloom was an enthusiastic supporter of the introduction of US tests

<sup>348</sup> Dr Dow's Witness Statement [PEN.017.1680] at 1684

<sup>349</sup> Ibid [PEN.017.1680] at 1684

<sup>350</sup> Professor Cash – Day 48, pages 43–44 and 130 – to buy a kit and start testing would be 'ethically unacceptable'. See also Professor Cash's letter of 12 February 1985 to the CMO [SNB.013.2233] – most of the emerging commercial kits seemed to have a false positivity rate which was 'embarrassingly high'.

<sup>351</sup> Day 50, page 39

<sup>352</sup> Day 51, pages 55–56

<sup>353</sup> Day 49, page 102

<sup>354</sup> Dr Macdonald's Statement [PEN.017.0559] at 0561

<sup>355</sup> Day 51, pages 58–59; Dr McIntyre's statement [PEN.017.0552]

in the early part of the year but, on 9 July 1985 at a meeting of the Central Committee for Research and Development in Blood Transfusion, acknowledged the need for a proper evaluation of the tests. The Chairman, Dr Gunson, expressed the view that until a proper evaluation of the available tests had been carried out within the PHLS and the BTS the tests should not be used for routine screening of blood donations.<sup>356</sup>

**30.214** The risk of false positive results in the routine use of the available US test systems was a significant issue at least until August 1985.<sup>357</sup> This was a substantial issue affecting donors and the blood transfusion services. In addition, the deficiencies in the US test kits (in particular the lack of uniformity and comparability among the several manufacturers' tests due to inconsistencies in the test sera provided) undermined the reliability of the results. It would not have been responsible to have introduced test kits manufactured in the US without evaluation in the UK.

**30.215** Most other experts were consistently in favour of evaluation. The EAGA ad hoc Expert Working Group was set up to design and possibly oversee the technical evaluation project. Professor Tedder commented that field trials were required and he expected the MH/CB assay to be subjected to evaluation. On the evidence as a whole, evaluation was clearly a necessary step to provide assurance of the acceptability of any test for application in the UK and in Scotland in particular. Timing, and in particular whether the process became excessively protracted, remains a contentious issue.

#### *The timing of an evaluation exercise*

**30.216** It seems clear that, in the circumstances of the development of HIV test kits, the evaluation of any given test kit, whether by a regulatory body or by the manufacturer, involved at least two stages: (i) the progressive testing of prototypes until the manufacturer was in a position to proceed to full-scale marketing and (ii) the validation of the kit supplied for routine application as conforming to the specification and level of performance developed by prototype testing. Marketing would be impossible without the conventional set of claims having been exposed to evaluation and found to be consistent with the evaluation results. However, the issue whether to proceed to marketing was squarely one for the manufacturers. There was no regulatory control in the UK, though manufacturers had a clear indication of the likely attitude of the UK health authorities. The letter of 21 January 1985 sent to producers intimated that information would be required at the evaluation stage to substantiate claims made for the product.<sup>358</sup> The views of the health departments would be likely to affect market perceptions. There was no obstacle, however, to submitting kits for evaluation: Abbott were able to do so before they were able to meet market demand in the autumn of 1985. What was required was enough material to meet the requirements of the body carrying out the evaluation. Abbott duly began the process.

**30.217** Although not selected for the second stage UK evaluation exercise, Abbott was originally the principal candidate as supplier of US systems in Scotland. The West of Scotland BTS in particular had a long association with the company. In the period following the general introduction of testing, using the selected Organon and Wellcome test systems, Abbott kits were obtained to carry out the continuing evaluation of that system in comparison with Wellcome's system. It appears to be a reasonable inference

<sup>356</sup> Minutes [PEN.016.1142] at 1145

<sup>357</sup> When, approximately, the second generation Abbott and Organon tests, which were probably better than the original kits, became available.

<sup>358</sup> A copy of one such letter is [DHF.001.9140]

from what happened in fact that obtaining an alternative supply of US test kits in Scotland would have depended on Abbott, at least in 1985, when the choice of system was a live issue. As indicated in paragraphs 30.151–30.153, Dr Dow’s ‘mini-evaluation’ of the Organon and Wellcome test systems favoured Wellcome’s and, as between Wellcome’s kit and Abbott, the Abbott kit proved less specific than the Wellcome kit.

**30.218** Lack of specificity had been the issue with Abbott’s test kit since the company had entered into arrangements with British evaluators in February 1985 to carry out clinical trials of small quantities of the Abbott HTLV-III EIA Diagnostic test kit at the Regional Virus Laboratory at Ruchill, the North London Blood Transfusion Centre, Edgware, and Middlesex Hospital.<sup>359</sup> Dr Dow obtained Abbott kits for evaluation in the spring of 1985. If the company had obtained the support it sought from these contractual trials, there was no regulatory impediment to their introduction in the UK market. The company was unable to satisfy the FDA until March 1985 that the kit should be licensed in the US and it was found that there were problems of poor specificity with the first kits supplied for evaluation in Scotland.<sup>360</sup>

**30.219** It is apparent that Abbott’s problems had not been resolved when Dr Dow’s mini-evaluation began and had still not been finally resolved when Wellcome’s Wellcozyme test emerged as the favoured test system. As Dr Dow commented, the Wellcozyme test was British, appeared to be more robust and was user-friendly.<sup>361</sup> It was demonstrated by the evidence that evaluation of available US pharmaceutical companies’ kits from the spring of 1985 showed an unacceptable lack of specificity and that, when improved Abbott kits became available for comparison with the Organon and Wellcome test systems, the original problems had not been resolved so as to be competitive. In the circumstances, timing of the evaluation of imported kits is not a live issue. By the time acceptable kits became available, Wellcozyme was proven in evaluation.

### *Priorities in risk assessment in the United States*

**30.220** Policy makers and transfusion practitioners in the UK emphasised the need to protect donors from risks associated with test system that produced high percentages of false positive results. The comparative positions in the United Kingdom and the United States of America have been set out in paragraphs 30.41–30.47 in discussing the need for local evaluation of imported products. As noted in those paragraphs, it had been commented as early as 1985 in the paper *Blood Policy and Technology* (paragraphs 30.12–30.17) that the US approach subordinated the interests of donors to those of recipients, a position unacceptable in a public sector transfusion service.

### *Timing of routine screening*

**30.221** Specificity was a substantial issue affecting donors and the blood transfusion organisation and resolving it was critical to progress towards routine screening. There were, however, other factors that required time to deal with.

**30.222** Dr Dow discussed the practical issues that arose from the introduction of ELISA testing.<sup>362</sup> Completely new washing and reading equipment was required. A spectrophotometer was required. Trained staff, working space, pipetting equipment,

<sup>359</sup> Letter from Abbott to DHSS dated 11 February 1985 [DHF.001.9169]

<sup>360</sup> Dr Dow’s Witness Statement [PEN.017.1680]

<sup>361</sup> Ibid [PEN.017.1680]

<sup>362</sup> Ibid [PEN.017.1680] at 1681–82

timers and incubators were required to perform the tests. Staff had been accustomed to RIA technology (in Scotland largely through use of Abbott Diagnostics Ausria-II HBsAg test) since 1975 and the introduction of ELISA technology required re-training. Similar considerations had been behind the NBTS preference for RIA technology at the early stages of development of the MH/CB assay. It is difficult for the Inquiry to put a value on the work involved in carrying the changes into effect but the impression given was that it was not inconsiderable. On any view it was a factor that had to be dealt with relative to the test system selected for routine use. The preparations were set out in Professor Cash's letter dated 2 August 1985 (paragraph 30.187). The work was put in hand and there is no basis in the evidence for criticism of the rate of progress thereafter towards full implementation of routine screening.

### **Availability of US test kits in 1985**

**30.223** In the circumstances, the ability of commercial companies to supply the needs of the UK, and in particular Scotland, for test kits for routine use is a secondary matter, although it is not wholly irrelevant. Abbott's intention to supply the European demand from Delkenheim, Germany was delayed: their factory there did not begin to supply kits until the autumn of 1985. Abbott's test appears to have been approved for use in France on 24 July 1985.<sup>363</sup> How the official position evolved in France is unclear.<sup>364</sup> A WHO publication indicates that a 'surveillance scheme' was commenced there in July 1985.<sup>365</sup> While that was in progress, routine screening for antibodies to HIV was officially implemented in August 1985.<sup>366</sup> It appears that approval for use of the Abbott kit was granted before surveillance was begun and before routine screening became official policy. Whatever the regulatory position, it appears to be clear that, from approval in July 1985 until Delkenheim began production, Abbott could only have supplied France from Chicago and that Chicago did not have enough kits to satisfy domestic demand until mid-July 1985.<sup>367</sup> To provide kits for France, Abbott had to modify its method of cloning H-9. That was achieved in mid-July 1985 and supplies to France began a week later.<sup>368</sup> It is not possible to form a view whether Abbott could have supplied the UK, and Scotland in particular, on a commercial basis before the opening of Delkenheim but it is reasonably clear that supplies could not have come on-line before late July 1985 and only then if they could have been shipped from Chicago at that time.

**30.224** Dr Dow's evidence is conclusive as to availability of Abbott kits in Scotland from about July 1985. His mini-evaluation in July 1985 was restricted by the shortage of supplies of kits for evaluation. Fewer than 5000 kits were supplied for the continuing evaluation of Abbott's system until the selection of Wellcome's system was finally decided in West of Scotland. On the evidence available to the Inquiry, there was not a sufficient supply of Abbott kits to suggest that the company could have met Scottish market demand for general use for screening of blood for transfusion before the first phase of evaluation was complete.

<sup>363</sup> Crewdson, J. *Science Fictions* [PEN.017.1057] at 1067

<sup>364</sup> *Ibid* [PEN.017.1057] at 1066–67

<sup>365</sup> Habibi, B. 'Summary of Experience in France Regarding Screening and Confirmatory Tests', in Petriciani et al (eds), *AIDS The Safety of Blood And Blood Products* (World Health Organisation) [LIT.001.5536]

<sup>366</sup> The evidence of Professor Cash – Day 48, page 185 – that routine screening was introduced in France in about May 1985 appears to have been wrong.

<sup>367</sup> Crewdson, J. *Science Fictions* [PEN.017.1057] at 1068

<sup>368</sup> *Ibid* [PEN.017.1057] at 1067

*Delay caused by or contributed to by administrative decisions***The United Kingdom position**

**30.225** In an Inquiry such as this it was inevitable that there would be questions as to whether the administrative process caused or contributed to delay in the implementation of routine screening for HIV. The resolution of issues surrounding the decisions of UK Ministers and Departments relative to the use of test kits in England and Wales is not within the competence of this Inquiry. It is not a 'Scottish matter', a matter that relates to Scotland and is not a reserved matter. In addition, at a practical level, decisions taken in England could not have been investigated fully in the absence of representation of the Department of Health. Dr Smithies, a central figure over the material period, did not feel able to assist the Inquiry.<sup>369</sup> It appears, further, that either not all of the discussions at the time were recorded or the Inquiry does not have all of the relevant records (paragraph 30.103).

**30.226** That apart, it is clear that, at the time, the introduction of HIV testing was not treated as a UK policy issue. Dr Scott's minute of 8 February 1985 (paragraph 30.167) expressed regret that a policy decision on testing had not been taken at a UK level. Whether his regret was appropriate is immaterial: the minute reflected the reality that Scottish transfusion policy on this matter was the sole responsibility of Scottish Ministers and their SHHD advisers.

**The Scottish position**

**30.227** Before discussing the role of Scottish officials and Ministers, it is important to recall the overall time-frame for the critical discussions and decisions. The announcement of the isolation of HTLV-III by Dr Gallo's team, and their prototype ELISA to screen blood, on 23 April 1984, included Ms Heckler's prediction that a test to screen the blood supply with 100% certainty would become widely available within six months. There was, in fact, no test available for marketing until early March 1985. Continuing problems with lack of specificity postponed the date at which an effective screening test was available from Abbott until late July 1985 (if one accepts the approval of the kit by French authorities on 24 July as a reliable indicator that the test had achieved a level of specificity acceptable to France). The MH/CB research test was in use from 4 July 1984 and the Cheingsong-Popov article on 1 September 1984 showed that the test was highly specific: there were almost no false positives. Following scale-up, and the resolution of production problems, the CAMR Porton antigen came on-line in late spring 1985. The MH/CB project was not government controlled: it was a private sector commercial project. Kits were in Dr Dow's hands for testing in July/August 1985.

**30.228** Progress in developing test kits, in the USA and in England, was rapid. In England, it was driven by Professor Weiss and Professor Tedder. The UK Government was informed of progress, albeit to a limited extent. The scope for Scottish Government agencies to influence the rate of development was limited. Realistically, it was in the hands of those with commercial interests in the success of their products.

**30.229** However, whether or not to introduce screening in Scotland was plainly a Scottish matter. The SHHD elected to follow the lead of the DHSS in relation to evaluation. A joint approach to resolving issues relating to the introduction of screening is not obviously inappropriate. A number of specifically Scottish issues arise, however:

<sup>369</sup> Response from Patrick Hennessy at the Department of Health (on behalf of Dr Alison Smithies) dated 01 April 2011 [PEN.017.0504]



- Whether Scottish officials and advisers were fully integrated into the process so as to be able to represent Scottish interests and positions.
- Whether the information Scottish officials and advisers had was adequate to enable them to assess Scottish interests.
- Whether factors that materially affected the process were of equal weight throughout the UK, or differed in weight so that a separate outcome for Scottish practice would have been possible or appropriate.
- Whether purely Scottish factors could or should have resulted in earlier introduction of screening in Scotland than in the rest of the UK.

### Participation of Scottish officials and experts

**30.230** From a purely Scottish point of view, specifically the view of the SNBTS, it was unfortunate that the very experienced team at the West of Scotland BTS did not have the opportunity to participate in the initial field tests of kits proposed at the meeting on 28 June 1984 referred to in Dr McClelland's oral evidence. It was envisaged that the results would influence practice throughout the UK. There is nothing to indicate, however, that if they had participated the outcome would have been different and Scottish experts were involved in oversight of the process.

**30.231** From early 1985, the EAGA was the most influential advisory group dealing with matters relating to HIV/AIDS. Professor Cash and Dr McClelland were members and Dr McClelland was also a member of the sub-group set up to consider screening tests. Dr McClelland was an active contributor to the work of EAGA and its sub-group. He and Dr Gunson were responsible for the design of the programme for the evaluation of test kits. The discussion and amendment of the proposals at the meeting of the sub-group on 1 March 1985 supported a laboratory assessment of the kits followed by a large scale field assessment. The scale of the main evaluation (10,000 specimens) and the sub-division of specimens into aliquots sufficient to ensure that all kits could be tested at the PHLS, leaving sufficient specimens for evaluation tests in the proposed second phase of the exercise, were developed in discussion to which Dr McClelland was party.<sup>370</sup>

**30.232** Professor Cash was critical of the approach adopted by the DHSS to the evaluation programme, in his written statement and in the course of his oral evidence.<sup>371</sup> Professor Cash's comments do not help to answer the question whether the information Scottish officials and advisers had was adequate to enable them to assess Scottish interests. Apart from other considerations, he accepted that there were never enough test kits available to do what he wanted, a fact which he came to appreciate.<sup>372</sup>

**30.233** That there were limited supplies of test kits was clear from the evidence of Dr Mitchell and Dr Dow. Dr Dow's work was directly affected. Much of Professor Cash's argument about the relative efficiency of a NBTS/SNBTS evaluation fails in light of the evidence about supplies.

---

<sup>370</sup> Meeting minutes [SNB.001.0172] at 0172-73

<sup>371</sup> Professor Cash's Witness Statement [PEN.017.1038] at 1041

<sup>372</sup> Professor Cash – Day 48, page 43. See footnote 215 of this chapter, above.

**30.234** The first phase of the evaluation, involving 220 samples, seems to have taken about four to four and a half months to the end of July 1985<sup>373</sup> and the extensive field study stage was never carried out as an integrated exercise. There was an extensive evaluation in Manchester and Edgware and other transfusion centres carried out tests to inform the selection of kits. There is a need to consider whether there were factors relevant to Scotland that indicated that Scotland could and should have taken an independent approach. There may have been factors that materially affected the process that were not of equal weight throughout the UK, or differed in weight so that a separate outcome for Scottish practice would have been appropriate.

**30.235** The possibility of a Scottish evaluation exercise was mooted at the start of 1985. The Scottish Transfusion Directors decided to take action themselves. Professor Cash intimated the decision to all Scottish RTDs and to Dr Bell.<sup>374</sup> There was a clear will at that stage to proceed independently in Scotland.

**30.236** That proposal was stopped by Dr McIntyre, SHHD and by the discussions that followed his intervention. Professor Cash's evidence was clearly to the effect that the proposed Scottish evaluation in West of Scotland could have led to earlier screening in Scotland. From the evidence of Dr Dow and Dr Mitchell, however, it appears that there would have been problems in obtaining kits in sufficient numbers to carry out an evaluation of the scale required to provide reliable data, as already noted. Not only would it have been necessary to get access to all of the relevant US kits, it would have been necessary to have access to the MH/CB assay. Professor Weiss, Professor Tedder and Wellcome all had interests in aspects of that assay as developed for further use. Scottish attempts to become involved in work with Professor Weiss and Professor Tedder were not successful. It is not apparent how access to their material could have been obtained otherwise. Without that, any Scottish evaluation would have been seriously deficient. In the event, the proposal was probably stopped to maintain the concord with the UK Department of Health. However, in substance, without satisfactory evidence that an evaluation of appropriate scale could have been undertaken, all that one is left with is Dr Mitchell's evidence that West of Scotland was well placed to do the work in terms of skill and experience and that pride was hurt by being denied the opportunity.

**30.237** There is a theoretical possibility that, had there been an independent Scottish evaluation and had it produced reliable findings, cases of infection might have been prevented. The necessary hypothesis for that, however, includes so many elements that the possibility becomes vanishingly small as they are applied sequentially. Scotland did not have the necessary containment facilities. Timing is an issue; the availability of test kits to complete the project is an issue; availability of commercial kits on the market to meet the demand of the treating centre is an issue; and the risk of false negatives compounds the difficulties as a whole. Further, the wide range of issues around dealing with donors had not been addressed, in the UK as a whole or in Scotland in particular, by this time. So far as the SNBTS was concerned, the need for decisions on these matters had been identified in Dr McClelland's paper of 15 May 1985. It was necessary for these issues to be dealt with before screening began. Professor Cash's view that routine screening could have been introduced earlier in Scotland than in the United Kingdom as a whole is not supported by the evidence as a whole. It is also difficult to reconcile with the views of Dr McClelland and Dr Mitchell.

---

<sup>373</sup> Discussion with Professor Cash left the period uncertain – Day 48, pages 104–105.

<sup>374</sup> Letter to Dr Mitchell copied to Transfusion Directors and Dr Bell [SNB.005.9713]

**Concern about delay**

**30.238** It was evident to the Inquiry that, from the beginning of 1985, there was anxiety about when testing of donated blood for the AIDS virus would be introduced in the UK. Haemophilia doctors, and Professor Bloom in particular, were anxious that US test kits should be introduced as soon as they became available. His letter of 31 May 1985 put concern for haemophilia patients and patients undergoing surgery above other interests, including those of donors, and proposed that re-testing and confirmatory testing and donor counselling should be left over to be dealt with as separate issues.<sup>375</sup> Professor Bloom's concern at the delay, as he saw it, is understandable: he represented a particular and specific interest. The same can be said of the letter sent by Professor Bloom, Dr Forbes and Dr Rizza to the *BMJ* in June 1985 to advocate the rapid introduction of screening for HTLV-III antibody of all blood donations, particularly since three commercial test kits had been approved by the FDA by that date. It also referred to the risk to patients with haemophilia of using cryoprecipitate or unheated blood products and also to the risk to patients undergoing blood transfusion.<sup>376</sup>

**30.239** Although the June 1985 letter was said to be written on behalf of the Haemophilia Reference Centre Directors throughout the UK, the situation for patients with haemophilia in England and Wales was more difficult than in Scotland at that time. NHS heat-treated Factor VIII and Factor IX products were not in routine issue in England and Wales and the only heat-treated products available were commercial. Patients in Scotland had the benefit of heat-treated Factor VIII products produced by the PFC from December 1984 and would have heat-treated Factor IX from October 1985.

**30.240** On the other side of the debate, transfusion doctors had concerns about whether the tests being developed in the USA were sensitive and specific enough for large-scale screening in the UK. Again, the topic was discussed in terms of the whole of the UK. Professor Cash raised some of these issues in his letter to *The Lancet* published in March 1985 and signed by all of the Scottish Regional Directors and most of the English Reference Centre Directors.<sup>377</sup> It recorded the authors' belief that commercial testing kits were likely to give high rates of false positive results. They contended that careful consideration should therefore be given before such kits were introduced for the screening of blood donors in the UK, both for the benefit of the blood supply and for the sake of the donors themselves. The contemporaneous letter from physicians in California also highlighted the danger of missing positive samples if the cut-off value for a positive sample was set too high.<sup>378</sup> The views of the Transfusion Directors were strongly expressed and, in view of the differing policy positions adopted at the time in the US, presented a more acceptable position for the UK in general, and Scotland in particular, relative to the need for evaluation.

**30.241** The March 1985 letter represented Professor Cash's point of view at the time. That view was also reflected in his unpublished response to the letter sent by Professor Bloom, Dr Forbes and Dr Rizza, published in the *BMJ* in June 1985.

<sup>375</sup> Letter from Professor Bloom to DHSS re: introduction of FDA-approved tests [DHF.002.5510]

<sup>376</sup> Bloom et al, 'HTLV-III Haemophilia and Blood Transfusion', *British Medical Journal*, 22 June 1985 [LIT.001.0333]

<sup>377</sup> Ala et al, 'HTLV-III Antibody in Sequential Plasma Samples from Haemophiliacs 1974-84', *The Lancet*, 2 March 1985 [LIT.001.0374] at 0375

<sup>378</sup> Carlson et al 'HTLV-III Antibody Screening of Blood Bank Donors', *The Lancet*, 2 March 1985 [LIT.001.0374]

**30.242** Professor Cash's evidence on these matters suggests that in his view, at mid-1985, the introduction of testing should have been postponed. There may be some attraction in the argument: in an ideal world one would cross all the 't's and dot all the 'i's before proceeding. That would have added to delay, however, and it is inconceivable that such a suggestion would have been acceptable against the background of growing pressure for testing to be introduced.

*Abandoning the second phase of evaluation*

**30.243** Pressure to introduce screening increased over the summer of 1985. The events are set out in the Preliminary Report at paragraphs 8.130–133 and in the paragraphs above. The Transfusion Directors themselves, in their Working Party advising on screening, concluded that the evaluation of the kits in the Blood Transfusion Service should take place but that it was not possible to complete that evaluation prior to arrangements being undertaken for the introduction of screening.<sup>379</sup>

**30.244** The second phase, which was the field study in transfusion centres, was truncated and information about it does not appear to have been available to Directors when they made their final preparations for screening, including their choice of kits. So, all that was available was the information from the first phase, which (as far as blood donors were concerned) only involved 220 samples.

**30.245** The evidence of Professor Cash, Dr Mitchell and Dr McClelland, though differently expressed, was to the effect that the second phase was an important element in the evaluation process and that abandonment of it weakened its reliability. That must be so, if the original decision was valid and more than a laboratory test with local evaluation was required for confidence in the selected test systems.

**30.246** However, the exercise that took most time, and was the principal cause of any potentially unacceptable delay that may have occurred, was the CAMR laboratory process. The perception of EAGA at the time (as expressed by the Chairman, Dr Acheson) was that the exercise had been carried out with expedition.<sup>380</sup> Professor Cash and Dr McClelland were both present at the EAGA meeting on 30 July 1985, as was Dr Covell. This was an important meeting concerned with progress towards the local evaluation of the two selected kits, among other topics. The Inquiry has not uncovered contemporaneous evidence of complaints that the CAMR exercise had not been carried out with the speed appropriate for a virological evaluation of the sensitivity required. Professor Tedder was also at the meeting on 30 July 1985. He had an opportunity to protest if progress with the production contract had been affected by delay caused by the Phase 1 evaluation. From the minute of the meeting it is not possible to identify any critical comment relating to the time taken.

**30.247** If the first phase of the exercise was required in any event, local evaluation, whether a requirement of the original specification or not, would have followed. There was no unnecessary delay in Scotland and no delay overall. Whether a different approach, perhaps involving virologists with transfusion expertise, as advocated by Professor Cash, could have been carried out more expeditiously involves considerable speculation as to who would have been engaged, how much time would have been required and whether the exercise would have succeeded. In his letter to Professor Cash dated 7 August 1984,

---

<sup>379</sup> First Version of Report [SNB.001.0357] plus corrigendum [DHF.001.7532]

<sup>380</sup> Minutes of Meeting [SNB.001.0432] at 0434

Dr McClelland noted one significant problem: it was highly unlikely that there was a facility in Scotland that could have undertaken the work of producing significant quantities of HIV antigen.<sup>381</sup>

**30.248** Further, the change of direction does seem explicable. In January 1985 it was probably not anticipated that the first phase of evaluation would take the four to four and a half months it did and by the summer the landscape was different: new 'editions' of the tests were coming on-line with assured increased effectiveness. Screening had become even more urgent and the idea of completing and reporting on the field evaluation had to be abandoned.

**30.249** So, in short, it appears not unreasonable to have decided in January 1985 to assess all available kits in an attempt to guide transfusion services as to which to purchase. Even if it was unreasonable, the alternative of simply buying whatever US kits could be obtained as soon as they were available and starting with them would have led to other problems. If it had been decided to take that alternative approach, a sufficient supply of test kits would not have been available until the end of July 1985. Further, the false positive issue would not have been avoided.

**30.250** More significant, perhaps, is to consider what would have happened had the UK simply begun routine testing as soon as Abbott kits were licensed in the United States and were available for marketing abroad. This would have been after late July 1985 at the earliest. Undoubtedly, if they had been first generation kits, similar sorts of problems to those which occurred in the US would have ensued, given the problems with the H9 cell line discussed above. The alternative policy, of awaiting the development of improved kits before acting, would have been open to serious criticism: until improved kits were actually developed and tested, it would have required an article of faith to promote a testing strategy on the hypothesis that they would necessarily appear.

**30.251** The Inquiry has not found reliable evidence of (i) what happened with the Electro-Nucleonics kit, which was assessed in the UK evaluation and which was approved in the US only days after Abbott, or (ii) what kits were used in the other countries which started screening early, such as Australia. There cannot have been insurmountable supply problems in these other countries unless they had developed their own test systems. Even if the Electro-Nucleonics kit had been available and used in the UK, however, it would also have suffered from the 'H9 problem' and therefore liability to false positive results, because it too was manufactured from the HTLV-III<sub>B</sub> isolate.

### *Other questions*

**30.252** One further question is material: the necessity for kits to have the approval of the FDA for use in the USA before introducing them for screening of blood in Scotland. Dr Lane suggested in July 1985 that this was necessary for BTS marketing purposes. That would not have been relevant in Scotland, however, as, in terms of the chronology set out, the FDA approval was granted before any kits were introduced for screening in Scotland. More generally, the decision that local evaluation was necessary implied that the FDA approval was not conclusive of the suitability of kits for screening in Scotland or the UK more generally.

---

<sup>381</sup> Dr McClelland's letter to Professor Cash [SNB.006.5977]

**30.253** Further, it was considered that, as Dr Smithies put it, such a stipulation might not act in Wellcome's interests. It would not have been in the best interests of any UK manufacturer to have imposed on top of the requirements of UK evaluation a requirement to satisfy the FDA under a regulatory system that had no direct applicability in the UK. On any view that would have exposed the domestic product to two separate evaluation processes and, in the case of the FDA's procedures, at least a risk of significant delay.

**30.254** In addition, there were serious concerns about the US process that had been applied in 1985 in evaluating the systems for use in the US, in particular about the provision of different sera samples to each manufacturer, undermining the comparisons that could usefully be made among test results. It would not have been possible to be confident that the FDA's assessment of any UK-produced test system would have been on an equal basis with the earlier exercise: there was no reference panel of samples against which to test that.

**30.255** In short, subjecting UK products to a need for approval of the FDA before introducing them for use in Scotland would not have been a rational exercise of judgment by any UK or Scottish Government agency.

## Conclusions

**30.256** The production of screening tests for antibodies to HIV in 1984 and 1985 involved research and development work, in the USA, in France and in England, that was carried out with remarkable expedition and commendable success.

**30.257** In the UK generally, and in Scotland in particular, the role of government agencies in relation to HIV research is best understood as that of interested spectators as private sector institutions proceeded to build on earlier research in investigating human retroviruses and to develop (i) an independent British HIV isolate and (ii) a unique anti-HIV assay, conceptually distinct from US models, using proprietary systems and methodology which were commercially confidential generally and in part protected by patents.

**30.258** Suggestions that UK BTS researchers, and in particular SNBTS researchers, could have made more rapid progress with evaluation of an acceptable assay than was achieved by private sector researchers are without foundation. Scotland, in particular, had no laboratory with containment facilities sufficient for the safe handling of live HIV and, in addition, the MH/CB assay was proprietary and information about it was not made available to Scottish scientists when it was requested. The DHSS-sponsored first phase evaluation was the best public sector process available. If progress had depended on the public sector bodies involved, the criticism of the patient core participants that they represented 'a startlingly diverse and unstructured collection'<sup>382</sup> might have been relevant, though variety is not necessarily adverse to progress. The criticism is, however, without substance.

**30.259** Progress towards implementation of screening was not inhibited by the involvement of government agencies, largely because those who had commercial interests to promote pursued solutions independently and succeeded in producing marketable products on a commercial basis that enabled policies on the introduction of screening to be implemented as soon as was practicable.

---

<sup>382</sup> Closing Submission – Patient interests [PEN.019.0552] at 0555

**30.260** The UK Government had an interest in the development of a UK test which government agencies were keen to promote. This could have delayed implementation of routine screening if imported products of acceptable quality had been available in appropriate quantities to meet UK market demand before British commercial products were available. In the event that did not happen. Though truncated in the end, the evaluation programmes applied equally to all manufacturers.

**30.261** By the date of implementation of routine screening, imported products had not matched British commercial products in terms of specificity.

**30.262** There is no legitimate ground for criticism of the processes adopted for the introduction of anti-HIV screening that can be founded on delay. It was achieved as soon as was reasonably practicable. In any evaluation exercise, carried out in such circumstances, a tension is likely to exist between the exigencies of full scientific rigour and the need for progress.

## CHAPTER 31

### THE INTRODUCTION OF SCREENING OF DONATED BLOOD FOR HEPATITIS C

#### Introduction

**31.1** This chapter concerns the introduction of screening for antibodies to the Hepatitis C virus (HCV) in the blood donor population in Scotland. It will follow the progress towards and up to the introduction of UK-wide screening on 1 September 1991.

**31.2** The relevant period began when the Chiron Corporation of California announced in May 1988 that it had isolated and cloned a protein of the blood-borne non-A, non-B Hepatitis (NANB Hepatitis) virus. At the same time, Chiron was working to develop and release tests to detect antibodies to the virus, which in time became known, as the Hepatitis C virus. First generation tests were made available to other parties from 1989. The availability of antibody test kits opened the way for scientists such as virologists and transfusionists to assess and try to understand the tests and to gauge their value and usefulness in screening blood donations quickly, effectively and accurately, and counselling potentially large numbers of donors. Developing knowledge provided policy makers and their advisers, at government and institutional levels, with information required to formulate and implement policies on the introduction of screening. This chapter will discuss the chronological development of government policy by examining the work of the government's in-house advisers and independent advisory committees.

**31.3** The introduction of screening for antibodies to HCV (anti-HCV) was initially examined in Chapter 9 of the Preliminary Report in paragraphs 9.87 to 9.291. Since that section was written, the Inquiry has examined more written documentation on this topic and gathered more information on the background to screening, as well as heard a great deal of oral evidence. This chapter will therefore set out a fuller and more focused account of the introduction of screening than was possible in the Preliminary Report.

#### Hearings of evidence

**31.4** The interval between the availability of tests for the Hepatitis C virus in 1989 and the introduction of screening of donated blood for the virus in the United Kingdom in September 1991 was identified as a topic requiring to be considered at the Oral Hearings of the Inquiry.

**31.5** All the witnesses who gave evidence to the Inquiry on the topic, in writing or at Oral Hearings, were asked to consider a standard list of questions.<sup>1</sup> The standard list of questions was accompanied by an 'extended narrative'. This consisted of the paragraphs of the Preliminary Report from 9.247 to 9.283, with insertions to reflect material discovered after publication of that report.<sup>2</sup>

#### Chiron's breakthrough in May 1988

**31.6** The factual background to Chiron's discovery, and its role in defining the aetiology of Hepatitis C, are narrated in Chapter 16, *Knowledge of Viral Hepatitis 3 – 1986 Onwards*. In the initial announcement of the discovery on 10 May 1988, it was stated that Chiron had

---

<sup>1</sup> Schedule of questions for witnesses [PEN.017.2159]

<sup>2</sup> Extended narrative [PEN.017.2165]



developed a prototype immunoassay that might lead to a screening test for non-A, non-B Hepatitis virus antibodies.<sup>3</sup> In this chapter there is further discussion of the development and marketing of Chiron's assay, but it is appropriate first to set the scene with a brief summary of the developing picture.

**31.7** Chiron claimed that its research team had discovered 'a long-sought blood-borne hepatitis non-A non-B virus', not *the* virus that caused NANB Hepatitis, implicitly acknowledging the understanding at that time that there might be other causes of NANB Hepatitis. The development of immuno-diagnostic products for screening for NANB Hepatitis antibodies was advertised as a possibility, though it was emphasised that Ortho Diagnostic Systems, a subsidiary of Johnson & Johnson, would market any products which were developed.<sup>4</sup> The proprietary claims for intellectual property rights in and derived from the discovery were intimated at the outset. Some parts of the press release were more concerned with marketing than scientific accuracy.<sup>5</sup> Typically, the information published was less than explicit in disclosing the science underlying the discovery.

**31.8** The Chiron research team had not isolated and cloned the whole virus. Later research would show that the significant entity that had been identified, and specifically targeted by the tests tentatively announced by Chiron at this stage, was limited to one of the proteins of the virus, identified as the NS4 protein.<sup>6</sup> Not all genetic types of HCV have NS4 proteins. Limitations on the usefulness of a potential Ortho test related to this characteristic were noted as discussion of the adoption of the test progressed, and would emerge in practice when it first became available. In the meantime, however, Chiron's press release was optimistic in tone and the claim of the effectiveness of the proposed test was broad.

**31.9** In explaining briefly how the test would be used, the press release stated:

[B]lood banks will be able to apply a relatively simple assay procedure, using a plate coated with the virus protein, to screen for blood infected with hepatitis non-A, non-B virus. Antibodies from the infected blood bind to the plate, which is then rinsed – if the antibodies are present, a second coating of indicator antibodies will signal a color.<sup>7</sup>

**31.10** Just over a week after the initial announcement, on 19 May 1988, a shorter article containing similar information appeared in the journal *Nature*.<sup>8</sup> The journalist who wrote the piece in *Nature* appears to have drawn on the Chiron press release as source material.

**31.11** The announcement of the Chiron research was repeated in the journal of the American Association of Blood Banks (AABB), *Blood Bank Week*, dated 13 May 1988.<sup>9</sup> The comments published were cautious, reflecting a degree of scepticism in the absence of scientific details.

<sup>3</sup> Chiron press release [PEN.016.0290]

<sup>4</sup> Ibid [PEN.016.0290] emphasis added

<sup>5</sup> Dr Dow – Day 67, page 87

<sup>6</sup> Chapter 16, *Knowledge of Viral Hepatitis 3 – 1986 Onwards*, paragraph 16.31

<sup>7</sup> Chiron press release [PEN.016.0290] at 0292

<sup>8</sup> 'Candidate cause identified of non-A, non-B hepatitis', *Nature*, Vol 133, 19 May 1988 [SGH.002.8036]

<sup>9</sup> See Chapter 16, *Knowledge of Viral Hepatitis 3 – 1986 Onwards*, paragraph 16.18

**31.12** The *Blood Bank Week* article gave further details of the test kit that was in development:

Chiron Corp. of Emeryville, CA, is submitting a screening test (ELISA) to detect antibodies to the viral particles, to the Food and Drug Administration for approval. The test, if approved, could prevent patients from receiving infected blood and help reduce the amount of blood discarded, possibly eliminating the need for the surrogate tests currently used, ALT and anti-HBc.<sup>10</sup>

**31.13** This information indicated a change of direction. Dr Brian Dow commented that when Chiron isolated their protein clone they used a radio immuno-assay (RIA) and reported on that in various papers in 1989, but it was never marketed.<sup>11</sup> Instead, the test was developed as the enzyme-linked immuno-assay (ELISA), which Ortho proceeded to market, as anticipated in the article.

**31.14** The *Blood Bank Week* article became a topic for discussion at the SNBTS Directors meeting on 14 June 1988. It was noted that Ortho Diagnostic Systems would soon market an ELISA test for NANB antibody. It was agreed that Professor John Cash would contact Ortho to enquire about the availability of the test in the UK.<sup>12</sup>

**31.15** Scientific details of the discovery were not released until April 1989 when two articles were published in the journal *Science*. The first article described the isolation by Chiron of a cloned protein derived from NANB Hepatitis.<sup>13</sup> The second, published in the same edition, gave details of the specific screening test developed to detect antibodies to the NANB Hepatitis virus that Chiron had discovered.<sup>14</sup> How that was achieved is described in Chapter 16; *Knowledge of Viral Hepatitis 3 – 1986 Onwards*, paragraphs 16.22–16.26. The Choo article in *Science* designated the hepatitis virus isolated by Chiron as ‘hepatitis C’ or ‘HCV’ and identified it as a major cause of both community-acquired and post-transfusion NANB Hepatitis, while recognising that other agents might be involved in transmitting NANB Hepatitis.<sup>15</sup>

### Professor Cash contacts Ortho

**31.16** On 5 July 1988, Professor Cash wrote to Dr Ginger Rosenberg of Chiron in the USA, asking for access, in due course, to some of their kits for SNBTS to evaluate.<sup>16</sup>

**31.17** On the same date, Professor Cash also wrote to Ortho in England seeking confirmation that Ortho would be marketing the recently announced Chiron kit. In addition, he asked when the kit would be marketed in the UK for full donation testing.<sup>17</sup>

<sup>10</sup> ‘Hepatitis Non-A, Non-B Discovered’, *Blood Bank Week*, 13 May 1988 [SNB.002.4411]

<sup>11</sup> Day 67, page 93: see Kuo et al below, [PEN.017.2764]. RIA was used by the Houghton team in the research phase leading to the announcement of the discovery

<sup>12</sup> Minutes of SNBTS Directors Meeting, 14 June 1988 [SNB.002.7333] at 7337

<sup>13</sup> Choo, et al, ‘Isolation of a cDNA Clone Derived from a Blood-Borne Non-A, Non-B Viral Hepatitis Genome’, *Science*, 1989; 244:359–362 [LIT.001.0629]

<sup>14</sup> Kuo, et al, ‘An Assay for Circulating Antibodies to a Major Etiological Virus of Human Non-A, Non-B Hepatitis’, *Science*, 1989; 244:362–364 [PEN.017.2764]

<sup>15</sup> The need for a ‘type C’ hepatitis virus or viruses had been postulated by Feinstone and others in 1973: Chapter 14, *Knowledge of Viral Hepatitis 1*, paragraphs 14.64–14.68

<sup>16</sup> Letter [SNB.008.3584]

<sup>17</sup> Letter [SNB.008.3585]

**31.18** Mr Follett, of Ortho UK, replied to Professor Cash on 19 July:

Ortho ... do have an agreement with Chiron to develop and market the product but I do not know precisely when this product will be available. The best information I have been able to obtain is that the product may be available towards the end of 1989.<sup>18</sup>

**31.19** Mr Follett emphasised that there was a great deal of work to do regarding manufacturing and trials before the product would be available. There was a noticeable gap of time between the Ortho letter to Professor Cash of July 1988 and the suggested availability of the test in late 1989. While 12 months to develop an assay might appear to be quite a long time, Dr Dow commented in oral evidence that it probably takes longer nowadays to develop something into a useable assay that can be launched commercially.<sup>19</sup> In the event, Ortho had supplies of its first generation ELISA available for sale for 'in vitro diagnostic use' at the end of November 1989, as forecast.<sup>20</sup>

### **UK Health Departments<sup>21</sup> discussion of need for a new advisory group, July 1988**

**31.20** When Chiron made its announcement in May 1988, the United Kingdom Government did not have an advisory body competent to provide an assessment of the possible value of the American research, and in particular of the usefulness of the ELISA test in screening blood donors, as an aid to informing policy.

**31.21** Early in 1988 Dr Harold Gunson (Consultant Advisor to the Blood Transfusion Service in England and Wales)<sup>22</sup> had discussed with Dr Brian McClelland (SNBTS Regional Director, Edinburgh and SE Scotland Blood Transfusion Service) and Dr Hilary Pickles (DoH) the formation of a UK group to determine policy with respect to transfusion-transmitted diseases.<sup>23</sup> There appears to have been no progress with the proposal until July 1988.

**31.22** Coincidentally, and apparently separately from the above, on 14 July 1988 Dr E L Harris (Deputy Chief Medical Officer, England and Wales), sent a memorandum to various officials in the Health Departments, including Dr John Forrester (SHHD), proposing the creation of a group with a wide remit, an Advisory Committee on the Virological Safety of Blood (ACVSB).<sup>24</sup> It noted that concerns had been raised at a recent meeting of the Expert Advisory Group on Aids (EAGA) about the lack of advice available to ensure, generally, the virological safety of blood in the UK. Since viruses other than HIV1 and HIV2 were involved, EAGA was not felt to be an appropriate group for this. Having reviewed the existing advisory bodies, Dr Harris concluded that there was no suitable existing body and suggested a new advisory group. The new group would advise on tests for NANB Hepatitis, among other virus infections. To avoid both budgetary issues, and the need to refer the proposal to Ministers, the new group would be brought under the wing of

<sup>18</sup> Letter [SNB.008.3586] (*emphasis in original*)

<sup>19</sup> Day 67, page 93

<sup>20</sup> Letter from Ortho Diagnostics to Professor Cash dated 27 November 1989 [SNB.006.1560]

<sup>21</sup> The DHSS ceased to exist on 28 November 1988 in terms of the Transfer of Functions (Health and Social Security) Order 1988 when it was split into two. Health functions were taken over by the Department of Health (DoH) from that date. Since accurate designation is not relevant for the purposes of this chapter, the Department will be referred to as the DoH throughout.

<sup>22</sup> Dr Gunson's position was the nearest equivalent to Professor Cash's in Scotland and for convenience he is referred to as the National Director of the NBTS.

<sup>23</sup> Introductory comments in the Minutes of the First Meeting of the UK Advisory Committee on Transfusion Transmitted Diseases held on Friday 24 February 1989 [SNB.006.1975] stated that the meeting between Drs Gunson, McClelland and Pickles was 'about a year' before that first meeting of the ACTTD.

<sup>24</sup> Dr Harris' memo [SGH.003.1265]

an existing body, the Advisory Committee on the NBTS.<sup>25</sup> Dr Harris included suggestions for its terms of reference and membership. He did not consider that there was a need to consult Ministers on the proposal and hoped to be able to bring the group together 'shortly'.

**31.23** The EAGA's role had already become controversial. Dr McClelland observed in oral evidence that both he and Professor Cash had been members of the EAGA and made themselves 'unpopular' by exploring how other infection-related matters could be dealt with on a UK basis. This had not been acceptable to the Chairman of the group, as the EAGA's remit was intended to concentrate exclusively on AIDS.<sup>26</sup>

**31.24** Dr Harris's memorandum did not appear to be a reaction to Chiron's announcement. The note on NANB Hepatitis commented: 'no direct marker at present; dispute over indirect markers. No routine testing now'.<sup>27</sup> Around this time people involved in blood transfusion issues were anticipating developments in NANB Hepatitis research and Chiron's announcement was known in UK transfusion circles, but it was not referred to in Dr Harris' memorandum.

**31.25** In a letter dated 18 July 1988 to Dr Pickles, Dr Forrester (SHHD) welcomed the proposal to create the ACVSB.<sup>28</sup> He agreed with the proposal that Dr Robert (Bob) Perry (PFC) should be a member of the new committee and proposed Professor Stan Urbaniak (SNBTS, Aberdeen) as the member for the SNBTS. That proposal appears to have been made without reference to Professor Cash or the SNBTS. Dr Forrester was happy to act as an observer.

**31.26** Professor Cash also welcomed the creation of the proposed group, though it appears that he was not fully informed. In a letter dated 19 July 1988 to Dr Pickles he advised that he was pleased to learn (from Dr Pickles) that discussions were taking place which would hopefully lead to the establishment of a UK group which would concern itself with the long-term problems associated with the microbial screening of blood donations.<sup>29</sup> It appears, however, that he was unaware that Dr Forrester had already made a suggestion as to who would be a suitable member from the SNBTS. Professor Cash indicated in his letter that he would appreciate the opportunity, in due course, to provide an input into the membership of the new committee.

**31.27** The proposal for a new group under the aegis of the DoH did not resurface until October 1988, by which time the proposal had changed and the scope of the DoH proposals had become broader.

#### *Formation of two advisory groups: ACVSB and ACTTD*

**31.28** Mr Malcolm A Harris wrote to Mr Duncan Macniven (Assistant Secretary at SHHD) on 25 October 1988.<sup>30</sup> He attached a draft submission to Ministers on the setting up of the Advisory Committee on the Virological Safety of Blood (ACVSB).<sup>31</sup>

<sup>25</sup> Ibid [SGH.003.1265] at 1266

<sup>26</sup> Day 68, page 160

<sup>27</sup> Dr Harris' memo [SGH.003.1265] at 1266

<sup>28</sup> Letter [SGH.003.1264]

<sup>29</sup> Letter [SNB.006.1010]

<sup>30</sup> Letter [SGH.003.1257]

<sup>31</sup> Draft submission [SGH.003.1235]

**31.29** By way of background, the draft commented that concern over the safety of the blood supply had been heightened by greater public and clinical awareness of the potential for viral contamination and new developments in product liability legislation. The need for a new advisory body was set out:

Decisions on testing for particular viruses involve a range of disciplines. Clinical and scientific expertise must be balanced by expertise representing the practicality and cost/benefit of testing. Neither the CSM the CBLA nor the BTS have the remit or expertise to take this broader approach. Their conflicting interests are ultimately in no-one's best interest.

The new advisory group will embrace the expertise of all interested groups ....

There is no suitable existing body. All of the UK must be covered.<sup>32</sup>

**31.30** The terms of reference proposed were:

To advise the Health Departments of the UK on measures to ensure the virological safety of blood, whilst maintaining adequate supplies of appropriate quality for both immediate use and for plasma processing.<sup>33</sup>

**31.31** Mr Harris asked for confirmation that the SHHD was content with the proposals and in particular that:

- (i) the committee would operate on a UK basis;
- (ii) the committee would report to the CMOs of all four health departments;
- (iii) the terms of reference were acceptable;
- (iv) the membership and observers arrangements were acceptable.<sup>34</sup>

**31.32** Mr Macniven replied by letter dated 11 November 1988 and confirmed his agreement with the proposals.<sup>35</sup> He was content that the committee should operate on a UK basis and report to the Chief Medical Officers (CMOs) of all four health departments. The terms of reference were acceptable, as was its proposed membership. The proposed Scottish members remained Dr Perry and Professor (then Dr) Urbaniak. It is not known how Mr Macniven reached his views.

**31.33** In the meantime, concern had been growing in the Blood Transfusion Services over the lack of progress in making provision for uniform advice on microbiological testing, as the EAGA had 'withdrawn from the field'.<sup>36</sup> The issue arose at a meeting of the Directors of the SNBTS on 13 December 1988, primarily in the context of AIDS. Dr Gunson and Dr William (Bill) Wagstaff of the English NBTS were in attendance, as was Professor Cash. The minutes of the meeting noted that the DoH had indicated some nine months previously that it would take the initiative, but that this had not happened 'and meanwhile certain problems needed to be addressed'.<sup>37</sup> Mr Robert (Rab) Panton (SHHD) reported that his medical colleagues would welcome the formation of a professional group. After discussion, it was agreed that the UK Blood Transfusion Services should establish a group to advise

---

<sup>32</sup> Ibid [SGH.003.1235] at 1236

<sup>33</sup> Ibid [SGH.003.1235] at 1238

<sup>34</sup> Letter [SGH.003.1257]

<sup>35</sup> Letter [SGH.003.1252]

<sup>36</sup> Minutes of a Directors' Meeting Held in the HQ Unit on 13 December 1988 [SNB.002.7350] at 7351

<sup>37</sup> Ibid [SNB.002.7350] at 7351

the Departments of Health on policy. Professor Cash and Dr Gunson, together with the SHHD, would put pressure on the Department of Health to bring that about.

**31.34** In relation to the introduction of surrogate donation testing for NANB Hepatitis (a topic discussed more fully in Chapter 27 of this Report), the meeting agreed that the task would be dealt with by the proposed group: Scottish Directors would not commence surrogate testing until the DoH and the SHHD supported and funded it. Discussion of Chiron's test was not noted in the minutes of the meeting.<sup>38</sup>

**31.35** The decisions at the meeting of SNBTS Directors on 13 December 1988 had immediate impact. On 9 January 1989 Dr McIntyre wrote to Dr Pickles. He sent her an extract from the meeting, pointing out that Dr Gunson and Dr Wagstaff had been present. He expressed his concern that if the Health Departments did not establish an advisory committee, the Transfusion Services would do so. He wrote:

This method of approaching the problem we consider to be unsatisfactory and we suspect that the decisions reached might be influenced to a considerable extent by the views of the Transfusion Directors. As this is a matter which has policy implications and will be of considerable interest to Ministers we feel that this Advisory Committee should be set up jointly by the Departments.<sup>39</sup>

**31.36** Dr McIntyre went on to observe that in Scotland there was 'considerable pressure' from the SNBTS to fund the introduction of additional virological testing, but the SHHD was of the opinion it should be tackled on a UK-wide basis. He asked for reassurance that the Department of Health would take steps in this matter, as the SHHD 'would not like to be forced into a course of action which might have repercussions for the UK as a whole'.

**31.37** The issue of the formation of the ACVSB was followed up by a letter dated 13 January 1989 from the Parliamentary Under-Secretary of State for Health, Roger Freeman, to the then Parliamentary Under-Secretary of State at the Scottish Office, Michael Forsyth, asking for Mr Forsyth's agreement to the proposal.<sup>40</sup> Mr Freeman commented that it seemed timely for the Blood Transfusion Services and all other interested parties to 'act in unison on this important matter'. Mr George Tucker (Assistant Secretary, SHHD and Mr Macniven's successor) told the Inquiry in oral evidence that it was common for government officials to consult initially on a proposal or plan, before the Ministers would correspond directly and notify their agreement.<sup>41</sup>

**31.38** On 6 February 1989 Mr Macniven sent a memorandum to Mr Forsyth's Private Secretary to recommend that the Minister should agree to Mr Freeman's proposals.<sup>42</sup>

**31.39** Mr Forsyth wrote to Mr Freeman on 8 February to confirm his agreement.<sup>43</sup> The Scottish members of the committee remained Professor Urbaniak and Dr Perry at this stage.

**31.40** The UK Health Ministers' decision to set up the ACVSB, originally proposed the year before, was intimated in a letter of 8 March 1989 sent out by Dr Harris.<sup>44</sup> Ministers believed

---

<sup>38</sup> Ibid [SNB.002.7350] at 7353

<sup>39</sup> Letter [SGH.003.1251]

<sup>40</sup> Mr Freeman's letter [SGH.003.1242]

<sup>41</sup> Day 69, page 96

<sup>42</sup> Memo [SGH.003.1233]

<sup>43</sup> Letter [SGH.003.1232]

<sup>44</sup> Letter [SNF.001.1263]

it was 'of the utmost importance that the UK Blood Transfusion Services act in unison on this subject, and with the benefit of the best advice available'. Government policy aimed at securing common action throughout the Health Departments was established at this time.

### **The initial meetings of the two groups**

**31.41** The decision at the meeting of the SNBTS Directors on 13 December 1988 to form a UK blood transfusion services group on microbiological testing was implemented very efficiently. The resulting group, the Advisory Committee on Transfusion Transmitted Diseases (ACTTD), held its first meeting on 24 February 1989.<sup>45</sup> This was about six weeks before the group established by the Departments of Health, the ACVSB, first met. Dr Gunson, in his introduction to the initial meeting of the ACTTD, was able to report that the DoH was in the process of forming another group with a brief that would be much wider than simply blood transfusion medicine. It appears to have been understood at that stage that the remit of the ACVSB would be very broad, and that the ACTTD's remit would be narrower, concentrating on transfusion-transmitted diseases.

**31.42** The ACTTD had three members from Scotland: Professor Cash, Dr Ruthven Mitchell and Dr Eddie Follett, (Hepatitis Reference Laboratory, Ruchill Hospital, Glasgow) along with four English members.<sup>46</sup> Dr McClelland thought members would have been invited by Dr Gunson.<sup>47</sup> He added that a working group like this tended to consider where they could find the best input, rather than looking at it on a political or geographical basis.

**31.43** Dr Mitchell commented in his statement that membership of the ACTTD was nominated by peer opinion and based on 'individual interest, knowledge and ability'.<sup>48</sup> He was to be a member of both the ACTTD and the ACVSB, and assumed this was because he represented the largest transfusion centre in Scotland. Professor Cash confirmed in his statement he had nominated Dr Mitchell for membership of the ACTTD as he had led the SNBTS team responsible for testing kit evaluations and could be a valuable link between the ACVSB and the ACTTD.<sup>49</sup>

**31.44** The terms of reference adopted by the ACTTD at its first meeting were:

1. To consider the epidemiological, clinical and laboratory aspects of diseases which may be transmitted by the transfusion of blood and blood products.
2. To determine the appropriate policy which should be implemented by the UK Blood Transfusion Services for the control of transfusion-transmitted diseases.
3. To advise the Departments of Health accordingly.<sup>50</sup>

**31.45** Dr Gunson's introduction to the first meeting of the ACTTD on 24 February 1989<sup>51</sup> recognised that the ACTTD and the ACVSB had different roles.

---

<sup>45</sup> Minutes [SNB.006.1975]

<sup>46</sup> Those English members were Drs Contreras, Gunson, Mortimer, and Wagstaff

<sup>47</sup> Day 69, page 1

<sup>48</sup> Dr Mitchell's Statement [PEN.017.1901]

<sup>49</sup> Professor Cash's Statement [PEN.017.2094] at 2095

<sup>50</sup> Draft Terms of Reference [SNB.006.1923]

<sup>51</sup> Minutes [SNB.006.1975]

**31.46** Dr Gunson told the meeting that Ortho had approached him with respect to conducting trials of the Chiron test in the UK. He undertook to report to the committee when further details became available.<sup>52</sup>

**31.47** The ACVSB held its first meeting on 4 April 1989<sup>53</sup> when the committee adopted the terms of reference outlined in Mr Harris' submission to Ministers quoted above. They added a qualification, however:

Note remit is UK-wide. Our concern is matters of major policy, not the detailed implementation of policy. The intention is that any proposed changes in requirements or practices of one of the major groups (transfusion service, fractionators, regulators) that has major implications for the others are brought to this group first for discussion.<sup>54</sup>

**31.48** Terms of reference of related groups were noted as follows:

- the UK Advisory Committee on Transfusion Transmitted Diseases (ACTTD) would be considering many of the same issues as the ACVSB, but only from a transfusion viewpoint;
- a BTS/National Institute for Biological Standards and Control (NIBSC) group formed between the NBTS/SNBTS and the NIBSC to formulate scientific guidelines for the standardisation and safety of blood and blood products; and
- the Advisory Group on Hepatitis, which provided 'medical advice to the Chief Medical Officers of the Health Departments on all aspects of communicable hepatitis' and had the appropriate technical expertise for detailed consideration of the technical aspects of screening donors and plasma for various forms of hepatitis, leaving the ACVSB to consider the wider policy issues.<sup>55</sup>

**31.49** The ACVSB was chaired by Dr Harris. The initial members comprised Dr Gunson (NBTS), Dr Lane (BPL), Dr Minor (NIBSC), Dr Mortimer (PHLS), Dr Summerfield (Middlesbrough Haemophilia Centre), Dr Tuddenham (MRC) and Professor Zuckerman (Professor of Medical Microbiology). As regards the two members from Scotland, by the first meeting, on 4 April 1989, Professor Urbaniak had been replaced by Dr Mitchell, although Dr Mitchell did not in fact attend the first meeting.<sup>56</sup> Dr Perry remained a member of the ACVSB from its inception.<sup>57</sup> There was to be one Scottish observer from the Scottish Home and Health Department and Dr Archie McIntyre took on that role.<sup>58</sup> One important consequence of the selection of Scottish members was that Professor Cash was not involved in the work of the ACVSB while Dr Gunson, his equivalent in the NBTS, was involved. Dr Perry was a member as a fractionator and not because he had expertise in the microbiological safety of blood.<sup>59</sup> Members were chosen in an individual capacity, and not as representatives of their parent organisations.<sup>60</sup> The omission of Professor Cash was to have consequences.

---

<sup>52</sup> Ibid [SNB.006.1975] at 1978

<sup>53</sup> Minutes [SNF.001.1219]

<sup>54</sup> ACVSB paper 'Terms of Reference' [SNB.001.9366]

<sup>55</sup> Ibid [SNB.001.9366]

<sup>56</sup> Note of Meeting of the Advisory Committee on the Virological Safety of Blood [SGH.003.1228]

<sup>57</sup> Day 68, page 2

<sup>58</sup> Ibid, page 14

<sup>59</sup> Ibid, page 7

<sup>60</sup> Ibid, page 18



**31.50** Over the period to mid-1991 which was of particular importance in the context of this chapter there were a few changes in membership of the ACVSB. Dr Jeremy Metters replaced Dr Harris as DCMO and as chairman of the committee by 3 July 1989. Professor Tedder, Middlesex Hospital, joined and attended the second meeting of the committee on 22 May 1989. Dr Tuddenham resigned before the ninth meeting on 25 February 1990 and was replaced by Dr Wensley. Dr Summerfield did not attend regularly. But otherwise the membership of the ACVSB was stable and meetings were well attended.

**31.51** At the beginning of the meeting on 4 April 1989, Dr Harris made a comment that was to have important consequences for relationships between the ACVSB and the transfusion services and, in particular, the ACTTD:

He reminded members that their advice on the subjects under discussion could be publicly sensitive and should not be discussed outside the Committee, unless specifically indicated.<sup>61</sup>

**31.52** The minutes recorded that it was the intention that the next meeting of the committee should concentrate on viral hepatitis.<sup>62</sup>

**31.53** The second meeting of the ACTTD took place on 19 May 1989.<sup>63</sup> From reviewing the minutes, it appears that comparatively little time was spent discussing developments in Hepatitis C screening. Dr John Barbara (NBTS, Edgware, North London) reported that ordinary donor samples saved and stored from the tri-centre trial of ALT testing (discussed in Chapter 27, *Surrogate Testing of Donated Blood for non-A, non-B Hepatitis*, paragraphs 27.245–27.246) were being tested with the trial Ortho anti-HCV assay at a rate of 400 per day, before proceeding with selected groups. The test was running consistently with the manufacturer's expectations. Under the heading in the minutes 'Anti-HCV testing of donations from Scotland' it was noted:

Professor Cash reported that the SNBTS would be interested in taking part in evaluative trials of the Ortho Pharmaceutical Company's Chiron test and said he would be grateful if Dr Gunson would contact him about this matter. In particular the West of Scotland centre has a bank of frozen donor samples already tested for ALT, from which further samples are available of i.v. IgG known to have produced raised ALT levels in recipients.<sup>64</sup>

**31.54** Dr Dow commented in oral evidence that Professor Cash, as National Medical Director, was keen to ensure that the SNBTS remained at the forefront of test developments.<sup>65</sup>

**31.55** The second meeting of the ACVSB on 22 May 1989 tackled the topic of hepatitis.<sup>66</sup> Members advised that although colleagues in the US considered only one virus caused NANB, there may be two or more. The Chiron test was estimated to pick up only approximately 50% of cases and there was a need for caution. There had been enormous progress and once the sequence was published it would be possible to test without recourse to Chiron. In oral evidence, Dr Perry said that he was unclear what that meant other than that the release of data could pave the way for other manufacturers to come

---

<sup>61</sup> Minutes [SNF.001.1219]

<sup>62</sup> Ibid [SNF.001.1219] at 1220

<sup>63</sup> Minutes [MIS.001.0009]

<sup>64</sup> Ibid [MIS.001.0009] at 0012

<sup>65</sup> Day 67, page 103

<sup>66</sup> Meeting [SNB.001.9416]

up with tests.<sup>67</sup> This appears to be a plausible explanation. Dr Perry could not recall any sense in which the ACVSB was waiting for a British developed test to become available, and using that rather than relying on one that originated in the USA.<sup>68</sup> However, the minute remains somewhat obscure.

**31.56** The minutes noted that the DoH would keep the issue of testing under review. The use of Chiron or surrogate testing would be influenced by Chiron data once released; the Medical Research Council (MRC) might be asked to consider the data. The minute notes that members regarded the matter as a 'priority'.<sup>69</sup>

**31.57** The ACVSB met for the third time on 3 July 1989. Dr Metters was now its Chairman. The meeting considered the topic of non-A, non-B Hepatitis.<sup>70</sup> Dr Philip Mortimer had attended a recent conference, and come away with the view that 'there was a persuasive case that the Chiron test results were reliable'. As a result the Chairman asked for all available data on NANB Hepatitis to be compiled and given to the committee for consideration at the next meeting.<sup>71</sup>

**31.58** In his evidence Dr Perry agreed that the impression created by the reported discussion was that there was no detectable sense of urgency in the ACVSB to introduce testing at this time, stating that:

[T]here was a greater emphasis on understanding the science than there was in saying, "We must introduce a test as soon as possible" .... There was certainly no discussion ... of a putative date at which the test could or should be introduced.<sup>72</sup>

**31.59** Dr Perry went on:

My general sense of the meeting was that there were some exciting international developments in relation to a specific HCV test but that it was far from clear when or if a test suitable for routine use (including confirmation) would emerge.<sup>73</sup>

**31.60** So far as the committee was concerned, all options were to be kept open. At this stage, that was understandable. Apprehension that the Chiron test would identify 50% of cases of virus infection in donations left 50% of cases unidentified. Depending on the outcome of early studies of the evaluation of the Ortho test in use in the UK population, ALT and anti-HBc were the only tests currently available that might provide surrogate screening in the UK donor population for agents other than HCV.

**31.61** In his statement Dr Perry responded to a question whether it was a correct impression to derive from correspondence around this time that the principle of introducing a further test designed to reduce the incidence of post-transfusion hepatitis had not yet been determined. He replied:

I believe this impression is correct. It was certainly periodically emphasised by Dr Metters at ACVSB meetings that the primary purpose of the committee was

---

<sup>67</sup> Day 68, page 27

<sup>68</sup> Ibid, pages 27–28

<sup>69</sup> Meeting [SNB.001.9416] at 9418

<sup>70</sup> Meeting [SNB.001.9513]

<sup>71</sup> Ibid [SNB.001.9513] at 9515. It is likely Dr Mortimer had attended an Ortho symposium in Paris on 30 June 1989.

<sup>72</sup> Day 68, page 35

<sup>73</sup> Dr Perry's Statement [PEN.017.2108] at 2111

to establish the policy and principle for introduction of new screening tests. At this time such a policy had neither been stated or agreed – notwithstanding the fact that many believed it to be only a matter of time.<sup>74</sup>

**31.62** Dr Perry added in oral testimony that he would not have considered himself, in summer 1989, to be someone who thought it was only a matter of time before testing for Hepatitis C was introduced, although he came to that view fairly soon afterwards.<sup>75</sup>

**31.63** When asked about Dr McIntyre's view, stated in a letter to Professor Cash on 2 August 1989,<sup>76</sup> that testing would be introduced simultaneously throughout the UK, Dr Perry thought it was the 'accepted view of the committee, that this would be a UK decision and implemented in a co-ordinated manner across the UK'.<sup>77</sup>

**31.64** Dr Perry had no knowledge of the formal position in Scotland on the procedure for translating a 'UK decision' into local application. He added in his statement: '[R]ather it was understood that a decision by DOH (and presumably English Ministers) would be replicated in Scotland'.<sup>78</sup>

### Events in summer 1989

**31.65** In the meantime, as the summer of 1989 progressed, several interrelated issues emerged, including collaboration between the NBTS and SNBTS at a practical level in relation to evaluation of Ortho's kit and the introduction of screening; Ortho's marketing strategies; and expectations of the role of government in the introduction of screening.

**31.66** In June 1989 Professor Cash had arranged with Ortho to obtain kits for research evaluation. A preliminary report on the project, by Dr Dow, Mr A Barr and Dr Mitchell, was prepared in October 1989 and is referred to below. SNBTS had a clear and obvious interest in developing an understanding of the new test as soon as possible given the central importance of eliminating or reducing the transmission of infection by transfusion. However, Professor Cash offered a more particular explanation.

**31.67** Professor Cash commented in oral evidence that the SHHD, through Dr McIntyre, had previously 'banned' Dr Mitchell's team from involvement in the testing of HIV kits as it was to be done 'centrally'.<sup>79</sup> With the HCV test kits, the SNBTS was determined to have some control and to do their own test of the earliest kit they could obtain. He feared that the SHHD would defer to the DoH in London, as they had done with HIV testing.<sup>80</sup> The SNBTS concern, according to Professor Cash, was the effect it would have on donor perception of the screening if there was controversy over its accuracy, especially; in the initial stages a confirmatory test was unlikely to be available.<sup>81</sup>

**31.68** Professor Cash was keen that the SNBTS should generate their own independent data as quickly as possible, that could be used as a 'lever' for influencing central action later on.<sup>82</sup> This 'lever' was a way to get Dr Mitchell and his team involved in UK-wide

---

<sup>74</sup> Ibid [PEN.017.2108] at 2111

<sup>75</sup> Day 68, page 36

<sup>76</sup> Dr McIntyre's letter [SGH.002.8026]

<sup>77</sup> Day 68, page 36

<sup>78</sup> Dr Perry's Statement [PEN.017.2108] at 2113

<sup>79</sup> There is a detailed description of the steps taken by SNBTS to evaluate HIV screening kits to be found in paragraphs 30.71–30.87 of Chapter 30, *Screening of Donated Blood for HIV*. The issue over testing using live HIV became complex.

<sup>80</sup> Professor Cash's Statement [PEN.017.2094] at 2096; Day 72, page 115

<sup>81</sup> Day 72, pages 114–115

<sup>82</sup> Professor Cash's Statement [PEN.017.2094] at 2096

testing that he envisaged would be run by the DoH.<sup>83</sup> He wanted to ensure that Scotland had 'a place in the team, the UK team', that was involved in evaluation of test kits.<sup>84</sup> He told the Inquiry in his statement that the SNBTS thought that engagement with Ortho might expedite outcomes from their confirmatory testing developments.<sup>85</sup>

**31.69** Evaluation of the Ortho kits proceeded, and information was exchanged between the NBTS and the SNBTS. Dr Gunson wrote to Professor Cash on 26 July 1989 to express his pleasure that the SNBTS was to test 5000 samples with the Ortho kit.<sup>86</sup> Dr Barbara (Edgware, North London) had almost completed testing 9000 samples and the results would be sent to Professor Cash when available. The methodology adopted was explained by Dr Dow. A positive result on a first test was followed by repetition of the test, twice if the second test was negative. A sample which was positive on both the initial and one other of the two subsequent tests was classified as a 'repeat reactive'.<sup>87</sup> A sample that was reactive with the first test, but negative with the two subsequent tests would be classified as an 'initial reactive'.<sup>88</sup>

**31.70** Dr Gunson went on to emphasise the importance of close collaboration between the SNBTS and the NBTS. He concluded by saying:

My view is that we should not move until we know what our European colleagues are doing. For the U.K. it is important that the SNBTS and the NBTS act in close collaboration since I can foresee difficulties if one of us introduced the test unilaterally.<sup>89</sup>

**31.71** In his reply of 28 July 1989 Professor Cash confirmed that close collaboration seemed certain, since the SNBTS would not move unilaterally unless instructed to do so by the SHHD.<sup>90</sup> He commented that he had indicated to Ortho that the SNBTS would not be able to discuss contracts for supply of the test kits unless instructed to do so by the SHHD. Professor Cash agreed in oral testimony that he and Dr Gunson were planning to work together on the introduction of screening and that he was happy with that as the best course of action.<sup>91</sup> Ultimately, a common start date was agreed and implemented. However, there was not a uniform pattern of concerted action between the NBTS and the SNBTS in arriving at that outcome.

**31.72** Professor Cash also wrote to Dr McIntyre on 28 July 1989 to confirm the terms of a recent telephone conversation.<sup>92</sup> Dr McIntyre had indicated that the decision to commence routine donation testing, using the Ortho test, would be made by the SHHD and it would not be appropriate for senior SNBTS managers to liaise directly with Ortho. Professor Cash told the Inquiry in his statement that the letter was drafted primarily to confirm and put on record important conversations he had had with Dr McIntyre, and to ensure the SNBTS directors were fully briefed on SHHD policy.<sup>93</sup>

---

<sup>83</sup> Day 72, pages 116–117

<sup>84</sup> Ibid, page 116

<sup>85</sup> Professor Cash's Statement [PEN.017.2094] at 2096

<sup>86</sup> Letter [SNB.006.1574]

<sup>87</sup> Day 67, page 104

<sup>88</sup> Ibid, page 107

<sup>89</sup> Letter [SNB.006.1574]

<sup>90</sup> Letter [SNB.008.2606]

<sup>91</sup> Day 72, page 127

<sup>92</sup> Letter [SNB.008.2603]

<sup>93</sup> Professor Cash's Statement [PEN.017.2094] at 2097

**31.73** Dr McIntyre replied in a letter dated 2 August 1989. The terms and the tone of the letter are instructive:

As you are aware there is a UK Advisory Committee on the Virological Safety of Blood which is meeting regularly and considering the sensitivity and specificity of the tests available for a variety of infective agents including [the Chiron test and others]. If it is considered desirable to introduce a further routine screening test for blood donors I understand that this will be done simultaneously throughout the UK – as was done in the case of the current HIV test.

I am sending a copy of this letter to Dr Jeremy Metters, Deputy Chief Medical officer at the Department of Health and to administrative colleagues here in SHHD.<sup>94</sup>

**31.74** Dr McIntyre was a regular SHHD observer at ACVSB meetings, and Dr Perry thought he would have been aware of the DoH view that any new test would be introduced simultaneously throughout the UK.<sup>95</sup>

**31.75** Professor Cash wrote to the SNBTS directors on 3 August 1989.<sup>96</sup> In his letter he advised that he believed that it was only a matter of time before screening using the Chiron test was introduced and that while he did not know when screening would commence he thought the start date would be some time after April 1990. That was much earlier than screening in fact began. Professor Cash remarked in his Inquiry statement that at the date of his letter he thought the assessment of the Ortho kit would reveal a kit with acceptable specificity and sensitivity so that screening could commence.<sup>97</sup> Professor Cash's comment in his letter of 3 August that '[t]he decision to commence testing will be a UK one and will be made by the UK Departments of Health', was tempered by adding that '[t]he start date ... will, as with HIV-1, also be a matter for central government decision, with, of course, appropriate consultation with the UK BTS directors'.<sup>98</sup> He concluded his letter by stating that he had 'started a battle' with Ortho on the need for confirmation testing, which he intended taking as high as he could in the Departments of Health.

**31.76** Dr Mitchell's view at the time appears to have been that sensitivity and specificity of the test remained a problem that required improvement to the test to avoid the problems of false positive and negative results.<sup>99</sup>

**31.77** Dr Gunson wrote to his NBTS transfusion directors on 18 August 1989 and copied the letter to Professor Cash.<sup>100</sup> He emphasised the need to act in a coordinated fashion, both nationally and with Scotland, with regard to the introduction of routine screening. According to Mr McIntosh in oral evidence, the regional transfusion centres in England and Wales did not report to Dr Gunson; rather, they reported to their local health authorities. In his view, Dr Gunson and his central blood authority team did not have executive authority.<sup>101</sup>

---

<sup>94</sup> Letter [SGH.002.8026]

<sup>95</sup> Professor Cash's Statement [PEN.017.2108] at 2112

<sup>96</sup> Letter [SNB.006.1580]

<sup>97</sup> Professor Cash's Statement [PEN.017.2094] at 2098

<sup>98</sup> Letter [SNB.006.1580]

<sup>99</sup> Dr Mitchell's Statement [PEN.017.1901] at 1905

<sup>100</sup> Letter [SNB.006.1426]

<sup>101</sup> Day 70, page 83

**31.78** Mr Tucker was an Assistant Secretary in SHHD whose role was to ‘quality control check briefings and to channel advice to Ministers’.<sup>102</sup> He sent a memorandum to Mr Forsyth on 23 August 1989 regarding an article on testing for Hepatitis C which appeared in *The Guardian* on the same day.<sup>103</sup> Mr Tucker’s memo confirmed that the introduction of HCV screening of blood donors was a UK issue and that the DoH would take the lead, but that SHHD and SNBTS would be represented in meetings and the appropriate Minister would be consulted before any decision was taken.

**31.79** By this time there was growing concern within SNBTS that their Directors did not have sufficient information about the work of the ACVSB. The issue of the reporting of events at the ACVSB was discussed at the SNBTS Directors’ meeting on 29 September 1989.<sup>104</sup> By then, it was reported on behalf of Mr Panton that there had been progress. It would be in order for Dr Perry and Dr Mitchell, as members of the ACVSB, to report the Committee’s discussions and recommendations to the other SNBTS Directors. Miss Corrie, the minute taker, was to seek written confirmation of this from Mr Panton, and to ask if the Directors could have copies of the ACVSB minutes.

**31.80** At the SNBTS Directors meeting of 13 February 1990 it was noted that ‘it would be in order for Dr Perry and Dr Mitchell to report the discussions and findings of the Committee to fellow Directors, but ... the minutes could not be copied to them’.<sup>105</sup> The minutes could, however, be passed around and discussed at the Directors’ meetings informally. The same position was said to apply in the NBTS. Thus the provision for relaxation of confidentiality noted by Dr Harris at the first meeting of the ACVSB was given practical effect.

### Medical literature on testing in summer 1989

**31.81** Before returning to events in the UK, it is appropriate to note what was happening in the wider scientific community, as a great deal of research was being published at the time. As noted above,<sup>106</sup> *Science* published an article by Kuo and others on 21 April 1989 giving scientific information on the Chiron discovery and the research behind it.<sup>107</sup> A radio-immuno assay was used in the research phase leading to the announcement of the discovery. A radio-immuno assay utilises radioactive material and the research team was encouraged, according to Dr Dow, to discontinue use of that technology, and to develop an ELISA rather than expose workers in general laboratories to radioactivity. The researchers had also moved on from the initial clone and had found a slightly longer strip of the NANB Hepatitis virus genome.<sup>108</sup> The ELISA assay performed well using ‘well pedigreed’ NANB Hepatitis samples,<sup>109</sup> showing high levels of reaction in those samples when compared with reactions to alcoholic and other forms of non-viral hepatitis. The ELISA tested for C100 antibodies, a late-appearing antibody in terms of the period lapsed since infection. Researchers noted later that antibodies in drug addicts in the acute early stage of NANB Hepatitis were not detected by this test. The second generation tests developed later were able to detect earlier appearing antibodies, thus shrinking the ‘window period’ of infectivity.<sup>110</sup>

<sup>102</sup> Statement [PEN.017.2060] at 2061

<sup>103</sup> Memo [SGH.002.8008]; *The Guardian* article [SGH.002.8010]

<sup>104</sup> Minutes [SNB.002.4517] at 4518

<sup>105</sup> Minutes [SNB.002.4627] at 4628

<sup>106</sup> Paragraph 31.15

<sup>107</sup> Kuo et al, ‘An Assay for Circulating Antibodies to a Major Etiologic Virus of Human Non-A, Non-B Hepatitis’, *Science*, 1989; 244; 362–364 [PEN.017.2764]

<sup>108</sup> Day 67, pages 96–98

<sup>109</sup> ‘Well pedigreed’ samples were those from subjects, animal and human, who, clinically, were known to be suffering from NANB Hepatitis

<sup>110</sup> Day 67, pages 98-99

**31.82** With regard to the *Science* article, Dr McClelland commented in oral evidence that it would have been difficult to be confident about any estimate of the sensitivity of the assay when it was completely new. There was no reliable, independently certified set of known positives to use as controls. Furthermore, any new technique used by the research laboratory that developed it would work better than in the field: the research scientists would know its 'little ins and outs' and 'technical foibles'. They would almost always produce better results in the early days than would be produced by people from other laboratories.<sup>111</sup>

**31.83** *The Lancet* of 5 August 1989 contained an editorial concerning the Ortho test entitled 'Will the real hepatitis C stand up?'.<sup>112</sup> The editorial concluded: 'It would be logical to confer the title of hepatitis C on the newcomer'.<sup>113</sup> The issue also included a series of results of the new test system from Spain and Holland and two from Germany.<sup>114</sup>

**31.84** The editorial noted:

In general, the results support the sensitivity and specificity of the test system, and underline both the urgency of making the test system available for blood donor screening, and the importance of despositing [*sic*] the sequence of the viral genome in the GenBank database where it would be available to the wider scientific community.<sup>115</sup>

**31.85** The research reported from Spain was focused on prevalence in patients at high risk of infection.<sup>116</sup> Dr Dow was referred to Table I in the paper and was impressed with the figures for positive tests, as the percentage figures were as high as he would expect from high-risk groups.<sup>117</sup> The test at this stage appeared to have good sensitivity in high-risk groups where the virus would be expected.<sup>118</sup> The figure of 64% for positive reactions in a group of people with haemophilia was very close to the finding of anti-HCV positivity in patients with haemophilia in the (subsequent) Scottish paper.<sup>119</sup>

**31.86** The authors stated that:

Our results show that HCV accounts for most cases of post-transfusion hepatitis in Spain. Although seroconversion may occur during the acute phase of the infection (in about a third of cases), in more than half of our patients, anti-HCV antibodies were first detected 4-6 months after transfusion, and in some the antibody response was considerably later.<sup>120</sup>

<sup>111</sup> Day 69, pages 7–9

<sup>112</sup> 'Will the Real Hepatitis C Stand Up?', *The Lancet*, 5 August 1989 [LIT.001.3848]

<sup>113</sup> By the time of a subsequent editorial in *The Lancet* on 16 June 1990, 'Hepatitis C virus upstanding' [LIT.001.3879] it was stated that 'Hepatitis C virus is believed to be the main blood borne [NANB] hepatitis virus'

Day 67, page 123

<sup>114</sup> 'Will the Real Hepatitis C Stand Up?', *The Lancet*, 5 August 1989 [LIT.001.3848] at 3849

<sup>115</sup> Esteban et al, 'Hepatitis C virus antibodies among risk groups in Spain', *The Lancet*, 5 August 1989 [LIT.001.3834]. The 'risk groups' were noted as being: patients with post-transfusion NANBH, patients with chronic hepatitis, haemophiliacs, intravenous drug users, haemodialysis patients, homosexual men and female contacts of drug users.

Day 67, page 127

<sup>116</sup> See the high rates of positive results in those with post-transfusion NANBH, those with chronic NANBH and intravenous drug abusers shown in table 1 [LIT.001.3834] at 3835.

<sup>117</sup> Day 67, page 128; SNBTS Evaluation of the Ortho HCV antibody ELISA test system, Dr B Dow et al, October 1989 [SNB.006.1596]

<sup>118</sup> Esteban et al, 'Hepatitis C virus antibodies among risk groups in Spain', *The Lancet*, 5 August 1989 [LIT.001.3834] at 3836

**31.87** According to Dr Dow, the authors referred here to a time delay following infection and before the RIA would pick up the HCV antibodies.<sup>121</sup> The authors themselves commented: 'This delayed response could explain why anti-HCV was not detected in all our post-transfusion cases'.<sup>122</sup>

**31.88** The Dutch study in *The Lancet*<sup>123</sup> was a prospective study of patients undergoing heart surgery. Post Transfusion-NANB Hepatitis (PT-NANB Hepatitis) developed in nine patients, and four of those seroconverted. The authors commented:

We have shown that in a Dutch blood donor population the new anti-HCV RIA developed by Chiron specifically identifies blood products associated with NANB hepatitis in patients who have received transfusions .... Sensitivity of the assay for detecting probable NANB infected blood products was 67% in our study population.<sup>124</sup>

**31.89** The patients studied were in a group of people assumed to have a low incidence of HCV. The number of cases of PT-NANB Hepatitis was small. The authors concluded:

Despite its limited sensitivity, the high specificity of this first generation anti-HCV assay should permit greatly improved donor screening procedures for the prevention of PTH-NANB.<sup>125</sup>

**31.90** The German research published in the same issue of *The Lancet*<sup>126</sup> related to a study of donors at four German blood banks using the Ortho ELISA. By categorising donors in different ways the researchers found that samples from certain groups were repeatedly reactive. They observed, however, that in the absence of a confirmatory test, the true frequency of HCV infection in their population remained to be determined. A note of caution was sounded regarding confirmatory testing:

The use of the same recombinant antigen material – ie, that constituting the solid material in the EIA – for a confirmatory test (eg, immunoblot) would not be satisfactory scientifically.<sup>127</sup>

**31.91** The same edition of *The Lancet* contained a second letter from researchers in Germany.<sup>128</sup> This study looked at patients rather than donors, using the Ortho ELISA tests. Researchers looked at patients with acute and chronic NANB Hepatitis and at high-risk patients – haemophilia patients, patients on haemodialysis and drug addicts. They reported:

Seroconversion seems to occur late after onset of disease since acute post-transfusion NANBH patients have a lower prevalence of anti-HCV than chronic cases, and seroconversion occurred at 3-4 months post exposure in 3 patients with haemophilia. The low prevalence of anti-HCV in haemodialysis patients in our study may reflect a selected population.<sup>129</sup>

<sup>121</sup> Day 67, page 130

<sup>122</sup> Esteban et al, 'Hepatitis C virus antibodies among risk groups in Spain', *The Lancet*, 5 August 1989 [LIT.001.3834] at 3836

<sup>123</sup> van der Poel et al, 'Anti-hepatitis C antibodies and non-A, non-B post-transfusion hepatitis in the Netherlands', *The Lancet*, 5 August 1989 [LIT.001.3854]

<sup>124</sup> Ibid [LIT.001.3854] at 3855

<sup>125</sup> Ibid [LIT.001.3854] at 3855

<sup>126</sup> Kuhn et al, 'Antibody to hepatitis C virus in German blood donors', *The Lancet*, 5 August 1989 [LIT.001.3856]

<sup>127</sup> Ibid [LIT.001.3856]

<sup>128</sup> Roggendorf et al, 'Antibodies to hepatitis C virus', *The Lancet*, 5 August 1989 [LIT.001.3856]

<sup>129</sup> Ibid at [LIT.001.3856] at 3857



**31.92** On 26 August 1989 *The Lancet* published a letter written by Drs Contreras and Barbara from the North London BTC on the subject of 'Screening for hepatitis C antibody'.<sup>130</sup> The authors agreed that the Chiron/Ortho ELISA for anti-HCV was specific for the major agent causing post-transfusion NANB Hepatitis and was superior to all previous attempts at a test for the NANB virus. However, they struck a note of caution with regard to the screening of donors for anti-HCV:

As in any other assay, the predictive value of a positive result hinges on the prevalence of the marker in a given population. While the test scores well in panels of well-characterised NANB hepatitis sera and in samples from patients with a diagnosis of NANB hepatitis, we do not know the predictive value of the test in low prevalence populations, such as UK blood donors.<sup>131</sup>

**31.93** The authors went on to emphasise the importance of a confirmatory test to eliminate uncertain results, before realistic policies for generalised screening of blood donations could be implemented.

**31.94** In addition, the 26 August 1989 edition of *The Lancet* contained a letter by Professor Cash and Drs McClelland, Urbaniak, Brookes and Follett on the subject of screening for Hepatitis C.<sup>132</sup> They also emphasised the importance of a confirmatory test. Without such a reliable test there would be serious problems for blood transfusion services, which would probably be required to absorb the majority of counselling of sensitive donors. A repeatedly reactive ELISA test was 'suggestive but not definitive' evidence of the presence of HCV antibody. A confirmatory test which used the same antigen as the ELISA test was described as 'scientifically less than satisfactory' but 'better than nothing'. The authors urged Ortho to make available reagents and/or tests that would ensure that an assay system that was fundamentally different from the marketed ELISA test could be used for confirmatory testing.

### Supplementary and confirmatory tests

**31.95** As was implicit in the letter by Professor Cash and others, a 'confirmatory' test was ideally a test that was fundamentally different from the ELISA currently on the market, that would affirm the initial screening test, or not, and provide a reliable basis for diagnosis and counselling. Dr Dow commented that, in general terms, a confirmatory test would be better than a supplementary test.<sup>133</sup> Dr McClelland observed in oral testimony that the terms were very difficult to define because 'there are numerous definitions invented by various people'.<sup>134</sup> In his view, a confirmatory test should assist in deciding if a positive screening test result is a real or a false positive result. The type of test used for confirmation did not matter provided it could determine if an earlier test was truly positive. A 'supplementary' test, that simply repeated the initial screening test, was much less useful.<sup>135</sup>

**31.96** Professor Leikola observed in oral testimony:

[T]hat a true confirmatory test should be based on the principle that it is different from the original antibody/antigen reaction, in order to show from

<sup>130</sup> Contreras and Barbara, 'Screening for hepatitis C virus antibody', *The Lancet*, 26 August 1989: 505 [LIT.001.3858]. This referred to the NBTS assessment exercise discussed later: paragraphs 31.118–31.121

<sup>131</sup> Ibid [LIT.001.3858]

<sup>132</sup> Cash et al, 'Screening for hepatitis C virus antibody', *The Lancet*, 26 August 1989; 505 [LIT.001.3858]

<sup>133</sup> Day 67, page 140

<sup>134</sup> Day 69, page 24

<sup>135</sup> Ibid, page 25

another point of view that it really is a true reaction between the virus and the antibody.<sup>136</sup>

**31.97** The difficulty in the early days of anti-HCV testing was that there was only one antigen because only a small section of the virus had been isolated. As a result only one antibody was identified by the screening test, whether on initial or repeat testing. The recombinant immunoblot assay (RIBA) that Ortho developed later as a confirmatory test targeted the same antigen. For a test to be truly confirmatory it would be required to detect an antibody to some *other* part of the virus, or the virus itself. Because the RIBA looked for the *same* protein, it could only have been a 'supplementary' test and not 'confirmatory' of the initial screen result. By way of contrast, in later developments virus laboratories would test for the virus itself using a Polymerase Chain Reaction (PCR) test which was truly confirmatory because it is based on a different principle from the initial screening tests.<sup>137</sup>

### The position in Finland in 1989–90

**31.98** Professor Juhani Leikola assisted the Inquiry as expert witness and spoke to events in Finland, which provide a useful comparison to events in Scotland and in the UK as a whole. His general evidence had a basis in the work of the Finnish Red Cross. There were structural differences between the blood transfusion services in Finland and in the UK which have to be taken into account, but these do not invalidate the comparison. Finland is a small country, where the prevalence of NANB Hepatitis was very low, at less than one per cent. By the end of 1989, it was known to the UK Blood Transfusion Services, including the SNBTS Directors, that the Finnish Red Cross had arranged with Chiron to test samples at the same time as evaluation was proceeding in the United Kingdom.<sup>138</sup>

**31.99** Professor Leikola was approached by Ortho in the spring of 1989 and asked to arrange a study of their new test kit, together with researchers from Sweden and Denmark.<sup>139</sup> There was considerable contact between these countries in the blood transfusion field, although the organisation of their individual transfusion systems was different. Sweden and Denmark had independent hospital blood banks within hospital authorities, while in Finland the Finnish Red Cross organised a blood transfusion service on a countrywide scale.<sup>140</sup>

**31.100** In evaluating the Ortho assay, Finnish researchers looked at both material from a large prospective study done by Dr Freja Ebeling between 1987 and 1989 and local haemophilia patients.<sup>141</sup> Dr Ebeling's material was from a post-transfusion (PT) hepatitis study of 685 patients who had undergone open heart surgery. Hepatitis was diagnosed when the patient's ALT was found to exceed 2.5 times the upper normal value in one sample and 2 times the upper normal value in a second sample, and where non-viral causes could reasonably be excluded. Of the 685 coronary bypass patients, 11 developed elevated ALT levels during the six post-operative months, and were diagnosed as having acute NANB hepatitis by exclusion of non-viral causes, an incidence of infection of 1.6%. This research was subsequently written up in November 1990 in an article in *Transfusion*

<sup>136</sup> Day 71, page 111

<sup>137</sup> Professor Leikola – Day 71, pages 111-112

<sup>138</sup> Meeting Minutes [SNB.002.7350] at 7353

<sup>139</sup> Professor Leikola's Statement [PEN.017.1957] and *Hepatitis C and blood donation* – Unofficial translation from Finnish by Juhani Leikola [PEN.017.1828] at 1828

<sup>140</sup> Day 71, pages 81–82

<sup>141</sup> *Hepatitis C and blood donation* – Unofficial translation from Finnish by Juhani Leikola [PEN.017.1828]

*Medicine*.<sup>142</sup> A secondary object of the exercise had been to obtain samples for future evaluation of possible preventive strategies, and the material was available when Ortho provided kits for evaluation in the course of the project.

**31.101** Dr Ebeling's research group applied the Ortho ELISA and a Chiron RIBA 'confirmatory' research test to the panel of 685 frozen samples already collected. Samples from the 11 patients diagnosed with post-transfusion, NANB Hepatitis were tested. Seven of them had received a blood product from an anti-HCV positive donor, on the ELISA test. A further 1029 donor samples not associated with a PT Hepatitis case in the earlier phase of the project were tested and six of these were found to be anti-HCV positive on the ELISA test. The six samples were all associated with hepatitis (raised ALT) in a patient recipient, and five of these were shown to have seroconverted (developed HCV antibodies), based on the ELISA test.

**31.102** The group published the preliminary results of this research in a letter to *The Lancet* on 21 April 1990.<sup>143</sup> The letter referred to the earlier *The Lancet* publication by Dutch researchers<sup>144</sup> and agreed with their findings that it was possible that false-positive results would be achieved with the ELISA test when screening low prevalence groups such as blood donors. In false positive cases, the kit had failed to differentiate between non-infectious and infectious blood, which would make it difficult for blood transfusion centres to decide which blood units to discard and which donors to counsel.

**31.103** On the basis of this research, however, the scientists suggested the RIBA might be helpful in differentiating between an infective and a non-infective blood donor, and that reactivity to both antigens (511 and C100) was strongly associated with infectivity.<sup>145</sup>

**31.104** Professor Leikola said that the Finnish researchers were very keen to try the new Ortho kits on the 11 patients identified in the first phase of the project as having NANB Hepatitis. Of the five who had been found to be anti-HCV negative, two had an anti-HCV positive donor. Professor Leikola commented that this demonstrated the initial (ELISA) test was not highly sensitive, and those two patients might have been positive with use of the test kits developed later.<sup>146</sup> He also observed that the level of HCV antibody fluctuated in patients. Sometimes the level was below the cut-off level for positivity and these patients were considered to be HCV negative due to that fluctuation.<sup>147</sup>

**31.105** Despite Finland having a very low prevalence of NANB Hepatitis the development of the Ortho test was welcomed there as NANB Hepatitis was still the most common infectious complication of blood transfusion. The new screening test to detect antibodies offered major advantages.<sup>148</sup>

<sup>142</sup> Ebeling et al, 'Post-transfusion hepatitis after open-heart surgery in Finland – A prospective study', *Transfusion Medicine*; 1991, 1: 103–108 [PEN.017.1777]

<sup>143</sup> Ebeling et al, 'Recombinant immunoblot assay for hepatitis C virus antibody as predictor of infectivity', *The Lancet*, 21 April 1990; 335: 982 [LIT.001.0270]

<sup>144</sup> van der Poel et al, 'Anti-hepatitis C antibodies and non-A, non-B post-transfusion hepatitis in the Netherlands', *The Lancet*, 5 August 1989 [LIT.001.3854]

<sup>145</sup> Ebeling et al, 'Recombinant immunoblot assay for hepatitis C virus antibody as predictor of infectivity', *The Lancet*, 21 April 1990; 335: 982 [LIT.001.0270] at 0271 and Day 71, page 108. The C100-3 antigen was used in the ELISA test and a sub-sequence of the C100-3 antigen, 5-1-1, was used in the RIBA test

<sup>146</sup> Day 71, page 88

<sup>147</sup> *Ibid*, page 89

<sup>148</sup> *Ibid*, page 86

**31.106** Professor Leikola also provided the Inquiry with a translation of a memorandum he wrote in Finnish dated 10 October 1989.<sup>149</sup> It was intended for internal discussions and for the Finnish National Board of Health, which was responsible for the practical aspects of healthcare.<sup>150</sup> He commented in his memorandum: 'Thus, HCV is not responsible for all NANB hepatitis cases, and not all anti-HCV positive persons transmit this disease, but the association of HCV with NANB hepatitis is clear in Finland.'<sup>151</sup>

**31.107** The overall prevalence of HCV positivity in Finland was considered to be 0.73%. Professor Leikola commented in his memorandum that this was 'possibly slightly higher than in the rest of Scandinavia, which number is somewhat surprising considering the clinical background'.<sup>152</sup>

**31.108** The Finnish Red Cross did not require the permission of the National Board of Health to introduce screening, but did need their consent to increase the price of blood products to reflect the increased screening costs.<sup>153</sup> This proved to be a straightforward matter and consent was given by the Director General of the National Board of Health at a meeting in December 1989. The request did not have to go to a committee and permission was granted at a single meeting, in stark contrast to the situation that evolved later in the UK.<sup>154</sup>

**31.109** In the conclusion to the memorandum, Professor Leikola stated his concern at the lack of a confirmatory test, but added:

The repeatability of the screening test is, however, good. The FDA may register the test ... before the end of this year, and the American blood services will start using it as soon as possible. Testing may start soon next year also in Europe, wherever it is technically possible.<sup>155</sup>

**31.110** In his memorandum, Professor Leikola commented that whilst most hepatitis cases remained mild, they had a tendency to become chronic, and therefore, 'Since a specific test now exists that may reduce the blood inventory by as little as less than one per cent, a general screening test has to be introduced in our country to safeguard ... transfusion safety'.<sup>156</sup>

**31.111** The memorandum, from October 1989, discussed the possibility of commencing screening in Finland in the first quarter of 1990. In practical terms, the introduction of screening was relatively straightforward for Finland as there was only one, central, laboratory in the capital, Helsinki, and donations collected by mobile teams were taken there. The introduction of screening would have affected the working of only one laboratory service and would have been much simpler than having various different centres, each with its own laboratory. It would have to be a staggered start due to a limited number of testing kits and the pressures on the laboratory. The Finnish populations with higher prevalence would be screened first. 'A similar approach was used with anti-HIV screening which was started ... [in] Helsinki area donors.'<sup>157</sup> The memorandum concluded: 'Despite the costs

<sup>149</sup> *Hepatitis C and blood donation* – Unofficial translation from Finnish by Juhani Leikola [PEN.017.1828]

<sup>150</sup> Day 71, page 93

<sup>151</sup> *Hepatitis C and blood donation* – Unofficial translation from Finnish by Juhani Leikola [PEN.017.1828] at 1829

<sup>152</sup> *Ibid* [PEN.017.1828] at 1829

<sup>153</sup> Day 71, pages 94-95

<sup>154</sup> *Ibid*, page 102

<sup>155</sup> *Hepatitis C and blood donation* – Unofficial translation from Finnish by Juhani Leikola [PEN.017.1828] at 1829

<sup>156</sup> *Ibid* [PEN.017.1828] at 1829

<sup>157</sup> *Ibid* [PEN.017.1828] at 1829

and other difficulties anti-HCV screening has to be started at the [Finnish Red Cross] Blood Service as soon as it is technically possible.<sup>158</sup>

**31.112** In oral evidence, Professor Leikola said that it was not controversial to introduce screening in a staggered fashion across the country. They had used that pattern for the introduction of anti-HIV testing, and followed the same pattern with HCV without any obvious objections.<sup>159</sup>

**31.113** Routine testing duly commenced in Finland in the beginning of February 1990 and was extended to all blood donations by 1 April of that year.<sup>160</sup>

**31.114** Dr Ebeling and colleagues proceeded to study a group of haemophilia patients in Finland.<sup>161</sup> Finland was self-sufficient in the production of clotting factors. Until 1984, small pool lyophilized cryoprecipitate (manufactured from two to eight donors) was used exclusively to treat Haemophilia A, von Willebrand's disease and Factor VIII deficiency. The total population with bleeding disorders on the central register was 230 patients. Samples were received from 137 patients, all but ten of whom had haemophilia. Surrogate tests were performed and the patients were tested with the Ortho kits. Of the study group, 68 patients (50%) from a total of 137 were anti-HCV positive, with most of the samples demonstrating strong reactivity. There was a significant association of anti-HCV with raised levels of ALT in the blood.

**31.115** The research paper on this study noted that patients with severe haemophilia had Hepatitis C antibodies significantly more often than those with milder forms of haemophilia. In addition, anti-HCV positivity was significantly more common in AHF-20 (large pool concentrate) users than in cryoprecipitate users.<sup>162</sup>

**31.116** It was noted that HCV antibodies sometimes seemed to disappear and that the percentages brought out might underestimate the number of patients with a previous HCV contact. On the other hand, the results might have been skewed in the opposite direction since patients who already knew that they had liver disease might be more willing to participate in the study.<sup>163</sup> Chiron's new RIBA confirmatory test was available to test some of the anti-HCV ELISA positive samples and proved to be very specific. It was concluded that 'false positive results were only a minor source of error among these patients'.<sup>164</sup>

**31.117** Professor Leikola was asked in oral evidence if the difficulties faced by transfusion services in dealing with 'false positives' could justify delaying the introduction of a screening test. He commented:

[I]t was very clear that as long as the number of positives ... including false positives in the primary screening is low enough so we can handle figures that are less than one per cent, and explain to the donors what is the situation ... in our opinion at the time it would not prevent introducing such a test.<sup>165</sup>

<sup>158</sup> Ibid [PEN.017.1828] at 1830

<sup>159</sup> Day 71, page 92

<sup>160</sup> Witness Statement of Professor Leikola [PEN.017.1957] at 1958. Reference is made to Chapter 9, paragraph 9.7 and footnote 6 of the Preliminary Report for the dates other countries introduced HCV screening of blood donors.

<sup>161</sup> Ebeling et al, 'Antibodies to Hepatitis C Virus and Chronic Liver Disease among Finnish Patients with Haemophilia', *Annals of Medicine*, 1990; 22:393-396 [PEN.017.1773]

<sup>162</sup> Ibid [PEN.017.1773] at 1775

<sup>163</sup> Ibid [PEN.017.1773] at 1775

<sup>164</sup> Ibid [PEN.017.1773] at 1775

<sup>165</sup> Day 71, pages 116-117

## Initial evaluation in England

**31.118** Returning to events in the UK, as noted above at paragraph 31.69 evaluation of Ortho's assay proceeded in the United Kingdom in 1989. A preliminary report of the NBTS pilot study of the first generation Ortho test, dated 23 June 1989, was presented to the third meeting of the ACVSB, on 3 July 1989. It gave summary results of tests of 3282 donations and noted that there were 22 initial reactive samples and 14 repeat reactive samples.<sup>166</sup> The report was brief and provides little useful information for present purposes.

**31.119** A second report of the pilot study, dated 10 January 1990 but relating to work undertaken in early December 1989, was presented by Dr Gunson to the fifth meeting of the ACVSB on 17 January 1990. A total of 14,133 donations had been tested by North East Thames, Trent and West Midlands RTCs.<sup>167</sup> This report assessed the practical implications of introducing the Ortho ELISA test. All participants commented that 'the test was straightforward and easy to perform'.<sup>168</sup> However difficulties with equipment and software, process problems and the marked difference in positivity rates returned, made it difficult at that stage to estimate the costs involved in screening.<sup>169</sup>

**31.120** A full report on the evaluation of the Ortho HCV ELISA test system was included in the Report on the 'Multi-Centre UK NANBH Surrogate Marker Study' dated April 1990.<sup>170</sup> The report noted that Dr Gunson had arranged a supply of test kits from Ortho sufficient to enable testing of the sera already available from the surrogate marker study.<sup>171</sup> In total 9741 samples were tested: more than 3000 at each of three centres (North London, Bristol and Manchester).<sup>172</sup> The methodology was described: 'all initially reactive sera were retested in duplicate'.<sup>173</sup> Testing was completed by early October 1989. The study found a geographical variation in the prevalence of HCV seropositivity, ranging from 1:277 for Bristol (described as 'a rural base') to 1:120 for North London (a 'metropolitan area'). There was a correlation between raised ALT and HCV seropositivity.

**31.121** The report noted:

Although from the results obtained so far it appears that the Ortho HCV ELISA has an acceptable specificity and sensitivity, these issues can not be definitively addressed as part of this evaluation, as there were no samples with well established links with NANBH tested in this study. However, this first report on screening UK donors sera for anti-HCV will serve as a basis for the future implementation of this screening test in the UK Blood Transfusion Service.<sup>174</sup>

<sup>166</sup> National Study of Surrogate NANBH Markers in Blood Donors [SNB.001.9545]

<sup>167</sup> Fifth Meeting of Advisory Committee on Virological Safety of Blood 17 January 1990 [SNF.001.1491] at page 1505

<sup>168</sup> Ibid [SNF.001.1491] at 1505

<sup>169</sup> Ibid [SNF.001.1491] at 1506

<sup>170</sup> Multi-centre UK NANBH Surrogate Marker Study [PEN.016.0075]

<sup>171</sup> Ibid [PEN.016.0075] at 0120

<sup>172</sup> Ibid [PEN.016.0075] at 0120. A total figure of 9742 donors was given at 0121 of the report, but the total number of donors from the three centres is in fact 9741.

<sup>173</sup> The Inquiry is puzzled by this statement as it appears illogical to test for a third time if the first and second tests are positive. This methodology is confirmed at [PEN.016.0075] at 0121.

<sup>174</sup> Multi-centre UK NANBH Surrogate Marker Study [PEN.016.0075] at 0123

## Initial evaluation by Dr Dow and others in Scotland

**31.122** Work proceeded on a Scottish evaluation of the Ortho assay. A preliminary report of the study was dated 5 October 1989.<sup>175</sup> The study was instigated by Professor Cash, following up his statement of interest in evaluating the anti-HCV test made at the meeting of the ACTTD on 19 May 1989. Dr Dow was a member of the team that carried out the study. He agreed that it was an ambitious study, with nine objectives.<sup>176</sup> Professor Cash had arranged to obtain the kits in June 1989. The regions each submitted samples by the start of August and testing commenced on 2 August.<sup>177</sup>

**31.123** This study had a repeat reactive rate of 0.47% overall (13/2745). There were variations within Scotland, with Aberdeen having a rate of 0.35%, Dundee a rate of 0.49%, and Glasgow a rate of 0.55%.<sup>178</sup> Dr Dow thought that the overall figure was comparable to the German figures, and considerably lower than the rate the English study found in North London.<sup>179</sup>

**31.124** Of the group of 15 patients reported to have developed post-transfusion NANB Hepatitis, Dr Dow's team found only a third (five) of the group to be anti-HCV positive.<sup>180</sup> The limited positivity in this group of 15 people was due, according to Dr Dow, to their having been tested early in their illness. It became known later that the first generation tests were not sensitive enough to pick up HCV in its early stages. They would also have failed to pick up some of the HCV genotypes that were discovered later, for example those that did not have the NS4 protein that was detected by the early Chiron test.<sup>181</sup>

**31.125** Professor Leikola's attention was drawn to this finding of the study and he agreed it was a disappointing result. He told the Inquiry that this could have been due to the way in which cases of NANB Hepatitis were identified. Further, some of the patients from the group of 15 may have had antibodies that disappeared from their blood over a prolonged period of time. He agreed also that a late appearing antibody would have been difficult to pick up if the samples had been taken early on in the progression of the disease, but he did not think that blood samples that had been frozen would yield unreliable results. In relation to patients with haemophilia, the Scottish study obtained results that can be compared with the Finnish work. Of 146 patients with haemophilia in the West of Scotland, 92 (63%) were repeatedly reactive for anti-HCV.<sup>182</sup> Dr Ebeling found 68 of 137 haemophilia patients (50%) to be anti-HCV positive: paragraph 31.114.

**31.126** Dr Dow's study also looked at sera from donors implicated in 28 cases of transmission of non-A non-B Hepatitis. This revealed only six donors as repeatedly reactive for anti-HCV. On that basis it appeared that only 21% of cases of post-transfusion NANB Hepatitis had a donor identifiable as being anti-HCV reactive. The report commented on theoretically possible explanations: individuals could lose antibody over time at one end of the scale, or at the other may not have developed anti-HCV by the time the sample was taken.<sup>183</sup>

<sup>175</sup> SNBTS Evaluation of the Ortho HCV antibody ELISA test system, Dr B Dow et al, October 1989 [SNB.006.1596]

<sup>176</sup> Day 67, page 154. The objectives were set out in the preliminary report of the evaluation: [SNB.006.1596] at 1599

<sup>177</sup> SNBTS Evaluation of the Ortho HCV antibody ELISA test system, Dr B Dow et al, October 1989 [SNB.006.1596] at 1597

<sup>178</sup> Ibid [SNB.006.1596] at 1601, Table 1

<sup>179</sup> Day 67, page 155

<sup>180</sup> SNBTS Evaluation of the Ortho HCV antibody ELISA test system, Dr B Dow et al, October 1989 [SNB.006.1596] at 1609

<sup>181</sup> Day 67, pages 158–159

<sup>182</sup> Day 71, pages 100–101

<sup>183</sup> SNBTS Evaluation of the Ortho HCV antibody ELISA test system, Dr B Dow et al, October 1989 [SNB.006.1596] at 1610; Day 67, page 160

**31.127** The authors were disappointed that their study suggested that the Ortho test would have prevented only 21% of the PT-NANB Hepatitis cases. The report suggested this might be due to some cases being caused by another agent, a possible early suspicion of what came to be known of the different genotypes in existence.<sup>184</sup>

**31.128** Overall the report authors found that ‘the Ortho HCV ELISA test has been shown to have an acceptable specificity’.<sup>185</sup> The fact that the test took three hours to complete did not present difficulties to the team testing samples in Dr Dow’s laboratory.<sup>186</sup>

**31.129** The report had noted as ‘worrying’ an apparent diminution in the sensitivity of the HCV test kit as compared with the ‘Dev’ kit. Dr Dow offered an explanation for the difference between the kits at paragraph 8 of his statement:

The test kits used in the SNBTS evaluation comprised two lot numbers, DEV89038 and HCV101. The DEV kit was probably meant to be a Developmental kit (produced in smaller volumes) whilst HCV101 would have been one of the first production lot numbers.<sup>187</sup>

**31.130** In oral evidence Dr Dow added: ‘This was one of the first times we had seen a development kit being used to do an evaluation ... we [SNBTS] had actually requested a kit to evaluate it on our own behalf, rather than the company’s behalf’.<sup>188</sup> He explained that with a ‘dev’ kit the manufacturer can still make changes, which cannot subsequently be done with a ‘production batch’.<sup>189</sup>

**31.131** This was the first time the SNBTS had had access to a test for HCV. In his evidence to the Inquiry Dr Perry said that he thought it would have been too soon for this evaluation in Scotland to form the basis of a decision to use the Ortho test. It would have been seen as a Scottish contribution to a UK wide body of knowledge and would have been likely to have gone to the ACTTD for discussion.<sup>190</sup> He expected the SNBTS to be informed in their decision making by ‘wider UK and international experience of its suitability’.<sup>191</sup> The international experience was important in studying places or populations where the test was not effective. If there had been an ‘international experience where there were significant issues and problems, then clearly that would have affected our [SNBTS] decision to introduce’.<sup>192</sup>

**31.132** Professor Leikola commented in his statement that in a low prevalence country such as the UK, a very large study is required to produce a meaningful number of positive samples to test. He added in oral evidence that ‘we [Finland] had to test 15,000 blood donors that were connected with the patients, and that only gave 11 cases and six of them were positive’.<sup>193</sup>

---

<sup>184</sup> Ibid [SNB.006.1596] at 1625; Day 67, page 160

<sup>185</sup> Ibid [SNB.006.1596] at 1625

<sup>186</sup> Day 67, page 161

<sup>187</sup> Dr Dow’s Statement [PEN.017.1915] at 1917

<sup>188</sup> Day 67, page 121

<sup>189</sup> Ibid, page 122

<sup>190</sup> Day 68, pages 29–30

<sup>191</sup> Dr Perry’s Statement [PEN.017.2108] at 2110

<sup>192</sup> Day 68, page 31

<sup>193</sup> Day 71, page 121



**31.133** Professor Leikola wrote a review article published in 1993 entitled 'Viral Risks of Blood Transfusion'.<sup>194</sup> He commented on the identification and isolation of the first clone and the study in 1989 of the first generation assay by Harvey Alter and colleagues. The assay was reported in that study to look very promising for the diagnosis and prevention of NANB Hepatitis. The test gave positive results in a high percentage of US patients with NANB Hepatitis. European experience was less promising. There were reservations about the test. The review commented:

In subsequent studies from Europe, the percentage was, however, lower. The test was sufficiently specific to study high prevalence populations such as hepatitis patients but it gave many false positive results when applied in blood donor screening. There was no true confirmatory test since everything was dependent on only one recombinant antigen.<sup>195</sup>

### Encouragement from Ortho to conclude contracts

**31.134** Dr Gunson had indicated in his letter to Professor Cash dated 26 July 1989 that Ortho representatives were keen that he should be in contract with them for test kits.<sup>196</sup>

**31.135** On 23 August 1989 representatives of Ortho attended a meeting in London with members of both the NBTS and the SNBTS.<sup>197</sup> Dr Mitchell attended and provided a report for Professor Cash two days later.<sup>198</sup> Johnson & Johnson (Ortho) had recently released material to Abbott Laboratories under licence. In addition to a royalty, the agreement ensured that Abbott would not develop any form of test similar to Ortho's test. The letter disclosed that steps had been taken to ensure that Abbott would be at least a year behind in making a distinctive test available. Abbott would not have clinical trials done before the second half of 1990. The agreement was intended to ensure that there was no competition while Ortho built up a market share. Dr Mitchell recalled in his statement that the meeting with Ortho revealed a need to improve the company's first generation test, but Ortho was still very keen to have it introduced in the UK before it was licensed for use in its country of origin.<sup>199</sup>

**31.136** The doctors in attendance were offered kits at 1989 prices if a decision to purchase was made before the end of that year. The costs of ordering kits at 1990 prices would be higher. Ortho also offered packages combining kit sales and the provision of Ortho technology. However, Dr Mitchell advised that alternatives to the early purchase options did not have the same impact since they were purely hypothetical in terms of the next one or two years.<sup>200</sup>

**31.137** The Ortho representative was keen to know if, and how, a decision on HCV testing would be made. He was told it was subject to the advice of the ACVSB, and could not possibly be made before their meeting on 17 October 1989. In addition, it would take time for screening to be introduced as a number of other associated matters would have to be organised first, such as counselling of donors, staffing and finances. It was made clear to Ortho that if a decision to introduce screening was made, 'the UK would move

<sup>194</sup> Leikola, 'Viral Risks of Blood transfusion', *Reviews in Microbiology*, 1993; 32–39 [PEN.017.1723]

<sup>195</sup> *Ibid* [PEN.017.1723] at 1724

<sup>196</sup> Dr Gunson's letter [SNB.006.1574]. See paragraph 31.69

<sup>197</sup> The transfusion service representatives were Drs Gunson, Contreras and Barbara (NBTS) and Drs Mitchell and Follett (SNBTS)

<sup>198</sup> Dr Mitchell's report [SNF.001.1449]

<sup>199</sup> Dr Mitchell's Statement [PEN.017.1901] at 1905

<sup>200</sup> Dr Mitchell's report [SNF.001.1449] at 1451

in unity and that there would be a simultaneous announcement, as happened with the HIV antibody testing'.<sup>201</sup> Dr Mitchell told Ortho there was 'little likelihood that the Scottish Transfusion directors would wish to have any kits ... until a decision was made'.<sup>202</sup>

**31.138** Dr Mitchell's letter of 25 August 1989 to Professor Cash ended:

I wish to stress that no decision was made that no (*sic*) Department of Health was committed to any decision in advance of the recommendations of the Advisory Committee which will make its own decision following the Rome meeting and taking account of all the scientific evidence which is being made available.<sup>203</sup>

**31.139** In the domestic Scottish context, Professor Cash was again being reminded that policy was a matter for the ACVSB.

### Scientific meetings in autumn 1989

**31.140** The Rome symposium organised by Ortho on 14–15 September 1989 provided a new focus for consideration of the Ortho ELISA. Dr Mitchell and Dr Gunson attended the symposium. Each produced reports intended in the first instance for the ACTTD meeting due to be held on 9 October that year.<sup>204</sup>

**31.141** Dr Mitchell commented in his Inquiry statement that the symposium was an important meeting. There was optimism that sufficient alterations would be made to the test to make it suitable for widespread introduction.<sup>205</sup> However, his view of the test as reflected in his report was less than enthusiastic. He emphasised the lack of a confirmatory test and the need, so long as that remained the position, for some form or set of control samples to be issued with the test to ensure that sensitivity was maintained. His view was that results should be repeated on a number of occasions at subsequent donor attendances before donors were counselled or notified. He noted that some of the issues with the test were 'obvious in the data collected from the Scottish survey'.<sup>206</sup>

**31.142** Dr Gunson's first report of the Rome meeting also commented on the lack of a confirmatory test and emphasised that such a test for seropositive blood donors was urgently needed.<sup>207</sup> Chiron's proposed RIBA test had limitations but would resolve some false results. The ACTTD was asked to approve in principle the routine testing of blood donations for anti-HCV and to request the National Directors in England and Scotland to arrange for the simultaneous introduction of the tests at an appropriate time when a policy had been defined for handling the seropositive donors.<sup>208</sup>

**31.143** In the interval between the Rome meeting and 9 October, the British Blood Transfusion Society met in Durham. On the last day of the meeting (around 22 September) doctors from the NBTS and the SNBTS<sup>209</sup> met with Ortho representatives. Dr Mitchell

<sup>201</sup> Ibid [SNF.001.1449] at 1450

<sup>202</sup> Ibid [SNF.001.1449] at 1451

<sup>203</sup> Ibid [SNF.001.1449] at 1453

<sup>204</sup> Dr Mitchell's report [SNB.001.8678]; Dr Gunson's report [SNB.006.1456]; Meeting Minutes [MIS.001.0016]

<sup>205</sup> Dr Mitchell's Statement [PEN.017.1901] at 1907

<sup>206</sup> Dr Mitchell's report [SNB.001.8678] at 8681. The reference was to the study by Dr Dow and others – see paragraph 31.122 onwards

<sup>207</sup> Dr Gunson's report [SNB.006.1456]

<sup>208</sup> Ibid [SNB.006.1456] at 1460

<sup>209</sup> Dr Mitchell, Mr A Barr (SNBTS), Drs Gunson, Contreras and Barbara (NBTS)

produced a note of the meeting.<sup>210</sup> He reported that Dr Gunson had indicated that, in his view, it was likely that the ACTTD would recommend to the ACVSB on 6 November that screening should be introduced in the 1990/91 financial year, and thus would commence some time after 1 April 1990. It was anticipated that the meeting of the ACTTD on 9 October would finalise the details of the report or reports to the ACVSB. Ortho had indicated that a lead-in time of at least 90 days would be required but, given that period, Ortho could supply kits on a regular basis and have at least two different batches in centres at any one time. Dr Mitchell recorded that Dr Contreras was hesitant at the speed of introduction proposed, especially since no account had been taken of how donor counselling would be carried out. She considered that some of the data presented at Rome and elsewhere were imprecise and that there were many grey areas. Nevertheless, there was recognition that the implementation of the European Commission requirements for blood and blood products was imminent (in 1992) and that member state governments might have to 'subscribe to ... "State of the Art" technology'.<sup>211</sup> By this stage (October 1989) the Chiron/Ortho test was being used in a large number of blood transfusion laboratories, as well as many virology diagnostic laboratories, throughout the world, albeit no country had yet introduced the test for routine screening of blood donors.

**31.144** The ACTTD duly met on 9 October 1989, its third meeting.<sup>212</sup> Members were told that the ACVSB had requested a briefing paper on policy regarding anti-HCV testing of blood donors. The committee considered the two papers, written by Drs Gunson and Mitchell. In addition, a report from North West Thames RTC on surrogate markers for NANB post-transfusion hepatitis was discussed. It was agreed Dr Gunson's paper should be amended for presentation to the ACVSB, to incorporate information from the paper prepared by Dr Mitchell, and the North West Thames report, and to reflect a number of textual amendments proposed by the committee.

**31.145** Dr Gunson duly amended his report for presentation to the ACVSB.<sup>213</sup> The main recommendation in Dr Gunson's amended report was that: 'Routine screening of blood donations for anti-HCV should be introduced when practical .... The committee [ACVSB] is asked to approve the routine testing of blood donations for anti-HCV in principle'. The recommendation was subject to the following conditions:

- There should be a defined policy for counselling and management of seropositive donors.
- A confirmatory test for seropositive blood donors was urgently needed. The RIBA put forward by Chiron had limitations.
- The routine use of the test should not commence until an FDA licence was in place.
- Pilot studies involving routine prospective use of the test in RTCs on freshly collected samples (as opposed to library frozen/thawed samples) should be established as soon as possible.

---

<sup>210</sup> Meeting note [SNB.002.4553]. The note and the meeting are further described at paragraph 9.145 of the Preliminary Report.

<sup>211</sup> Ibid [SNB.002.4553] at 4554

<sup>212</sup> Meeting minutes [MIS.001.0016]

<sup>213</sup> The report is part of the papers relating to the ACVSB meeting [SNF.001.1383] at 1405-06

**31.146** The fourth meeting of the ACVSB took place on 6 November 1989.<sup>214</sup> Dr Gunson spoke to his paper and told the committee that the ACTTD recommended that routine screening should be introduced only after a confirmatory test became available, after the FDA had approved the test and after urgent pilot studies had been carried out in this country to consider the feasibility of using the kits on freshly collected samples and to assess how they could be integrated into normal working practices.<sup>215</sup> The ACTTD considered that routine testing for anti-HCV would reduce the incidence of NANB Hepatitis. Estimates of the extent of the reduction ranged from 20–60%.

**31.147** The Chairman, Dr Metters, summed up the views of the ACVSB. They broadly took on board the recommendations of the ACTTD, but stopped short of approving the introduction of routine testing in principle. The feeling of the committee was that while the test represented a major step forward, the committee needed to know a great deal more about it, and there was a need for a confirmatory test. The ACVSB would support the general introduction of the test if the FDA approved it and the pilot trials showed the test to be feasible and non-problematic. Pilot studies would be carried out in Brentwood, Birmingham and Sheffield, of the feasibility of adding the kits to routine practice.<sup>216</sup>

**31.148** Dr Perry (who had not attended the meeting) commented in his Inquiry statement that, upon reading the documents, he thought Dr Gunson was trying to convey to the ACVSB the views of Transfusion Directors that the implementation of testing was inevitable. Dr Gunson was recommending to the ACTTD that the test was effective and should be taken seriously and ultimately introduced.<sup>217</sup> The minutes of the ACVSB recorded ‘a much more cautious position’.<sup>218</sup> According to Dr Perry this may have been due to the views of influential members such as Professor Zuckerman, Professor Tedder and Dr Metters.<sup>219</sup> He recalled that the ACVSB Chairman, and some of the expert Virologists, considered Dr Gunson’s approach to be ‘premature’.<sup>220</sup>

**31.149** In his written statement Professor Leikola commented that he thought the outcome of the meeting of the ACVSB noted above was ‘quite reasonable’.<sup>221</sup> In oral evidence, he qualified that statement. He said that he was a little surprised to see no clear cut decision to implement screening of donors. There was a recommendation of sorts and it was considered useful to have the test. But he explained that at this stage the FDA had not even licensed it for export, and therefore everything was on a preliminary and research level. It was ‘sort of natural that the committee was in general ... in a positive mood towards a future screening by this test but decided then to wait and see the developments and make a definitive decision later on’.<sup>222</sup> The minutes were not clear as to the committee’s commitment, but he understood the minutes to indicate that once FDA approval was given, and there was a confirmatory test, the decision would be positive if there were not any major problems.<sup>223</sup> On his understanding of the decision, that there were these automatic triggers, he thought the outcome of the meeting was reasonable.<sup>224</sup>

<sup>214</sup> Meeting minutes [SNB.001.9563]

<sup>215</sup> Ibid [SNB.001.9563] at 9566

<sup>216</sup> Ibid [SNB.001.9563] at 9567

<sup>217</sup> Day 68, page 47

<sup>218</sup> Ibid, page 49

<sup>219</sup> Ibid, page 50

<sup>220</sup> Dr Perry’s Statement [PEN.017.2108] at 2114

<sup>221</sup> Professor Leikola’s Statement [PEN.017.1961]

<sup>222</sup> Day 71, page 127

<sup>223</sup> Ibid, pages 128–129

<sup>224</sup> Ibid, page 128

**31.150** Dr Gunson reported the cautious views of the ACVSB to the next meeting of the ACTTD on 22 November 1989.<sup>225</sup> Dr Perry commented in oral evidence that ‘it was probably an outcome that was predicted ... everyone knew at that point that the UK was not ready to implement HCV testing’.<sup>226</sup>

**31.151** It appeared to Dr Perry that it was typical of the cautious approach of a government department not to make a policy decision until it was proved to be deliverable and all its consequences were known.<sup>227</sup> He thought the policy makers in the government were naturally more cautious than the practitioners who delivered the services would have wanted. In his view, that conflict would always be present.<sup>228</sup> Professor Leikola appeared to be in agreement with this view in his initial statement to the Inquiry on this topic. In relation to this period, Professor Leikola observed that opinion was divided between the views of the practical transfusionists and the academics.<sup>229</sup> He thought that Dr Gunson was a practical transfusionist.<sup>230</sup>

### Export permit and ‘confirmatory test’ in November 1989

**31.152** As appears from the discussion so far, one of the factors which featured in discussions of the possible introduction of screening in the UK over the period 1989 to 1990 was whether the FDA in the USA would approve the test for use there. In his statement Dr Perry expressed the view that waiting for the FDA to license the test kit was intended to provide the UK with evidence of satisfactory performance in the absence of a formal UK evaluation. There was no similar licensing regime in Britain. It would have been embarrassing if the test had been introduced in the UK and the FDA then refused to license it for use within the USA. He thought Ortho was unlikely to have retained their earlier export licence if the FDA had rejected the application to ‘license’ it in the USA.<sup>231</sup> In his statement, Dr Dow commented that:

The FDA were notoriously strict controllers of the quality of test kit systems. To be informed that a kit was FDA-approved meant that the manufacturers were expected to keep the same sensitivity and specificity over all lots that were produced, thus ensuring that the kits were robust quality products.<sup>232</sup>

**31.153** By way of contrast, a different, more casual, attitude to FDA licensing was reflected in a Department of Health memorandum dated 30 January 1985 relating to the introduction of screening for HIV.<sup>233</sup> The memorandum, entitled: ‘Evaluation of HTLV III kits: Some thoughts for consideration’, noted that ‘USA firms will have obtained *some sort* of FDA clearance before marketing in the UK starts’.<sup>234</sup> A different DoH memorandum dated 21 January 1985 stated: ‘We also discussed whether or not any reference should be made to tests not being accepted in the UK unless they had FDA approval ... FDA approval was in any case *one* of the factors to be considered in any evaluation’.<sup>235</sup> Dr Dow’s view is preferred: as a scientist with practical experience of the way the system operated, he

<sup>225</sup> Meeting minutes [SNB.006.2041]

<sup>226</sup> Day 68, page 51

<sup>227</sup> *Ibid*, page 53

<sup>228</sup> *Ibid*, page 54

<sup>229</sup> Professor Leikola’s Statement [PEN.017.1957] at 1958

<sup>230</sup> Day 71, page 130

<sup>231</sup> Dr Perry’s Statement [PEN.017.2108] at 2115

<sup>232</sup> Dr Dow’s Statement [PEN.017.1915] at 1920–21

<sup>233</sup> Memo [DHF.002.7016]

<sup>234</sup> Emphasis added

<sup>235</sup> Memo [DHF.002.7101] emphasis added

had direct knowledge of the working of the FDA. The reference to 'some sort of FDA clearance' indicates a lack of understanding on the part of the official.<sup>236</sup>

**31.154** Ortho Diagnostic Systems Ltd (the UK Company) wrote to Professor Cash on 27 November 1989, intimating that an export permit had been approved by the FDA for the Ortho ELISA test.<sup>237</sup> This meant Ortho could supply their product labelled for 'In vitro diagnostic use' instead of 'Research use only'. Dr Perry agreed in oral evidence that this was an optimistic early signal that the FDA would license the test for routine use within the USA.<sup>238</sup>

**31.155** On the same day, Ortho Diagnostic Systems Inc, New Jersey, faxed a second letter to Professor Cash, announcing that they had 'just completed production of a small number of prototype confirmatory tests in [their] RIBA (Immunoblot) format'.<sup>239</sup> The letter provided some details of the test format. Ortho hoped at the time of writing to introduce this confirmatory test in the first quarter of 1990. The American company intimated that C-100 antigen (the HCV protein) could not be made available to investigators for testing at that stage. The faxed letter indicated that three separate bands of antigen were used in the RIBA.

**31.156** The letters did not indicate that Ortho's ELISA had been approved by the FDA for use in the USA. One could not infer that the FDA had completed by this stage the investigations necessary for domestic purposes. However, it would be an over-cynical view to suggest that the FDA would release for use by the rest of the world a test about which it had material concerns. Dr Mitchell's report on the Rome Symposium referred to above noted that Ortho anticipated FDA licensing according to 'the agreed timetable'. The export permit was an encouraging development. It was sufficient for Finland and some other European countries to introduce routine testing in early 1990.

**31.157** It appears to be clear that information about the RIBA confirmatory test was published at the Rome symposium discussed above. Dr Mitchell appended to his report of the symposium a circular distributed by Ortho giving preliminary information on a RIBA confirmatory test then currently under evaluation.<sup>240</sup> The information was the same as set out in the faxed letter to Professor Cash on 27 November.

**31.158** Dr McClelland was asked in oral evidence about the usefulness of the first RIBA as a confirmatory test. He commented that there was a general acceptance amongst most virologists that the immunoblot tests such as the RIBA and Western Blot 'were a useful addition and provided valuable extra information to interpret the result of a positive ELISA test'.<sup>241</sup>

**31.159** He commented further in his statement:

The advantage of RIBA or WB is that with these methods a sample that gives a positive reaction with a screening test can be further analysed to show the reaction of the sample with different components of the virus, and can give additional help in distinguishing a false positive from a true positive result.<sup>242</sup>

<sup>236</sup> Professor Cash shared Dr Dow's view of the rigour of FDA assessment – see paragraph 31.210

<sup>237</sup> Ortho letter [SNB.006.1560]. At the time of writing the Preliminary Report it was known that this and the next letter [SNB.006.1561] had been written and copies were obtained later. See paragraph 9.162 of the Preliminary Report.

<sup>238</sup> Day 68, page 58

<sup>239</sup> Fax [SNB.006.1561]

<sup>240</sup> Circular [SNB.002.4555]

<sup>241</sup> Day 69, page 23

<sup>242</sup> Dr McClelland's Statement [PEN.017.2491] at 2497

**31.160** Dr McClelland thought the RIBA represented added value and information.<sup>243</sup> He added, however, that some groups of virologists, notably one led by Professor Tedder, felt the RIBA tests 'were a waste of time'.<sup>244</sup>

**31.161** Dr Dow had his own concerns about the value of the RIBA as a 'confirmatory' test. He commented in his statement:

[T]he first generation RIBA was based on only two specific HCV recombinant proteins which were both products of the same area of the genome (the non-structural (NS) 4 region). As both these recombinant proteins were the coating materials for the solid phase ELISA microwell, it was predicted that the same cross-reacting antibodies would produce (false positive) reactives in both ELISA and RIBA systems.<sup>245</sup>

### **The end of 1989: comment**

**31.162** In the course of 1989, the NBTS and the SNBTS each obtained test kits from Ortho for evaluation. There is no evidence to suggest that they could have been obtained earlier. Dr Gunson and Professor Cash agreed that the two services should act in close collaboration and envisaged difficulties if either should introduce the test unilaterally. Each proceeded with evaluation.

**31.163** By the end of August 1989, UK commentators appear to have formed a generally favourable view of the first generation Ortho test, but there were still reservations. Drs Contreras and Barbara were concerned about the predictive value of the test in low HCV prevalence populations, such as UK blood donors. Professor Cash, Dr McClelland and others thought that without a confirmatory test there would be serious problems for the Blood Transfusion Services in differentiating between true and false positives. There was concern that repeat and supplementary testing based on a common antigen source – both in initial screening kits and in the early RIBA format – failed to provide the confirmation required.

**31.164** The preliminary report of the NBTS pilot study was available in June 1989, with a second report in January 1990. As finally reported, in April 1990,<sup>246</sup> the study found that the first generation Ortho HCV ELISA tests appeared to have an acceptable level of specificity and sensitivity, albeit these issues could not be addressed definitively as part of the evaluation. There were no samples with well established links with NANB Hepatitis available to be tested.

**31.165** While Dr Dow's study in October 1989 reported disappointing results in a group of 15 patients 'known' to be positive for transfusion-transmitted NANB Hepatitis, the study nonetheless concluded that the Ortho test had an acceptable level of specificity. There is no doubt, on Professor Cash's evidence, that the Glasgow laboratories were the most experienced researchers in this area in Scotland at the time. They were the right people to carry out the assessment of the Ortho ELISA kits.

**31.166** As discussed above, a very different approach was adopted in Finland. The Finnish National Board of Health was open to advice from the Finnish Red Cross. The

---

<sup>243</sup> Day 69, page 28

<sup>244</sup> Ibid, page 24

<sup>245</sup> Dr Dow's Statement [PEN.017.1915] at 1919

<sup>246</sup> Report of Multi-centre UK NANBH Surrogate Marker Study [PEN.016.0075]

Red Cross did not need consent for the introduction of tests, but did need consent to raise prices: the consent was easily obtained. Professor Leikola was concerned at the lack of a confirmatory test but thought that, in light of the risk of chronic illness, since there was a test it had to be introduced. It was duly introduced in February 1990. Local circumstances are important. What was acceptable in Finland would not necessarily have been acceptable in the UK. Competent experts may reasonably take different views.

**31.167** The Inquiry accepts that there would have been difficulties in introducing the Chiron test kit for routine use at the end of 1989. It was not licensed by the FDA for export until November 1989, the need for a confirmatory test had not been met and pilot testing in the UK was thought necessary. It is of concern, however, that there was no firm intention to recommend screening once these conditions had been met. On 9 October 1989 the ACTTD had Dr Gunson's report, agreed amendments, and was prepared to submit it to the ACVSB. From the terms of the amended report, the ACVSB was fully informed when it met on 6 November as to the conditions that had to be met for the introduction of the test in the UK. On the information available, FDA approval, at least for export, could have been seen to be imminent after the Rome meeting. The ACVSB appeared unwilling to go further than offering support for 'general introduction' if the three conditions were met, and to developing an economic case for the DoH to fund routine use of the test. The date fixed for the next meeting of the committee was 17 January 1990. It would be six weeks before the ACVSB was expected to resume consideration of the issue. Professor Leikola's surprise that there was no firm decision on 6 November is understandable. Associated with the lack of a firm intention to introduce routine screening, was the decision that there was no case for introducing surrogate tests for NANB Hepatitis. In combination, the decisions put action on hold over the end of 1989 and early 1990.

### Events of 1990

**31.168** The ACVSB met for the fifth time on 17 January 1990.<sup>247</sup> The pilot study agreed to in November 1989 had been completed and approximately 5000 tests had been conducted at each of three centres, Brentwood, Birmingham and Sheffield. The percentage of repeatedly reactive donors at these centres was, respectively, 0.61%, 0.28% and 0.18%.<sup>248</sup>

**31.169** There was a full discussion of NANB Hepatitis and the issue of HCV testing. By now the FDA had approved the Ortho ELISA for export. Professor Zuckerman proved to be a powerful voice at that meeting. He recommended a delay in the introduction of testing until the FDA had approved the test for use in the USA and thought the FDA was unlikely to license the test in the absence of a confirmatory test (although by now information about the forthcoming Chiron RIBA confirmatory test was quite widely known).<sup>249</sup>

**31.170** It was also the understanding of Dr Rotblat of the DoH that the FDA was unlikely to approve the test at this stage. If the minutes are reliable, Dr Gunson did not comment that an export licence had already been granted. However, Professor Zuckerman added in a letter considered by the ACVSB that 'the introduction of screening could not be delayed much beyond FDA approval'.<sup>250</sup> He noted in his letter that test kits were being

---

<sup>247</sup> Meeting Minutes & Associated Documents [SNF.001.1491] at 1493

<sup>248</sup> Report of the pilot trial dated 10 January 1990 [SNF.001.1491] at 1505

<sup>249</sup> Meeting Minutes & Associated Documents [SNF.001.1491] at 1494 and paragraph 9.172 of the Preliminary Report

<sup>250</sup> Ibid [SNF.001.1491] at 1512



developed by other manufacturers and added at the meeting that the committee should keep an open mind on other, newer test kits, which should be available within the next 12 months.<sup>251</sup>

**31.171** The minutes record mixed views from others in attendance. For example, Professor Tedder was reluctant to make recommendations at that time as so little was known about the virus and its antibody markers, but Dr Mortimer was keen to introduce screening and considered that if routine use of the test began there should soon be a better test to move on to.<sup>252</sup> Dr Mitchell felt that it was possible to deal with donors who tested positive, without causing undue alarm. Dr Gunson explained that the transfusion services were under a great deal of pressure, not just from Ortho but from the press and, increasingly, from clinicians in the field. He felt that 'each centre must now consider how to set up the test and what extra resources they would need to do so'. In oral testimony Dr Perry denied there were widely divergent opinions at that meeting, just simply various views about different aspects of testing, according to individual areas of expertise.<sup>253</sup> Cost was an important consideration, but a strict cost/benefit analysis was never a topic for discussion at the ACVSB.<sup>254</sup>

**31.172** Dr Perry told the Inquiry the ACVSB members did not vote.<sup>255</sup> As a matter of procedure, each member had to express a personal view and it was for the Chairman to elicit such consensus as could be identified. The Chairman, Dr Metters, would summarise the main views of the committee and members were invited to agree or disagree with him.<sup>256</sup> At this stage there was insufficient consensus to form a definite recommendation or decision.<sup>257</sup> There was an emphasis on understanding scientific principles and a desire to be sure the test was appropriate before a policy could be announced.<sup>258</sup>

**31.173** The general consensus of this meeting was summed up by the Chairman: routine testing was not to be introduced in advance of the FDA decision and not enough was known scientifically at that time as yet.<sup>259</sup> After further discussion the committee agreed that the costs of introducing testing in each region should be looked at now, Professor Zuckerman's figures on the number of possible cases of chronic liver disease that could be prevented by the introduction of testing should be further refined and the committee could give no further scientific advice at that point, but would discuss the matter further at the next meeting (in April) which would be after the International Hepatitis Meeting in Houston. There was no clear recommendation that testing should be introduced as soon as the FDA had given the green light to the US blood banks.<sup>260</sup>

**31.174** The minutes of the meeting recorded Dr Metters as saying that 'funding would have to be found from the existing ... allocation'.<sup>261</sup> The minute clearly recorded Dr Metters' understanding of UK Government policy: there would be no new money for screening and health boards (at least in England and Wales) would have to find the necessary funds within their existing budgets.

---

<sup>251</sup> Ibid [SNF.001.1491] at 1495–96

<sup>252</sup> Ibid [SNF.001.1491] at 1496

<sup>253</sup> Day 68, page 66

<sup>254</sup> Ibid, page 69

<sup>255</sup> Ibid, page 76

<sup>256</sup> Ibid, page 70

<sup>257</sup> Ibid, page 70

<sup>258</sup> Ibid, page 71

<sup>259</sup> Meeting Minutes & Associated Documents [SNF.001.1491] at 1496–97

<sup>260</sup> Professor Leikola's Statement [PEN.017.1961]

<sup>261</sup> Meeting Minutes & Associated Documents [SNF.001.1491] at 1496

**31.175** Dr Perry's note of the fifth meeting of the ACVSB also recorded that:

[The] majority view was that [there was] sufficient evidence of test positive/infectivity correlation to justify implementation – overriding factor was question of product liability .... Agreed not to introduce test in advance of FDA approval but very compelling reasons to implement quickly following U.S. decision.<sup>262</sup>

**31.176** It was put to him in oral evidence that his note suggested that a 'fly on the wall' at the meeting, ie a completely independent observer, would have concluded that the committee was in favour of introducing the test, the deciding factor being the question of product liability. In response Dr Perry agreed that is how it read, and that while his hastily written note did not contain a full record all of the arguments put forward for and against the introduction of testing, it would have reflected at least the 'mood' of the committee as detected by him.<sup>263</sup> Notwithstanding his reservations about his note, there is no reason to think that what Dr Perry recorded failed to reflect the discussion: yet the absence of any reference in the minutes of the meeting to product liability as a factor (when Dr Perry's note suggests it was the overriding factor in favour of implementation) raises a question whether the formal minutes fully reflect the discussion that took place.

**31.177** On 16 March 1990 the ACTTD met for the fifth time.<sup>264</sup> It noted that the ACVSB had at its last meeting deferred the decision to introduce routine screening of blood donations for anti-HCV.

#### **Discussion at April meeting: change of tone since January?**

**31.178** The sixth meeting of the ACVSB on 24 April 1990<sup>265</sup> was dominated by discussion of HCV testing. The meeting followed two symposia. One, sponsored by Ortho, was held in London in February 1990. The other, sponsored by Abbott, was held in Chicago on the same day as the Ortho symposium. Dr Andrzej Rejman (Senior Medical Officer at the DoH and member of the ACVSB Secretariat) attended the Ortho symposium. Dr Mitchell and Professor Zuckerman attended and reported to the ACVSB on the Abbott conference. Reports of the proceedings appear to have had a significant influence on the committee. In particular, one of the factors that appear, at least in retrospect, to have influenced the decision of the committee on HCV testing was the report of the Ortho symposium.

#### *The Ortho symposium*

**31.179** Papers for the ACVSB meeting in April, circulated in advance, included documents apparently assembled by Dr Rejman and relating to the Ortho symposium. The papers included a brief synopsis of the contribution of each of a number of speakers, together with an abstract of the presentation of each speaker to the symposium. The bundle was prefaced with the secretariat's impressions of the event.<sup>266</sup>

**31.180** At the invitation of the Chairman, Dr Rejman opened the discussion on the Ortho symposium by expressing the view that 'the overall impression was that the test was not sensitive or specific enough for reliable testing' and that a confirmatory test and more information about the significance of positive results were needed before the Ortho test could be used for the routine screening of healthy donors. Dr Mortimer is reported to

---

<sup>262</sup> Ibid [SNF.001.1491] at 1500

<sup>263</sup> Day 68, pages 75-76

<sup>264</sup> Meeting Minutes [SNB.001.8763]

<sup>265</sup> Note of Meeting [SGH.002.7947]; Meeting Minutes [SNB.001.9761]

<sup>266</sup> Report on Ortho HCV Symposium [SNF.001.1628]

have said at the ACVSB meeting that there was an underlying feeling against screening because of the lack of confirmation tests, but that:

He thought confirmatory testing would become available within a reasonable time and that the routine screening of blood donors could not be delayed for a long time.<sup>267</sup>

**31.181** Professor Zuckerman, who again was a powerful voice at the meeting, echoed disappointment at the outcome of the symposium. He said that the non-specificity and sensitivity of the Chiron/Ortho test had been the main talking points at the London symposium.<sup>268</sup>

**31.182** Dr Barbara had presented a paper to the symposium on 'HCV and Blood Transfusion Service'.<sup>269</sup> In his view, the ELISA test was a 'turning point of years of frustrating search' for the agent of NANB Hepatitis, but left many important questions for the transfusion service, which were being researched. In particular, his abstract stated that 'the predictive value of a positive anti-HCV result in a blood donor in relation to transmissibility of NANB Hepatitis is still under active study'.<sup>270</sup> The imminent availability of supplementary tests from Ortho was welcome and was expected to reveal relevant information. Dr Barbara had also commented in his paper that Chiron had recently described cDNA polymerase chain reaction for HCV RNA which would shed some light on the infectivity of anti-HCV positive donors.<sup>271</sup>

**31.183** Dr Rejman's note of Dr Barbara's presentation recorded concern about how to address the issue of 'false-positive' donors. It struck a note of caution in the summary: 'Several "HCVpos[itive]" donors have not transmitted either transaminitis or HCV. How can "false positives" be addressed, this is of great concern?'.<sup>272</sup>

**31.184** Dame Sheila Sherlock in her 'HCV and Autoimmunity' abstract presented at the London symposium, noted that, in that context, 'Clearly the relation of anti HCV to actual hepatitis C disease must be clarified. Better tests are needed for the hepatitis C virus'.<sup>273</sup>

**31.185** The summary of the paper by Dr G Dusheiko entitled 'Hospital diagnosis of HCV' concluded: 'The Ortho test is in its infancy, it is not infallible and there are no QC [quality control] panels available to check its reactivity'.<sup>274</sup>

**31.186** The notes of Dr Mortimer's presentation recorded further caution: 'There are no confirmatory tests at present .... The Ortho HCV [antibody] is a late [antibody], appearing 130-150 days post-transfusion .... Presence of [antibody] does not mean/imply infectivity'.<sup>275</sup> Dr Mortimer had stated in his short abstract that the Chiron/Ortho test 'detects an antibody thought to be present in many who have been infected with HCV'.<sup>276</sup>

<sup>267</sup> Meeting Minutes [SNB.001.9761] at 9762

<sup>268</sup> Ibid [SNB.001.9761] at 9762

<sup>269</sup> Report on Ortho HCV Symposium [SNF.001.1628] at 1636

<sup>270</sup> Ibid [SNF.001.1628] at 1637

<sup>271</sup> Ibid [SNF.001.1628] at 1638

<sup>272</sup> Ibid [SNF.001.1628] at 1636

<sup>273</sup> Ibid [SNF.001.1628] at 1652

<sup>274</sup> Ibid [SNF.001.1628] at 1654

<sup>275</sup> Ibid [SNF.001.1628] at 1641. The word 'necessarily' in the second sentence would improve the accuracy of this note: Dr Perry, Day 68, page 84.

<sup>276</sup> Report on Ortho HCV Symposium [SNF.001.1628] at 1643

*Ortho symposium: a contrasting view*

**31.187** Following his attendance at the Ortho symposium, Dr Frank Boulton (Deputy Director of the Edinburgh Blood Transfusion Centre) wrote a letter on 21 February 1990 to Professor Cash,<sup>277</sup> Dr Boulton felt very strongly that the screening of donors should be introduced at the earliest opportunity. The test was not perfect, but there was little doubt people had contracted HCV as a result of transfusions which they would not have received if there had been screening for HCV antibodies. He was concerned that the SNBTS would face future litigation from people infected with HCV from blood that could have been screened.

**31.188** Dr Boulton had, in addition to a letter, composed a five page report of the material presented at the symposium.<sup>278</sup>

**31.189** The contrast between the negative tone of Dr Rejman's comments and Dr Boulton's observations raises issues, reflected in Dr Perry's evidence, as to the part played in the discussion by academic virologists, and about the role of the secretariat.<sup>279</sup> Dr Perry suggested that, at this point 'the best [was becoming] the enemy of the good'.<sup>280</sup>

**31.190** Professor Cash said in oral evidence that he agreed with Dr Boulton's view. He had been satisfied with the results of the first study done in Glasgow. The specificity of the Chiron/Ortho test was acceptable. He thought at the time that no test for HCV was going to be perfect and 'something was better than nothing'.<sup>281</sup>

*The Abbott symposium*

**31.191** As noted above, Dr Mitchell and Professor Zuckerman reported to the ACVSB on a conference held by Abbott in Chicago on the same day as the Ortho symposium. Dr Mitchell brought back a list of guidelines dated 8 February 1990, issued by the American Association of Blood Banks (AABB), the American Red Cross and the Council of Community Blood Centres.<sup>282</sup> Despite the absence of FDA licensing, these organisations were willing to issue guidelines for screening for anti-HCV. They directed that screening should commence as soon as FDA approval had been given. Professor Leikola thought they must have had some knowledge that the RIBA confirmatory test was coming, and consequently the FDA approval would not be far behind it.<sup>283</sup>

**31.192** Professor Cash sent a copy of the guidelines to Dr McIntyre at the SHHD with a letter dated 19 February 1990.<sup>284</sup> According to a manuscript note on the letter dated 5 March 1990 (written by Mr Roderick Angus, SHHD<sup>285</sup>), Dr McIntyre copied the guidelines to Dr Pickles of the DoH in London. Mr Angus went on to note that he had spoken to a civil servant in the DoH who told him the press statement had: 'stirred up a hornets nest. She asked for further info on it, in particular was the statement issued'.<sup>286</sup>

<sup>277</sup> Letter [SNB.014.1644]

<sup>278</sup> Report of HCV Symposium Organised by Ortho [SNB.014.1645]

<sup>279</sup> A note of the meeting prepared by Dr Perry [SNF.001.1710] at 1711, reported that discussion on HCV testing was 'dominated by reports and discussions by academic virologists!'

<sup>280</sup> Day 68, page 136

<sup>281</sup> Day 72, page 137

<sup>282</sup> Guidelines for Planning the Implementation of Anti-HCV Testing of Blood and Components for Transfusion [SNB.001.9825]

<sup>283</sup> Day 71, page 134

<sup>284</sup> Letter [SGH.002.8477]

<sup>285</sup> Confirmed by Mr Angus in his Statement [PEN.017.2084] at 2086

<sup>286</sup> Letter [SGH.002.8477]

**31.193** Mr Angus himself commented in his Inquiry statement that he could not recall the specific circumstances but thought:

[I]t would be reflecting the unexpectedness of the American announcement and the expectation of calls for the immediate introduction of similar testing in the UK. The reference to having “stirred up a hornet’s nest” reflects that unanticipated nature of the announcement rather than any anger felt by anyone.<sup>287</sup>

**31.194** Dr Mitchell thought Dr McIntyre’s communication with the DoH indicated that there were significant developments on their way and, once the main impediment had been removed, screening should be introduced in the UK.<sup>288</sup>

**31.195** Professor Cash in his oral testimony did not disagree with the suggestion put to him that upsetting the ‘hornet’s nest’ was caused by bringing into very sharp focus the likelihood of the USA introducing screening in early course, and this being at odds with the seemingly slow progress in the UK.<sup>289</sup>

**31.196** However, that apart, information about the AABB guidelines was clearly circulating within the SHHD and the DoH before the ACVSB meeting.

#### *The ACVSB minutes*

**31.197** At the ACVSB meeting itself, Professor Zuckerman stressed that the major cause of PTH was the NANB virus. He commented on the Abbott symposium. He noted that there was evidence of different ‘strains’ of the Hepatitis C virus which would have serious implications for diagnosis and the development of vaccines. He commented on the findings of US studies showing that the predictive level of anti-HCV positivity for infection was about 77% and recommending that positive donors should be deferred. He also reported the results of testing Abbott’s RIBA test and remarked on his view that the RIBA was not good enough to use routinely as a confirmatory test. He thought that the conference had been rather promotional in character.<sup>290</sup>

**31.198** Professor Tedder tabled a paper on the use of a modified PCR assay for the detection of HCV sequences in anti-C100 positive donations.<sup>291</sup> The PCR test, unlike the ELISA and RIBA tests, detected Hepatitis C antigen, rather than antibody. Study had shown the method to be a useful confirmatory test for detecting virus particles in the bloodstream. The assay was not, in its present form, suitable for mass screening needs, but recent modifications of PCR technology indicated its potential for large scale-testing.

**31.199** Dr Mitchell reported on proceedings at the symposium hosted by Abbott.<sup>292</sup> He said that the vast majority of Hepatitis C cases were not transfusion-related. With high-risk groups, anti-HCV positivity was high, but in a cross section of blood donors concordance was much lower. As discussed above, he reported that the AABB had directed that testing for anti-HCV should be introduced as soon as FDA approval had been given.

---

<sup>287</sup> Mr Angus’ Statement [PEN.017.2084] at 2086

<sup>288</sup> Day 69, page 171

<sup>289</sup> Day 72, page 135

<sup>290</sup> Meeting Minutes [SNB.001.9761] at 9763; Professor Zuckerman’s notes from the International Viral Hepatitis and Liver Disease Conference [SNF.001.1700]

<sup>291</sup> The paper was later published in *The Lancet*, 16 June 1990 [LIT.001.0263]

<sup>292</sup> Meeting Minutes [SNB.001.9761] at 9762

**31.200** Before opening the subject of testing to general discussion, the Chairman of the ACVSB, Dr Metters, reported that France, Belgium and Luxembourg had introduced routine screening of blood for HCV antibody. Italy had introduced the test on a voluntary basis. He went on to remark that, from the reports, the science seemed to have advanced little from the time of the previous meeting of the committee.<sup>293</sup> There were still questions whether the anti-HCV test was reliable and a useful step forward or whether it still created too many problems at that stage.

**31.201** After further contributions, the Chairman summed up the discussion:

- there was inadequate scientific data to support the introduction of the Ortho test for routine screening;
- a confirmatory test was needed which could be used in the RTCs and not just specialised laboratories;
- the FDA had not yet approved the test and it would be reassuring if the regulatory authority in the country of origin had done so;
- there was a need to learn more about the donor panels and the significance of positive reaction to the hepatitis C antibody test;
- a prospective study involving 25–50,000 donors would generate sufficient positives for confirmatory testing.<sup>294</sup>

**31.202** Dr Metters was concerned that there should be no confusion about the respective roles of the ACVSB and the ACTTD. He said:

The ACVSB advised Ministers on the virological safety of blood. The UKBTS Committee considered the operational implications of policy, gave the Department advice on safeguards against non-viral threats to blood and contributed to the advice on viral safety through input to the ACVSB.<sup>295</sup>

**31.203** The DCMO intended to write to Dr Gunson as Chair of the ACTTD in order to agree their respective roles. Dr Gunson was noted as confirming that he shared Dr Metters' view of the roles and thought there was no conflict between the committees. Whatever may have been the basis for the Chairman's concerns, the minute is further evidence that the decision whether to introduce HCV testing of blood donations was a matter of policy, to be decided by the government, on the basis of the expert advice of the ACVSB, rather than being a matter for the blood transfusion services. It is a matter for comment that, in emphasising the subordinate role of the ACTTD, Dr Metters implicitly accepted that it was the unqualified responsibility of the ACVSB to provide the government with the scientific advice required for formulating policy in this area.

**31.204** Dr Perry said in his Inquiry statement that he could not recollect the DCMO providing an explanation at the time of the need for his statement of intent. He speculated that 'the statement was intended to be an assertion of the authority of ACVSB to make policy recommendations ... and that ACTTD was subordinate to this authority'.<sup>296</sup> The question, however, is why such an assertion was required. It appears that, by this time, the respective roles of the ACVSB and the ACTTD had become an issue between them.

---

<sup>293</sup> Ibid [SNB.001.9761] at 9763

<sup>294</sup> Ibid [SNB.001.9761] at 9764. A subgroup including Dr Gunson and Dr Mitchell was set up to draft a protocol

<sup>295</sup> Ibid [SNB.001.9761] at 9765

<sup>296</sup> Dr Perry's Statement [PEN.017.2108] at 2109

**31.205** Dr McIntyre produced a note of the meeting for the SHHD that reflected the negative conclusions of the committee but confusingly recorded that 100,000 donors were contemplated for the proposed study.<sup>297</sup> Rather than proceeding to recommend that testing should be introduced, with or without conditions, the committee decided to initiate a large prospective study to investigate the significance of a positive test result and a sub-group was set up to prepare a protocol.<sup>298</sup> It was to include Dr Gunson and Dr Mitchell.

**31.206** Dr Perry reported back to Professor Cash in a personal note.<sup>299</sup> It was intended to convey his view of the meeting to a selected audience, whilst still being bound by the rules of confidentiality. Both he and Dr Gunson had felt there was sufficient data for testing to be introduced. He denied in oral evidence that he was suggesting in his note that the blood transfusion services were ready to introduce the test in April 1990. Rather, there was enough information for the government to make a policy decision that the test could, and should, be introduced in future. Other Western countries were beginning to introduce it and he thought the UK could adopt a more positive approach rather than hanging back and waiting for the science to improve.<sup>300</sup> He told the Inquiry in his statement that he shared this feeling with Dr Gunson.<sup>301</sup> He recalled this meeting as being the first point at which he thought there was information available to make a good case for the introduction of testing.<sup>302</sup>

**31.207** However, the outcome was that the meeting of the ACVSB on 24 April 1990 did not recommend the introduction of screening. Professor Leikola said in oral evidence about the material from the Ortho symposium:

It's very natural that in that kind of symposium, the investigators, they are not marketing people for this commercial manufacturer, but they want to have a critical approach to these tests and I think it's natural that they emphasise the fact that they have found, you know, that it's not a perfect test and so on. So much are not detected and so many are false positives also. But to draw this conclusion that it should not be introduced at that time, I think I, at least, couldn't make out of these abstracts.<sup>303</sup>

**31.208** With regard to Dr Rejman's comment that the test was not 'sensitive or specific enough for reliable testing', Professor Leikola pointed out in oral testimony that the tests were considered good enough by the Finnish authorities for screening to have been introduced in early 1990.<sup>304</sup> Professor Leikola commented in his Inquiry statement that the 'change of attitude of the ACVSB between January and late April was remarkable'. He added: 'The reservations as to routine screening had meanwhile grown'.<sup>305</sup>

---

<sup>297</sup> Note of meeting [SGH.002.7947]

<sup>298</sup> Meeting Minutes [SNB.001.9761] at 9764-65

<sup>299</sup> Dr Perry's note [SNF.001.1710]

<sup>300</sup> Day 68, page 101

<sup>301</sup> Dr Perry's Statement [PEN.017.2108] at 2115

<sup>302</sup> Day 68, pages 93-94

<sup>303</sup> Day 71, page 136

<sup>304</sup> Ibid, page 137

<sup>305</sup> Professor Leikola's Statement [PEN.017.1961] at 1962

### FDA approval May 1990

**31.209** On 2 May 1990, a week after the ACVSB meeting, the US FDA licensed the Chiron/Ortho anti-HCV ELISA test for use in the USA. Ortho announced on 4 May that the kits were being shipped to US blood centres and that screening of the US blood supply would commence immediately.<sup>306</sup> The announcement added that Ortho was supplying anti-HCV test kits to Europe, Japan, Canada and Australia.

**31.210** Professor Cash told the Inquiry in his statement, that FDA licensing was regarded as important. The scientific process of assessment of diagnostic kits by the FDA was rigorous. No kit licensing arrangements existed in the UK.<sup>307</sup>

**31.211** In his oral testimony Professor Leikola said that FDA licensing was not an important factor for the Finnish Red Cross. They had decided to proceed with the test based on their own observations and opinions on the Ortho kit. The earlier grant of an export licence to Ortho was enough for them to proceed, and they were not deterred by the possibility the FDA might refuse to license the test for use in the USA. Professor Leikola added that the FDA dealt with different issues when considering the blood transfusion system in the USA and their relationship with the blood banks and different laboratories. It was more complex in the USA. In Finland they had just one laboratory which had decided the test kit worked satisfactorily, and they did not expect the FDA to refuse to license its use 'in-country'.<sup>308</sup>

**31.212** If the FDA had refused to license the test in the USA, the Finnish Red Cross would have had to consider the reasons for that and decide if it was relevant to them and to consider any impact on their own screening system that might result. If there was something incorrect in the manufacturing of the test kit or inconsistencies between batches of the tests it would have impacted on the quality of the test kit and caused concern in Finland.<sup>309</sup>

**31.213** In a letter dated 11 May 1990, Ortho in the UK wrote to Professor Cash to confirm the arrival of its RIBA test: 'This exciting new assay is designed to detect the presence of antibodies to hepatitis C virus in samples that have given a positive result with the Ortho\* HCV antibody ELISA test'.<sup>310</sup> The letter from Ortho did not comment on whether the RIBA was developed as a 'confirmatory' or a 'supplementary' test, simply that it could detect the presence of antibody to HCV in samples which already tested positive with the ELISA. In later practice, the PCR test became the preferred confirmatory test as it detected the virus itself and was based on a different principle. Professor Cash considered the first RIBA to be a supplementary test, rather than a confirmatory test. But it did assist in convincing scientists that they had found a true positive.<sup>311</sup>

### July 1990 meeting of ACVSB brought forward

**31.214** Dr Metters wrote to members of the ACVSB on 5 June 1990.<sup>312</sup> He advised that the extended prospective study discussed at the last meeting to investigate the significance of positive findings from the anti-HCV ELISA test, was no longer considered appropriate

<sup>306</sup> Ortho announcement [SGF.001.2036]

<sup>307</sup> Professor Cash's Statement [PEN.017.2094] at 2101; see paragraph 31.152

<sup>308</sup> Day 71, pages 119–120

<sup>309</sup> Ibid, page 120

<sup>310</sup> Letter [SNB.004.5013]

<sup>311</sup> Day 71, page 112

<sup>312</sup> Letter re: ACVSB Meeting [SNB.002.0245]



'in light of subsequent developments'. These developments were said to be (unspecified) additional scientific information that had become available and the fact that the FDA had approved the Ortho test for routine use in the USA. He indicated a fairly urgent wish to bring the next ACVSB meeting (which had been fixed for 24 July) forward to 2 July and devote it entirely to Hepatitis C testing and felt the committee now needed to consider whether UK blood donations should be routinely screened for Hepatitis C.

**31.215** He set out the questions to be addressed:

1. What new information is available about the screening tests themselves, or on the use of supplementary (RIBA) and confirmatory (PCR) testing methods?
2. Has the FDA decision to approve the test and decisions of other countries to implement testing been influenced by some scientific or other information which has now become available?
3. Are there any advantages attached to either of the two tests currently available (Abbott and Ortho) in respect of specificity, sensitivity, operational ease of use, cost?
4. If routine testing were to be introduced what implications would this have for the UK BTS? How would positive findings (*sic* – probably 'findings') be dealt with? What supplementary or confirmatory testing would be required and where would this be carried out? How and when would the donor be counselled?
5. If testing is to be introduced in the UK should it be limited to whole blood or also extended to plasma donations bearing in mind the supposed efficacy of heat treatment? Are all current methods of viral inactivation successful in respect of hepatitis C?<sup>313</sup>

**31.216** On 6 June 1990 Dr McIntyre wrote a memorandum to Dr Young (DCMO, SHHD) commenting on Dr Metters' letter and the fast moving developments that were taking place.<sup>314</sup> Dr McIntyre had little doubt that the committee would recommend the introduction of the screening test. He remarked that the large prospective study planned at the last meeting was to be abandoned as it was no longer appropriate and advised that matters should be put on hold pending the ACVSB meeting on 2 July. Mr Panton of SHHD added a manuscript note to the memorandum, addressed to his colleague Mr Hogg, to tell him they should still press for funds despite the study being abandoned.

### Further new study

**31.217** The ACVSB met on 2 July 1990 for 'reconsideration' of the decision made at the committee's April meeting.<sup>315</sup> Dr Rejman outlined the sequence of significant events: the FDA had approved Hepatitis C screening, the USA had introduced it and other countries were following. He said that more studies had been carried out confirming that Hepatitis C testing reduced infection, and that RIBA was available as a supplementary test. The minute does not identify the additional studies although the agenda noted that a summary

---

<sup>313</sup> Note of a Meeting of the ACVSB on 02 July 1990 [SNB.002.0247]

<sup>314</sup> Memo [SGF.001.2034]

<sup>315</sup> Meeting Minutes [SNF.001.1705]

of the basis for approval by the FDA had been tabled. The proposed extended prospective study agreed at the previous meeting was 'no longer viable'. Professor Zuckerman felt it was time for screening to go ahead on public health grounds, although he thought counselling would pose some difficulty.

**31.218** After discussion, the committee concluded that it should recommend to Ministers that anti-HCV screening should be introduced, but that a pilot study was necessary first, to look at both the Abbott and the Ortho kits using the protocol drafted for the initial aborted study, to decide which was the better test kit.<sup>316</sup> The first two questions posed by Dr Metters appear to have been disposed of without separate discussion. Further study would resolve question 3. Question 5 was dealt with on what appears to have been a sensible basis: antiviral treatment was not guaranteed to be effective, and consistency required that all donations be treated alike. The matter of counselling, as focused in question 4, was discussed: national consistency on this was required and the working group would continue to look at the whole topic of counselling.

**31.219** Dr Gunson advised that Wellcome (a British company) was also developing a test which would be ready in September/October. The pilot study would go ahead without delay and frozen library samples would be kept so that donations could be retested later against other tests, such as Wellcome's, as they became available.

**31.220** A draft proposal for a three centre comparative trial of the first generation Abbott and Ortho tests was circulated at the ACVSB meeting.<sup>317</sup> The document noted that evidence from Finland indicated that supplementary testing at specialist laboratories should eliminate approximately two-thirds of the reactive samples. The comparison was to be done at North London, Newcastle and Glasgow RTCs, which would each carry out around 3500 tests. Confirmatory tests were to be carried out using Ortho RIBA, Abbott confirmatory test, and immunoassays based on other HCV proteins (if available). This study would take around four months to complete once finance was agreed. Contrary to the impression that might be created from the meeting having been advanced by three weeks, as Professor Leikola commented in his second statement, 'there was still no rush'.<sup>318</sup>

**31.221** According to Dr Mitchell, the comparative study was necessary because not all laboratories were using the same technology. Some were already familiar with Ortho technology and some with Abbott. It was important for the three laboratories involved to compare results from the two test systems and try to ensure they had detected the same thing.<sup>319</sup>

**31.222** Dr Perry thought the studies had different objectives.<sup>320</sup> In his statement, he resisted the suggestion that the time taken for the second 'replacement' pilot study was wasted. It would be best practice for a new test system, in this case Abbott's, to be validated. It would be useful to identify any problems, or advantages, with wide-scale use of either of the kits.<sup>321</sup> The second study would be looking at the relative performances of the two kits with a view to deciding if there were benefits from one over the other. The UK

<sup>316</sup> Ibid [SNF.001.1705] at 1707

<sup>317</sup> Draft proposal [SNB.006.1846]

<sup>318</sup> Professor Leikola's Statement [PEN.017.1961] at 1962

<sup>319</sup> Dr Mitchell's Statement [PEN.017.1901] at 1911

<sup>320</sup> Day 68, page 117

<sup>321</sup> Dr Perry's Statement [PEN.017.2108] at 2116

population could well have different characteristics from that in the US, and still relatively little was known of the Hepatitis C virus, so it made sense to look at both kits. If one kit had been better than another in one country, it did not mean it would be the best choice elsewhere.<sup>322</sup> While noting these possibilities, Dr Perry did not suggest any difference in format or indicate any underlying scientific reason that might have led to an expectation that there would be major differences between the two tests.

**31.223** It is observed in passing by the Inquiry that, in proposing this study, the ACVSB appears clearly to have been entering into the 'operational implications of policy' – the function of the ACTTD – and widening the area of responsibility accepted by the committee as articulated by Dr Metters on 24 April 1990. Having decided at their meeting on 2 July 1990 to recommend, as a matter of policy, that HCV screening of blood donors should be introduced, it is not clear why the ACVSB considered that it should become involved in deciding which test kit should be used by RTCs. On the face of it, that was an operational matter for the blood transfusion services, which fell within the remit of the ACTTD.

**31.224** In any event, the ACVSB underestimated the time it would take to assess the results of the pilot studies and decide its next step. The final report of the tri-centre study, incorporating Phases I and II, was not available until February 1991. Professor Leikola observed in his second statement that 'the outcome of the 2 July meeting meant at least half a year's delay in the introduction of the screening. As it turned out, the time span was more than two times longer'.<sup>323</sup>

**31.225** Professor Leikola was asked in oral evidence whether, in his view, screening had to be delayed until the Ortho and Abbott comparison was completed. He accepted that the comparison was necessary, but he did not feel it justified a delay in the introduction of testing.<sup>324</sup> He pointed out in his second statement that the comparison could have been undertaken while screening was up and running using the Ortho kit.<sup>325</sup> It could have been introduced in May 1991, after the FDA decision to license the Ortho test, and screening could have been given the 'go ahead' in July. Professor Leikola would not have expected there to be a major difference between the Ortho and Abbott kits: both were based on the same protein and the same patent from Chiron.<sup>326</sup> He noted that the philosophy in Finland was that 'if a new test seems to be inevitable, it pays off to start it as soon as possible, and then with flags waving'.<sup>327</sup>

**31.226** Professor Leikola commented in his initial Inquiry statement that a decision to introduce anti-HCV screening could have been made in June or July 1990:

[T]here was no clear mechanism for making a definitive decision concerning the whole UK. The time needed for practical arrangements in the blood centres could have been a maximum of four to five months, so the screening could have been in place in late 1990, possibly in October-November 1990.<sup>328</sup>

**31.227** This inevitably assumed a steady progression to implementation in a variety of blood transfusion centres once a decision had been made. Professor Leikola accepted in

<sup>322</sup> Day 68, page 119

<sup>323</sup> Professor Leikola's Statement [PEN.017.1961] at 1963

<sup>324</sup> Day 71, pages 125-26

<sup>325</sup> Professor Leikola's Statement [PEN.017.1961] at 1962

<sup>326</sup> Ibid [PEN.017.1961] at 1963

<sup>327</sup> Professor Leikola's Statement [PEN.017.1957] at 1958

<sup>328</sup> Ibid [PEN.017.1957] at 1959-60

oral evidence that it would have been much more achievable in Finland with one centre than in the UK where there was a variety of transfusion centres and organisations.<sup>329</sup>

**31.228** In his first Inquiry statement on this topic, Professor Leikola was asked to comment on the reasons for the delay in the decision to implement anti-HCV screening in the UK. He thought they were threefold:

- There was a lack of a proper prospective study on the incidence of transfusion transmitted hepatitis. There had been studies, but they were too small.
- There was pressure from the academic scientists in the ACVSB and ACTTD who preferred a cautious view of the usefulness of the test kits for routine use.
- There was also reluctance on the part of some blood centres to introduce screening, which would have involved them discarding an appreciable amount of blood donations and having to counsel an increased number of donors.<sup>330</sup>

In fact, on 9 October 1989, the ACTTD had recommended to the ACVSB that screening should be introduced (subject to conditions).

**31.229** In September and October 1990 Ortho intimated that a second generation anti-HCV ELISA test and a second generation RIBA confirmatory test would soon become available for clinical trials.<sup>331</sup> While the first generation ELISA detected antibodies to HCV non-structural (c100-3) antigen, the second generation ELISA detected antibodies to a combined, larger, non-structural (c200) antigen and a structural (c22-3) antigen. The second generation RIBA test was a four-antigen test, in which two additional antigens (c33c and c22) had been added to the first generation RIBA test (containing the c100-3 and 5-1-1 antigens). Two short papers presented at a Hepatitis C symposium in Los Angeles in November 1990 (attended by Dr Gillon, SNBTS, Edinburgh), concluded that the second generation ELISA offered improved sensitivity and specificity in a variety of clinical populations.<sup>332</sup>

**31.230** In the review paper published in 1993, mentioned in paragraph 31.133, Professor Leikola described the progress made with the introduction of second generation RIBA testing:

The sensitivity and specificity of the test have been improved by adding two more antigens to the assay, the non-structural protein C33c, and the structural core protein C22.<sup>333</sup>

**31.231** There were still reservations, however:

[T]he sensitivity of the confirmatory tests is not yet optimal, and it can be estimated that the true prevalence of anti-HCV antibodies in Northern European populations is approximately 0.05-0.1%, and it increases up to 1% or more in geographical areas where hepatitis viruses are more common.<sup>334</sup>

<sup>329</sup> Day 71, page 124

<sup>330</sup> Professor Leikola's Statement [PEN.017.1957] at 1959

<sup>331</sup> Minutes of UK Advisory Committee on Transfusion Transmitted Diseases on 13 September 1991 [SNB.001.8919] at 8920

<sup>332</sup> Dr Gillon's report of the symposium [SNB.005.1661]. The papers appended to Dr Gillon's report are at 1672 and 1675 respectively.

<sup>333</sup> Leikola, 'Viral Risks of Blood transfusion', *Reviews in Microbiology*, 1993; 32-39 [PEN.017.1723] at 1725

<sup>334</sup> *Ibid* [PEN.017.1723] at 1725

## November 1990 meeting of ACVSB

**31.232** By the time of the eighth meeting of the ACVSB on 21 November 1990,<sup>335</sup> a note had gone to Ministers intimating that the committee was in favour of introducing HCV screening. There was no indication whether or not Ministers had responded. It was anticipated that there would be a further submission following a decision at the meeting, as to which test would be most suitable.

**31.233** At the November meeting Dr Gunson reported on Phase I of the tri-centre pilot study.<sup>336</sup> Professor Cash said in oral evidence that one concern with using different kits was that a donor tested in Glasgow might be told they were positive for anti-HCV, but if tested in Edinburgh they could be negative. This was because different tests used different criteria and a borderline case could have different outcomes in different centres.<sup>337</sup> In the event, Dr Gunson reported that there was little to choose between the two tests: transfusion centres could decide individually whether to use the Abbott or Ortho kit, which might depend on the equipment already in their possession.<sup>338</sup> That was the only recommendation to come out of this study.<sup>339</sup> The minutes record confirmation by several members that better (ie second generation) tests were being developed and would shortly be issued. The inconsistencies in test results were noted by Professor Zuckerman at the meeting.<sup>340</sup>

**31.234** It will be necessary to return later in this chapter to the detail of some of that discussion. At this stage, it is noted that the committee agreed that the UK should introduce screening as soon as practicable, with individual RTCs deciding whether to use the Ortho or the Abbott test.<sup>341</sup> The minutes record that, 'A submission would go to Ministers regarding this significant policy decision and the Management Executive would consider the funding aspect'. Further action would depend on Ministers' policy decisions. Thus, there was no reference to any agreed method of informing the transfusion centres of the plan. No suggested date for introduction featured in the minutes of the meeting, although Dr Gunson reported some RTCs had asked for six months to set up testing.<sup>342</sup> According to Dr McIntyre's note of the meeting, the Chairman suggested 1 April 1991 as a start date.<sup>343</sup>

**31.235** The committee discussed some of the practical aspects of the introduction of testing, such as counselling. Dr Gunson said that the ACTTD would meet to discuss the problems of counselling donors and to develop a strategy.<sup>344</sup> Both Dr Gunson and Dr Mitchell felt that if the results of the pilot study giving six true positives out of 10,000 donors were borne out in practice, then counselling would be manageable.

**31.236** With regard to this meeting Dr Perry said in his statement to the Inquiry that it 'was widely understood that DoH and UK Ministers had ... established the principle of a common start date for testing and this position was periodically reiterated at ACVSB'.<sup>345</sup>

---

<sup>335</sup> Meeting Minutes [SNF.001.1777].

<sup>336</sup> Comparison of Anti-HCV tests using Abbott and Ortho test kits: Summary of Results [SNB.005.4749]

<sup>337</sup> Day 72, page 144

<sup>338</sup> Meeting Minutes [SNF.001.1777] at 1778

<sup>339</sup> Note of Meeting [SGH.002.8501] at 8502 and Meeting Minutes [SNF.001.1777] at 1779

<sup>340</sup> Meeting Minutes [SNF.001.1777] at 1779

<sup>341</sup> Ibid [SNF.001.1777] at 1780

<sup>342</sup> Ibid [SNF.001.1777] at 1780

<sup>343</sup> Note of Meeting [SGH.002.8501] at 8502. See paragraph 31.237 below.

<sup>344</sup> Meeting Minutes [SNF.001.1777] at 1781

<sup>345</sup> Dr Perry's Statement [PEN.017.2108] at 2117

***Communication of ACVSB decisions to Scotland***

**31.237** Dr McIntyre produced a note of the ACVSB meeting held on 21 November 1990 for his colleagues in the SHHD.<sup>346</sup> He reported that ‘some’ members wanted to start screening forthwith, but that the Chairman suggested 1 April 1991 was more realistic. Dr Perry attended this meeting and it was not clear to him, giving evidence to the Inquiry, who were the ‘some’ in favour of the forthwith introduction of testing.<sup>347</sup> There is no record in the committee minutes themselves of a suggested start date. The date may have been suggested in a discussion that took place ‘off agenda’. It may not have been adopted as the consensus decision of the meeting or, for some reason, may simply not have been minuted.<sup>348</sup>

**31.238** According to Dr McIntyre’s report, it was agreed that a submission would be drafted for the Ministers and copied to Scotland, Wales and Northern Ireland.<sup>349</sup> It was also recorded in the minutes that a submission would be sent to Ministers.<sup>350</sup> Mr Tucker explained that it was common for the DoH to send draft submissions to the individual health departments to demonstrate what they were putting forward to Ministers.<sup>351</sup>

**31.239** Dr Mitchell wrote a letter dated 23 November 1990 to Professor Cash following this meeting of the ACVSB.<sup>352</sup> He did not give a date for the commencement of screening but reported that it had been decided:

To introduce testing for anti HCV using either the Ortho or the Abbott test depending on local circumstances and experience of individual RTCs. The exact date of introduction would be at the earliest practical moment but it was reiterated that the UK would proceed in unity.

**31.240** Dr Gunson was to consult with English colleagues and distribute copies of his Phase I report to assess the likely update of the technical resources required and the likely start dates. There would be a report to the ACTTD meeting in Manchester in January.

**31.241** It appears to be clear that steps were in hand to explore the practical implications of implementation in England and Wales. Northern Ireland was not mentioned in Dr Mitchell’s letter, and it did not refer to any similar arrangement for Scotland. Professor Cash was not a member of ACVSB, as Dr Gunson was, and appears to have been left to consider the Scottish situation unguided by the ACVSB directly, with the benefit only of informal information from Dr Mitchell.

**Professor Cash advances matters in Scotland, November 1990**

**31.242** It appears that there were informal contacts between Professor Cash and Dr Mitchell, since Professor Cash was able to inform SNBTS colleagues that he and Dr Mitchell had a common view of the way forward. In response to Dr Mitchell’s report of the ACVSB meeting, Professor Cash wrote to the SNBTS directors on 27 November 1990:

<sup>346</sup> Note of Meeting [SGH.002.8501]

<sup>347</sup> Day 68, page 123

<sup>348</sup> As with discrepancies between the minutes of meeting on 24 April 1990 and other notes – see paragraphs 31.176 and 31.205 above

<sup>349</sup> Note of meeting [SGH.002.8501] at 8502

<sup>350</sup> Meeting Minutes [SNF.001.1777] at 1780

<sup>351</sup> Day 69, page 116

<sup>352</sup> Letter [SNB.005.3696]

I am advised by Ruthven [Mitchell] that we are a wee bit nearer to “D-Day” and we both believe that it would be to our corporate advantage to take a further step forward along the planning route.

It now seems clear that, in the context of quality, both the Ortho and Abbott kits ... are acceptable: the choice will be yours. We now need to know (as part of an information gathering exercise designed to obtain a UK consensus for a future simultaneous start date) when would be the earliest date you could start routine screening and have your counselling team in place.<sup>353</sup>

**31.243** Professor Cash was asked in oral evidence what he meant by ‘corporate advantage’. He thought it was no more than a reflection of his anxiety that the SNBTS ‘as a team, stayed as a team’.<sup>354</sup>

**31.244** Professor Cash’s view, stated in oral evidence, of what was meant by a ‘start date’ was the point at which transfusion centres would be in a position to test all blood products on their shelves in order for them to be pronounced safe on the same date. For centres to reach that stage, however, he stated that he would have been willing to accept that different centres would have to unwrap their kits and start testing their products at slightly different times.<sup>355</sup> A ‘slightly’ different start date would have been acceptable to him, as different centres had different logistical issues, but it would not have been acceptable for an individual centre to commence testing months in advance of the suggested date.<sup>356</sup> His ideal was for the individual transfusion centres to aim for the same completion date, when they could say all of the units of blood on their shelves were safe.<sup>357</sup>

**31.245** There was to be further debate about the meaning of the term ‘start date’. By the time Professor Cash wrote to Mr McIntosh four months later with the results of the agreements reached at the ACTTD meeting of 25 March 1991, the definition had been refined:

The definition of a start date now proposed will be exactly as stated – the date when routine HCV donation testing will commence. NBTS colleagues do not wish to accept the original proposal (which applied to HIV-1 testing) that the definition of a start date would be that on that date all RTC products issued would have been HCV tested.<sup>358</sup>

**31.246** The North of Scotland Transfusion Centre in Inverness replied on 6 December 1990 to Professor Cash’s letter of 27 November. The technical aspects of testing could be set up at short notice, but a system of donor counselling would be complicated and take around two months to establish.<sup>359</sup>

**31.247** The South East Scotland region replied to Professor Cash on 19 December in a letter composed by Dr Gillon.<sup>360</sup> The earliest date routine screening could start was 25 February 1991. They proposed to use the Abbott test system. Dr McClelland commented in oral evidence that the transfusion centre might have been ready in ‘purely transfusion’ terms,

<sup>353</sup> Letter [SNB.005.2555] *emphasis in original document*

<sup>354</sup> Day 72, page 148

<sup>355</sup> *Ibid*, pages 151-52

<sup>356</sup> As noted below, the context for this comment was that the Newcastle Centre broke ranks and implemented screening early: see paragraph 31.349 below.

<sup>357</sup> Day 72, page 153

<sup>358</sup> Letter [SGF.001.2026]

<sup>359</sup> Letter [SNB.004.7189]

<sup>360</sup> Letter [SNB.004.7202]

but in reality there would have been no ministerial approval or the necessary finance in place to proceed with screening.<sup>361</sup>

**31.248** Edinburgh and South East Scotland began preparations for routine testing in mid July, using stored samples to evaluate equipment. The SNBTS informed the Inquiry that its laboratory manager's records showed that the Edinburgh and South East Scotland BTS began testing all of their blood products for anti-HCV on 30 July 1991. That was done so that all products on the shelf on 1 September 1991 could be said to have been tested.<sup>362</sup>

**31.249** The Inquiry has been unable to locate any letters from other regional directors responding to Professor Cash's letter of 27 November 1990.

**31.250** On 21 December 1990, Mr Canavan (DoH) produced a note seeking Ministers' approval to commence screening in the NBTS, as a public health measure in line with the unanimous advice of the ACVSB that screening should be introduced as soon as practicable.<sup>363</sup> The note stated that, in view of the operational matters that needed to be discussed and finalised, it was unlikely that routine screening could be introduced before 1 April 1991.<sup>364</sup>

### Decision-making process in Scotland

**31.251** The development, and the effectiveness, of the management structures of the SNBTS is discussed in Chapter 17, *Blood and Blood Products Management*. From 1978 there had been a blood transfusion sub-committee of the CSA Management Committee, with a wide remit and delegated powers to deal with blood transfusion matters.<sup>365</sup> Notwithstanding the formal structural changes introduced in 1978, the Blood Transfusion Service would continue to be characterised by a high degree of local autonomy.<sup>366</sup> In 1990 the management structure of the SNBTS underwent a process of change. There had been concern that there had been a lack of professional management of the SNBTS under the existing system. The post of SNBTS General Manager was created. SNBTS Directors were made accountable to the General Manager on managerial aspects and professionally accountable to the National Medical and Scientific Director. There was one central body, the Management Board, through which all policy and strategic decisions passed.<sup>367</sup>

**31.252** Mr David McIntosh was appointed as the first General Manager of the SNBTS in February 1990, and subsequently became Chairman of the Board of Directors in May of the same year.<sup>368</sup> The Management Board met for the first time on 19 June 1990 to finalise its remit in the new structure.<sup>369</sup> Mr McIntosh gave oral evidence to the Inquiry on 29 November 2011. Professor Cash, as National Medical Director, had tended to liaise with medical colleagues within the SHHD directly, by-passing the CSA. Mr McIntosh said that, formally, Professor Cash became the Deputy Chairman of the Board at the same time as he was appointed. In formal terms, the Medical Director was now responsible to the General Manager and not vice versa.<sup>370</sup>

<sup>361</sup> Day 69, page 87

<sup>362</sup> Day 88, page 51

<sup>363</sup> Note [SGH.002.7893]

<sup>364</sup> Ibid [SGH.002.7893] at 7896

<sup>365</sup> See Chapter 17, *Blood and Blood Products Management*, paragraphs 17.41–17.43

<sup>366</sup> Ibid, paragraph 17.57

<sup>367</sup> Management of the SNBTS in the '90s – Report by the General Manager, 7 May 1990: [SNB.002.0832]

<sup>368</sup> Management of the SNBTS in the '90s – Part 1 – The Skeletal Structure [SNB.002.4674]

<sup>369</sup> Minute of Meeting [SNB.002.4726]. See Chapter 17, *Blood and Blood Products Management*, paragraph 17.83

<sup>370</sup> Day 70, page 7



**31.253** In his own view, Mr McIntosh had a clear understanding of what the relationships among parties should have been. As he saw matters, the individual health departments were responsible for presenting recommendations for decisions to their own Minister or Ministers.<sup>371</sup> The Scottish Health Service of the day was responsible to Parliament through the Secretary of State for Scotland and there were Ministers who would be responsible to him for health matters. Mr McIntosh was confident that Scottish decisions would take into account views from England, but that decisions would ultimately be made separately in Scotland. Scottish 'compliance' with English decisions could not be assumed. He made the point that the SNBTS would not have acted on any significant policy initiative without the authority to do so from the Secretary of State for Scotland, filtered through to them by the Health Minister or civil servants at the SHHD.<sup>372</sup>

**31.254** Whether his analysis was technically correct or not, there was a perception within the SNBTS of the relationships of the several participants, and disturbing such equilibrium as had been established in practice would not be easy. There were tensions as Mr McIntosh approached his task, as he saw it, of seeking to improve the previous administrative arrangements for the governance of the SNBTS.

**31.255** Mr McIntosh suggested in his statement that there were three periods of time in the lead-up to the introduction of testing: an initial period of 'genuine debate' about the necessity of HCV testing, a second period of 'genuine professional deliberation' and, from the end of March 1991 to the end of August of that year, a period of 'successive delays'.<sup>373</sup>

**31.256** It appeared to him that the view in Scotland in very early 1991 was that coordination with English implementation of testing was desirable and to be followed if at all possible.<sup>374</sup> The bodies in England that were advising and guiding decision making in Scotland had no responsibility for patient care in Scotland.<sup>375</sup> In formal terms, he was correct: the SNBTS was not directly dependent on Westminster funding. The allocation of expenditure from the Scottish block grant (determined by the Barnett formula from 1978) was purely a Scottish matter. But there was a single UK Government and, realistically, if there was a UK policy decision that screening should be introduced across the UK on a single date, reluctance to incur cost in England and Wales would have an indirect effect on what could be done in practice in Scotland.

### Slippage at the start of 1991

**31.257** Following on the DoH submission of 21 December 1990 seeking Ministers' approval to commence HCV screening of blood donors by the NBTS,<sup>376</sup> Mrs Sandra Falconer (SHHD) produced the following note on 4 January 1991:

[Mr Kennedy, DOH, Belfast] wanted to speak to Rab [Panton] about Hep C submission. He asked if we had put forward to Minister yet and if we had funding. Explained we were still working on submission and that bid for funding had been made but you were awaiting Mr Panton's return on Monday to discuss PES allocation & finalise submission.<sup>377</sup>

<sup>371</sup> Witness Statement of David McIntosh [PEN.017.2126] at 2128

<sup>372</sup> Ibid [PEN.017.2126] at 2129

<sup>373</sup> Ibid [PEN.017.2126] at 2133

<sup>374</sup> Ibid [PEN.017.2126] at 2130

<sup>375</sup> Ibid [PEN.017.2126] at 2141

<sup>376</sup> Note [SGH.002.7893]

<sup>377</sup> Handwritten note [SGH.002.7891]

**31.258** There was a meeting of the NBTS/SNBTS Liaison Committee on 7 January 1991.<sup>378</sup> Dr Gunson attended and expressed his concern that the DoH had not yet decided on a start date. It was suggested that it was probable that a date in May or June 1991 would be the earliest possible. Dr Gunson added that he thought the major problems were mechanisms for finding the money for the RTCs in England and Wales and for confirmation testing. Professor Cash's notes of the meeting state, 'The issue was one of DoH's disinclination to fund centrally and insist on cross charging i.e. increasing the unit cost of blood supplied to hospitals'. Professor Cash requested a more definitive description of 'start date'. Dr Gunson advised him that would be discussed at the next 'Microbiology Advisory Group Meeting' on 8 January.<sup>379</sup>

**31.259** After an interval of 10 months, the ACTTD met again on 8 January.<sup>380</sup> The minutes of the meeting noted that, 'It will be important for RTCs to start testing on an agreed date'. As with the ACVSB meeting of 21 November, the discussion on anti-HCV screening was dominated by setting out the details of the procedure to follow for positive test results. Dr Gillon attended and his paper on counselling of donors was also discussed. He agreed he would amend it in response to written comments from other committee members.

**31.260** On 16 January 1991 a short government memorandum was issued on behalf of Baroness Hooper, Parliamentary Under Secretary of State for Health, in response to Mr Canavan's note of 21 December 1990.<sup>381</sup> Screening for anti-HCV should be introduced as soon as practicable. No suggested date or timetable was given and no guidance was offered to suggest the commencement date. Baroness Hooper said there was no option but to introduce anti-HCV testing.

**31.261** On 21 January Mr Tucker sent a memorandum to Mr Panton passing on the information from Mr Canavan, that DoH Ministers had given their approval to the submission on HCV testing.<sup>382</sup> Mr Canavan did not know the start date, since some laboratories would require new equipment. There was to be a meeting of RTDs to explore the practical issues. Mr Tucker had suggested to Mr Canavan:

[T]hat it might be better to set a target of 1 April as the earliest possible date for introduction but leave it to Blood Transfusion Centres to come in line thereafter since to delay for the slowest could mean a long wait.

**31.262** He asked Mr Panton to proceed with a draft Scottish submission to Mr Forsyth, and to ascertain the earliest date the SNBTS could commence testing, whilst maintaining a 'UK approach'. It is not clear from the face of the memorandum if it was sent on that date. There is a further manuscript note by 'SF' – who is assumed to be Mrs Sandra Falconer – and that suggests it was not copied to Mr Panton until 14 February. Even then he was asked to work on the second, unrelated issue of 'handling charges for blood', described in the memorandum.

<sup>378</sup> Notes of NBTS-SNBTS Management Meeting, 7 January 1991 [SNB.011.7258]. In attendance were Dr Gunson, Professor Cash and Dr R J Moore

<sup>379</sup> As at 7 January 1991, it was expected that the next meeting of the ACVSB would be in late January 1991 (see [SNF.001.1777]). In the event it was held on 25 February 1991. It is unclear what meeting Dr Gunson had in mind. The only meeting that was held on 8 January 1991 was a meeting of the ACTTD.

<sup>380</sup> Meeting Minutes [SNB.001.8770]

<sup>381</sup> Memo [PEN.016.0259]

<sup>382</sup> Memo [SGH.002.7890]

**31.263** Mr Tucker commented in oral evidence that he would have preferred to set a target date for the introduction of screening; he would not have been comfortable with going to his Minister without a start date.<sup>383</sup> He suggested 1 April in his memorandum as the Public Expenditure Survey (PES) had been approved by Ministers in Scotland and funding was available for that date, adding in oral evidence: 'Then we could all move forward at the same time'.<sup>384</sup> Mr Tucker thought there would be no point in the DoH, or the SHHD, setting a date for screening if the transfusion centres themselves were not ready. There would have to be close consultation among the parties involved in decision making and implementation.<sup>385</sup>

**31.264** On 22 January 1991, Dr Gunson sent a memorandum to the Regional Transfusion Directors of England and Wales.<sup>386</sup> He advised them that routine testing would be put into action and asked for the earliest date they could commence screening. This appears to be Dr Gunson's equivalent to Professor Cash's letter to his Directors of 27 November 1990.

**31.265** Dr Gunson's memorandum was copied to Professor Cash, who replied on 24 January.<sup>387</sup> External factors – the kind of events that change history – had a bearing on what was practicable. On 14 September 1990, British forces were deployed to Saudi Arabia following Iraq's invasion of Kuwait. On 16 January 1991, the United States of America announced operation 'Desert Storm'. War had again impacted on the work of the SNBTS. Professor Cash advised Dr Gunson that anti-HCV testing could not commence until either the Gulf conflict had ended or the SNBTS teams had proved themselves able to cope with the pressures of both the conflict and HCV testing. The demands created in anticipation of the actual conflict were exhausting staff and Professor Cash judged that, when the troops went operational, the 'current frenetic activity' of the SNBTS would be sustained. Professor Cash added in his oral testimony that '90 per cent of the blood that was made available for British troops involved in the conflict in the Gulf came from Scotland'.<sup>388</sup> In his letter of 24 January to Dr Gunson, Professor Cash went on to say:

We remain firmly committed to starting on the same day as our NBTS colleagues and if pressed by Ministers I would suggest, in the circumstances, a May/June date should be considered. However, I would much prefer to wait another month and then respond to your letter.

**31.266** Dr McClelland agreed in evidence that the UK services, at that time, were preparing themselves for a potentially large number of casualties of the war in Iraq being flown to hospitals in the UK. In addition, the transfusion services were inundated with extra blood donations.<sup>389</sup> In the event, the military offensive comprised an initial prolonged aerial bombardment and a ground assault which commenced on 24 February and which ended when Iraqi forces agreed a ceasefire four days later, on 28 February. However, by that stage, the preparatory arrangements in anticipation of conflict had impacted heavily on the SNBTS.

---

<sup>383</sup> Day 69, pages 117-18

<sup>384</sup> *Ibid*, page 118

<sup>385</sup> *Ibid*, page 120

<sup>386</sup> Memo [SGF.001.2029]

<sup>387</sup> Professor Cash's reply [SGH.002.7887]

<sup>388</sup> Day 72, page 162

<sup>389</sup> Day 69, page 40

**31.267** On this occasion Professor Cash was supported within the SHHD.<sup>390</sup> Dr Gunson responded on 28 January, without reference to the demands created by conflict, and advised Professor Cash:

It was never my intention that anti-HCV testing should take place with great urgency. The reason I asked if it was possible to let me know by Tuesday feasible dates for the commencement of testing was because I have a meeting at the DOH on Wednesday to discuss this matter. It was not intended to pressurise RTCs to start testing in the immediate future which, I agree, is entirely impractical. For England and Wales, as you know, there is a matter of financial provisions for this testing to be sorted out.<sup>391</sup>

**31.268** The interpretation of this superficially rather puzzling letter is unclear. It may have been intended as support for Professor Cash, noting that England and Wales also had problems that might delay implementation. On the other hand, one cannot avoid the impression that Dr Gunson's views of the practicalities in England and Wales would always have precluded any commitment to urgent implementation of the decision to commence anti-HCV testing in the UK, including Scotland for the reasons noted above.

**31.269** In the meantime, the evaluation of test kits continued. On 24 January 1991 Dr Follett advised Dr Gunson of initial results from the Glasgow study, which indicated that the second generation Abbott anti-HCV test 'looks most promising .... Clearly the inclusion of the new C22 and C33 antigens has transformed this test'.<sup>392</sup> These antigens were introduced into the Abbott RIBA test, as indicated above.

### **Abbott's intellectual property problems**

**31.270** The intention to have an evaluation of 1000 Abbott ELISA kits was, however, frustrated. On 4 February 1991, Dr Follett wrote to Dr Gunson to say Abbott had supplied only four test kits. Abbott was prevented from providing further kits until 14 April as Ortho had taken out an injunction preventing their sale in the UK until after that date.<sup>393</sup> As indicated above, Abbott's licence had included restrictive provisions protecting Ortho's access to the market for one year.

### **Postponement from 1 April 1991**

**31.271** Dr Pickles of the DoH composed a memorandum on 5 February 1991, copied to certain members of the ACVSB but not to anyone in Scotland.<sup>394</sup> She commented that there were many problems with the proposed introduction of testing, such as choice of test, supplies, confirmatory testing and training of staff. Funding was still a very real concern. Following discussion with the RTCs, Dr Gunson had suggested to Dr Pickles that the start date should be 1 July, and she wondered if that would be too late. Dr Pickles set out her view:

My initial reaction was this would be OK. Attempting to go earlier would mean some stragglers would be left behind, the slight delay increased the chance of the finance being sorted out, and with the diversion of RTC resources to Gulf-

---

<sup>390</sup> Manuscript note on Professor Cash's letter [SGH.002.7887]

<sup>391</sup> Dr Gunson's reply [SNB.004.4574]

<sup>392</sup> Letter [SNB.006.3928]

<sup>393</sup> Letter [SNB.011.6960]

<sup>394</sup> Memo [PEN.016.0236]

related activities a short time date might not be feasible. Even that date was dependent on blood collection having been stable for the preceding 4 weeks, which should apply provided the ground war is over by then.

Do you agree? We will discuss in more detail at ACVSB, I presume.<sup>395</sup>

**31.272** 1 July had now emerged as the date of implementation of screening in place of 1 April. It is of importance to note the position on funding in England and Wales. As noted already, Dr Metters had stated at the ACVSB on 17 January 1990 that no new money would be made available for screening: funding would have to be found from existing allocations. Dr Pickles' memorandum indicates that, over a year later, the problem of funding in England and Wales had still not been resolved.

### **Funding in Scotland**

**31.273** Formally, the funding structure in Scotland was clear. In summary, SHHD funding came from the Scottish Office budget which was ultimately tied to the Treasury. The SHHD had its own Finance section which was overseen by the Scottish Office Finance Department. The SHHD had responsibility for the overall management and financing of the Common Services Agency, which in turn funded the SNBTS.<sup>396</sup>

**31.274** Mr McIntosh agreed with this summary put forward by Mr Tucker. However, as he recalled, the CSA took no part whatsoever in the chain of command as he saw it. Effectively, the SNBTS reported to Ministers through the Home and Health Department. He could not recall any CSA interest in the process of the introduction of anti-HCV testing.<sup>397</sup> This was consistent with the position that obtained generally, and as described in Chapter 17, *Blood and Blood Products Management*. The CSA was a conduit for budgeting and the allocation of funds, but it had no operational role in the formulation or implementation of policies directing or affecting the work of the SNBTS. Budgeting was provided through the mechanism of the annual PES; procurement was a separate issue.

**31.275** Mr Tucker told the Inquiry in his statement that there was a national procurement process. The Health Departments would seek to negotiate contracts on a national basis with the aim of obtaining the best value for money. The SHHD would not negotiate alone for products, as it would not have the purchasing power of the national procurement programme.<sup>398</sup> He added in his statement that SNBTS staff would not try to purchase outside of the nationally agreed contracts as it would have been far more expensive.<sup>399</sup>

**31.276** Mr Tucker commented that it was common for the DoH to take the lead in national issues. The SHHD was a smaller Health Department, with fewer resources; there was a general desire to make use of DoH resources. It made sense for the SHHD to be in partnership with the DoH and both obtained the same advice from the ACVSB. The DoH as the bigger organisation was better able to exert pressure on the Treasury.<sup>400</sup>

---

<sup>395</sup> Ibid [PEN.016.0236]

<sup>396</sup> Mr Tucker's Statement [PEN.017.2060] at 2061

<sup>397</sup> Day 70, page 96

<sup>398</sup> Mr Tucker's Statement [PEN.017.2060] at 2062

<sup>399</sup> Ibid [PEN.017.2060] at 2069

<sup>400</sup> Ibid [PEN.017.2060] at 2063

### *Public Expenditure Survey*

**31.277** On the agenda for the SNBTS management board meeting of 12 February 1991, it was noted in relation to the Public Expenditure Survey 1990 (PES90) that of a total sum of £2.5 million available for new developments, £1.1 million would be needed for anti-HCV testing.<sup>401</sup>

**31.278** On 12 February 1991 the Management Board of the SNBTS met 'to review the firmed up PES proposals for 1991/92'.<sup>402</sup> The agenda included testing for anti-HCV as 'Microbiological Screening – Anti-HCV'.<sup>403</sup>

**31.279** In the original bid (submitted to the CSA and the SHHD in June 1990),<sup>404</sup> total capital and revenue expenditure of £1.332 million had been sought (capital of £50,000 and revenue of £1.282 million) to introduce anti-HCV testing in 1991/92. In the revised bid, £1.223 million (£106,000 of capital and £1.117 million of revenue) was sought for that purpose. A detailed breakdown was provided.<sup>405</sup>

**31.280** It appears that the meeting in February 1991 may not have completed discussion of the detail of the bid for anti-HCV screening. It was planned to continue the discussion at a further board meeting in April 1991. It is however clear that the bid for the funding of screening for HCV was included in PES90, that it was successful and that (in contrast to the apparent state of affairs in England and Wales) the funding was available to commence routine screening in Scotland in April 1991.

**31.281** Mr Tucker commented in oral evidence that this implied that testing could begin in April 1991: the Minister had agreed testing as he had approved an allocation of funds in the PES for 1991/1992.<sup>406</sup> He said that there was no allocation of funds for HCV screening in the PES for 1990/1991.<sup>407</sup> That would have been drawn up in June or July 1989, and the need for funding would not have been known at that stage. The only money available for HCV screening in the financial year 1990/1991 would have been from the contingency fund, or spare money in the CSA budget. That led to a discussion of the use of the contingency fund.

### *Reserve/Contingency fund*

**31.282** The Inquiry asked the witnesses who provided statements whether, if screening had been introduced before the financial year 1991–92 (and specifically in year 1990–91), the money required could only have been found in the 'central reserve' (the contingency fund referred to in an SHHD memo of 2 July 1990).<sup>408</sup>

**31.283** All witnesses were referred to paragraph 2996 of the Minutes of the Meeting of the Management Committee of the CSA for the Scottish Health Service held on 20 June 1990:

The Committee noted the circulated paper dealing with plans for testing blood donations for Hepatitis C. It was likely that up to 100,000 tests per annum

<sup>401</sup> Agenda [SNB.002.7404]

<sup>402</sup> Minutes [SNB.002.7413]

<sup>403</sup> Management Board Meeting – Circulated PES Document [SNB.002.7426] at 7427

<sup>404</sup> See the Agenda for the Management Board Meeting which states 'The purpose of the [Management Board Meeting] is to review detailed bids based on the submission made in June 1990 to the CSA and the SHHD' [SNB.002.7404]

<sup>405</sup> Management Board Meeting – Circulated PES Document [SNB.002.7426] at 7430–31

<sup>406</sup> Day 69, page 121

<sup>407</sup> Ibid, page 141

<sup>408</sup> Memo [SGH.002.7930]

would be needed at a cost of £1.3 million. Should testing be started during the current financial year, funding would have to come from the contingency fund because there would be no additional finance available from Scottish Home and Health Department.<sup>409</sup>

**31.284** Mr Tucker explained in his statement that when the CSA received its annual budget allocation, 10% of each Division's budget would be held in reserve as a 'contingency fund'. Each element of the contingency fund was, however, related directly to the head of expenditure for which the PES bid had been made and was held in reserve for that head of expenditure. For example, the 10% of the budget for ambulances was held exclusively against any emerging needs of the ambulance service. The contingency fund was not available against unbudgeted expenditure generally.

**31.285** Mr Tucker thought it was very unlikely, if screening had been introduced early, that the CSA could have 'raided' the contingency fund. If there was a good case for urgent funding to be found, the CSA would have examined its financial priorities in divisions other than the SNBTS and looked for any unspent money that could be utilised.<sup>410</sup> If this was not possible the CSA could turn to the SHHD for unspent budgets. If this proved impossible, the request for funding for screening would 'go up the scale'<sup>411</sup> to the Scottish Office Finance Division to see if there was unspent money from a division such as Transport if, for example, a planned roads project had not gone ahead.<sup>412</sup>

**31.286** There were different views. In contrast to Mr Tucker, Mr Roderick Angus commented in his statement:

As part of the Public Expenditure Survey outcome, the Common Services Agency, of which the SNBTS was a division, was provided with a sum of money to be used as a 'contingency fund' to meet any in-year funding needs, this was also referred to as a reserve in some correspondence. Mr Donald, General Manager of the CSA, would have, in the first instance, been expected to fund the testing from within that 'contingency fund' rather than seeking additional funds from the Scottish Home and Health Department.<sup>413</sup>

**31.287** He went on to say that the minutes of the CSA Management Committee 'indicate that had screening been introduced before the financial year 1991–92, it could only have been paid for from the reserve'. If the contingency fund had been insufficient, additional funds could have been requested from Finance Division.<sup>414</sup>

**31.288** Mr McIntosh commented in his statement that the Inquiry's assumption, as reflected in the question, that the contingency fund was the only source of funds for screening was 'probably not correct'.<sup>415</sup> If it had been deemed necessary, Ministers could have brought implementation forward into the financial year of 1990–91. He thought it could have been financed in a number of ways which would probably include the use of the reserve fund. He felt confident that if the introduction of testing had been prioritised in the financial year 1990–91, the money for implementation would have somehow been

<sup>409</sup> Meeting Minutes [SNB.013.4871] at 4874

<sup>410</sup> Mr Tucker's Statement [PEN.017.2060] at 2065

<sup>411</sup> Day 69, page 113

<sup>412</sup> Mr Tucker's Statement [PEN.017.2060] at 2065

<sup>413</sup> Mr Angus' Statement [PEN.017.2084] at 2088

<sup>414</sup> Ibid [PEN.017.2084] at 2089

<sup>415</sup> Mr McIntosh's Statement [PEN.017.2126] at 2132

found for implementation before 1 April 1991. Mr McIntosh confirmed his view in oral evidence that he did not believe that finance was in fact an obstacle in Scotland.<sup>416</sup> He added that the SNBTS was not encouraged to think budgets were flexible, but he had found 'serious' amounts of money out of similar financial arrangements when necessary.<sup>417</sup>

**31.289** Another witness, Mr David Hogg (SHHD) commented in his statement:

Had the Hep C Testing commenced, however, within 1990-91 then technically the CSA/SNBTS would have to have funded from the remaining Revenue Allocation, including the 'Contingency Fund', although I am sure we within the Health Department would have gone back to Finance Division with a further in-year increased funding bid.<sup>418</sup>

**31.290** In the end, having regard to the evidence as a whole, it appears highly unlikely that funding in Scotland would have depended on technical budgeting issues: if a decision had been taken to commence screening for anti-HCV in Scotland in 1990–91 then the funds would have been found.

### **Start date becomes 1 July 1991**

**31.291** On 13 February 1991 Mrs Falconer (SHHD), sent a handwritten memo to Mr Hogg.<sup>419</sup> She commented that she had spoken to Ms Elaine Webb at the DoH and was advised that 'officially no date has been given'. The date would be discussed at the ACVSB meeting on 25 February, but confidentially the start date was hoped to be 1 July. Ms Webb had commented that 'the Department of Health did not want SNBTS or anyone outwith the office informed'.

**31.292** Mrs Falconer suggested in her Inquiry statement that it may have become effectively a matter of protocol. She observed:

I would suggest that DoH(E) colleagues requested that the 'unofficial date of 1 July' should not be shared because it would not be appropriate to suggest that a possible date had been set before the Advisory Committee had had an opportunity to discuss the matter at its meeting and agree a recommendation.<sup>420</sup>

**31.293** As her conversation with Ms Webb took place just 12 days before the ACVSB met, this appears to be a plausible explanation for the date remaining confidential until the committee had the opportunity to endorse it.

**31.294** Mr Tucker offered a different explanation for this, however. He said that Ms Webb at the DoH was a junior staff member who had inadvertently given an official start date to her SHHD counterpart and tried to mitigate this by saying the SNBTS should not be told. She may also have been concerned the date could be forwarded to the NBTS via the SNBTS.<sup>421</sup>

**31.295** Mr Hogg made an observation in his statement on the subject of why the start date was not to be openly discussed. He observed that the date 'must have been subsequently

---

<sup>416</sup> Day 70, page 30

<sup>417</sup> Ibid, pages 29–30

<sup>418</sup> Mr Hogg's Statement [PEN.017.2146] at 2149

<sup>419</sup> Memo [SGH.002.7886]

<sup>420</sup> Mrs Falconer's Statement [PEN.017.2120] at 2123

<sup>421</sup> Mr Tucker's Statement [PEN.017.2060] at 2067



confirmed at the aforementioned ACVSB meeting, as in D McIntosh's (SNBTS) letter to Dr McIntyre dated 12 March 1991 ... he clearly states 1 July 1991 as the agreed introduction date!'.<sup>422</sup>

**31.296** On 14 February 1991, Professor Cash advised Dr Habibi (Medical and Scientific Director, National Blood Transfusion Centre, France) that 'we (UK BTS) expect to start HCV donation screening in the early summer 1991 ...'.<sup>423</sup>

**31.297** On 15 February Dr Gunson wrote to the Directors in England and Wales to advise that screening would begin on 1 July 1991.<sup>424</sup> He warned that, if the Gulf war continued and blood donation levels were still very high, this date might have to be reconsidered. There were still matters to be considered at the meeting of the ACTTD on 25 March.

**31.298** Professor Cash wrote to Dr Gunson on 15 February, again saying he would like the SNBTS to stay in line with the NBTS/BPL.<sup>425</sup> Professor Cash asked for a common understanding of what a 'start date' meant. He suspected Dr Gunson would have to pursue Dr Metters' committee (the ACVSB) on these topics.

### Further slippage in timescale for introduction of screening

**31.299** Mr McIntosh described the period between the making of the decision to introduce screening (ie in late 1990) and the end of March 1991 as including 'genuine professional deliberation, aimed at investigating the validity, accuracy, reliability and operational practicality of available test materials and methods'. He thought this investigation was completed in time for anti-HCV testing to have been implemented throughout Scotland by 1 April 1991.<sup>426</sup> Funding for screening had been granted to the SNBTS and was in place for that date.

**31.300** On 21 February, Mr Mark Fuller from the DoH wrote to Dr Contreras.<sup>427</sup> The letter was copied to various individuals, including Dr Gunson and Dr Mitchell. At the meeting of the ACVSB on 21 November 1990, Dr Gunson reported that Ortho had brought out a second generation test, and had offered 2500 free test kits for use on frozen samples held at the North London Transfusion Centre.<sup>428</sup> Mr Fuller's letter was headed 'DH sponsored second round evaluation of HCV screening kits North London BTS, Colindale', and appears to have taken up this project. Dr Contreras was asked whether she was happy for the work to be done at her Centre. The letter does not specifically state that there was to be an evaluation of Ortho second generation kits. However, the instructions were given by Dr Gunson and the context supports the inference that they followed from the intimation in November. Professor Cash was of the view, stated in oral testimony, that this represented evidence that a decision had been made by the DoH to carry out an evaluation of second generation kits, before HCV screening of blood donors was introduced.<sup>429</sup> This is discussed further below.

<sup>422</sup> Mr Hogg's Statement [PEN.017.2146] at 2151

<sup>423</sup> Letter from Professor Cash to Dr Habibi [SNB.011.7042]

<sup>424</sup> Dr Gunson's Letter [PEN.016.0189]

<sup>425</sup> Professor Cash's Letter [SNB.005.1679]

<sup>426</sup> Mr McIntosh's Statement [PEN.017.2126] at 2133

<sup>427</sup> Letter [SNB.006.3947]

<sup>428</sup> Meeting Minutes [SNF.001.1777] at 1779

<sup>429</sup> Day 82, pages 24–25

**31.301** The ACVSB met on 25 February 1991.<sup>430</sup> Dr McIntyre attended as the SHHD observer. Dr Gunson did not attend and offered his apologies. The tri-centre study (North London, Newcastle and Glasgow) of the first generation Ortho and Abbott ELISA kits had been conducted in the second half of 1990 and a summary of the results of Phases I and II, dated February 1991, was presented to the committee.<sup>431</sup> All three centres reported that the tests were easy to perform. The Ortho tests were producing more initial screen positives than Abbott, but the repeatable positive rate was similar with both tests.<sup>432</sup> Dr Mortimer again reported results from the continuing pilot study. Significantly, he advised retention of the samples collected, for the evaluation of other candidate HCV tests, and that 'the Committee may wish to see the results from the second generation Ortho and Abbott tests'.<sup>433</sup> Professor Tedder tabled a paper which led to discussion:

The Committee discussed the likely availability of the second generation tests and operational factors which might influence the decision by RTCs as to which screening test to choose .... Members agreed it was important for proper evaluation of the Ortho and Abbott 1&2 tests to be carried out before RTCs decided which test they would adopt.<sup>434</sup>

**31.302** The Chairman's summary noted agreement on retention of the samples and that:

Any new test should be evaluated against the full 10,000 specimens to ensure it was at least as good as the tests already evaluated.

Ortho and Abbott 1 and 2 should in principle be available among others from 1 July for RTC's to choose.<sup>435</sup>

**31.303** The minutes do not record a change in the date participants had in mind for implementation of screening.<sup>436</sup> However, there was a clear weakening in commitment to any particular date, in so far as it was agreed that it was important for proper evaluation of the Ortho and Abbott 1 and 2 tests to be carried out before the RTCs decided which test to adopt, and availability of these tests 'in principle' by 1 July further qualified commitment.<sup>437</sup> The idea of an evaluation, incorporating second generation tests so that the RTCs could decide which to adopt, appears to stem from this meeting.

**31.304** However, that idea was not immediately appreciated. On 26 February Mr Bayne and Mr Panton of the SHHD met with Dr McIntyre<sup>438</sup> who had attended the ACVSB meeting of 25 February.<sup>439</sup> Dr McIntyre had confirmed the start date for screening was to be 1 July. Mr Bayne prepared a note of the meeting recording, in particular, that start date.<sup>440</sup>

<sup>430</sup> Meeting Minutes [SNB.001.8934]

<sup>431</sup> [PEN.016.0028] The final report was not available to the Inquiry when the Preliminary Report was written. Phase I results were discussed at ACVSB on 21 November 1990.

<sup>432</sup> Comparison of Anti-HCV tests using Abbott and Ortho 1st generation kits: Summary of Results of the trial – February 1991 [PEN.016.0028] at 0030

<sup>433</sup> Meeting Minutes [SNB.001.8934] at 8936

<sup>434</sup> Ibid [SNB.001.8934] at 8936

<sup>435</sup> Ibid [SNB.001.8934] at 8936–37

<sup>436</sup> Ibid [SNB.001.8934] at 8937

<sup>437</sup> Ibid [SNB.001.8934] at 8936

<sup>438</sup> The Extended Narrative [PEN.017.2165] mistakenly records this meeting as being with Mr McIntosh of SNBTS.

<sup>439</sup> Handwritten notes re: date of commencement for HCV testing [SGH.002.7880] and [SGH.002.7881]

<sup>440</sup> Note [SGH.002.7881]

**31.305** On 12 March 1991 Mr McIntosh wrote to Dr McIntyre on the topic of the 'Introduction of HCV testing'. Mr McIntosh referred in his letter to the 'agreed national (UK) introduction date (1 July 1991)'.<sup>441</sup>

**31.306** In a handwritten memorandum apparently dated 19 March, a message was sent by Mrs Falconer (who worked in the same Branch as Mr Panton)<sup>442</sup> to Mr Hogg. It noted the date of commencement of testing as 1 July 1991 and queried 'What about submission?'. She suggested he read the note of the meeting with Dr McIntyre and Mr Panton, written by Mr Bayne. The tone of her note suggested that the submission to the Minister had not yet been drafted. This prompted a note, of the same date and handwritten on the same document, from Mr Hogg to Mr Panton: 'To see and discuss next steps re the submission'.<sup>443</sup>

**31.307** In addition, this document contains a note that appears to be in Mr Panton's handwriting: 'Draft submission based on English one – shorter version. Other Ministers have agreed'. While the note is ambiguous, and might mean that a submission had already been drafted as a shorter version of the English submission, it is more likely to have been a drafting instruction along the lines suggested. Mr Tucker suggested in oral evidence that it was an instruction.<sup>444</sup> In his statement, Mr Hogg stated that he viewed it as an instruction that Mr Panton had addressed to him.<sup>445</sup> It reflected the reality of the relationship between the SHHD and the DoH: advice to Scottish Office Ministers needed only to be based on the text of the DoH submission. There was no independent input required.

**31.308** On 21 March 1991, the marketing manager of Ortho wrote to Professor Cash to advise that the second generation ELISA test was to be introduced, replacing the first generation test.<sup>446</sup> On the same day, the NHS Procurement Directorate sent a letter (possibly implementing the decisions of the ACVSB made at the February meeting) to Dr Gunson in respect of a phase two evaluation of the HCV screening tests. The letter stated:

The Department has agreed that there should be a 'second-round' comparative evaluation of Hepatitis C kits at the Newcastle, North London and Glasgow Regional Transfusion Centres ....

The work to be carried out by the NBTS should start in February for the North London RTC and March for the other centres and be completed by the end of April. After this any repeat positive samples previously not identified will be sent to the reference laboratory for additional (and confirmatory) testing.

In consideration of the work to be carried out in Phase II the approved limit of expenditure ... shall be by quotation to Mr Fuller, from each of the centres .... The screening kits involved in the evaluation have been ordered from, Ortho Diagnostic Systems, Organon Teknika and UBI ....<sup>447</sup> Tests from Abbott Laboratories will be done at Newcastle & Glasgow when available, the other tests being only done at North London.<sup>448</sup>

---

<sup>441</sup> Letter [SGH.002.7884]

<sup>442</sup> Day 69, page 120

<sup>443</sup> Memo [SGH.002.7880]

<sup>444</sup> Day 69, page 121

<sup>445</sup> Mr Hogg's Statement [PEN.017.2146] at 2150

<sup>446</sup> Ortho letter [SNB.005.5212]

<sup>447</sup> United Biomedical Inc.

<sup>448</sup> Letter [SNB.006.3953]

**31.309** As discussed below, just two days later, on 23 March, Dr Gunson telephoned Professor Cash to say that the commencement date for anti-HCV screening would be postponed. It is difficult now to understand why this should have been the case given that the letter from the Procurement Directorate expected the further evaluation to be completed by the end of April. Professor Cash could not explain this when asked in oral evidence. He observed, however, that the letter of 21 March to Dr Gunson from the Procurement Directorate, while very positive in tone, was from people who would not have 'the faintest idea' whether or not the kits were available. According to Professor Cash, Dr Gunson told him later the unavailability of second generation tests emerged as one reason for the delays.<sup>449</sup>

**31.310** The letter from the Procurement Directorate does refer to a March start for the evaluation in the Newcastle and Glasgow centres, in contrast to a February commencement in North London, suggesting a delay in the delivery of Abbott kits. In addition the letter makes reference to the Abbott kits being used at the Newcastle and Glasgow centres 'when available', possibly suggesting there was also a delay anticipated in the delivery of those kits. As noted above, Ortho's injunction against Abbott supplying further kits continued until 14 April, and this may have been the explanation for the anticipated delay. The evaluation was, however, expected to be finished by April and therefore would have been completed in time for a 1 July start date.<sup>450</sup>

**31.311** The general issue of delaying implementing a new screening test until a later generation of the test was available, was explored with Professor Leikola in his evidence to the Inquiry. Professor Leikola did not consider it necessary generally to delay the introduction of a test on the basis that better kits were on the horizon. In oral testimony he expressed the view that one would start screening with what was available and introduce better tests when they arrived. He did not think that time would be lost in the transition if a country had brought in screening with early test kits, and later replaced them with new and better kits.<sup>451</sup>

**31.312** He was asked if there was much work and time involved in introducing a second generation test to a laboratory which was already carrying out first generation testing. Professor Leikola thought that if the tests were basically similar, and did not require totally new machinery, it would not be difficult to do comparative tests on the two generations of kits to ensure the sensitivity and specificity had truly improved. He went on to say that the practicalities of actually introducing the new test would take time. First, the authorities would have to consider whether the manufacturer would be able to deliver enough of the new test kits. Secondly, work would be required to amend the legal agreements with the manufacturers of the first test, if necessary.<sup>452</sup>

**31.313** Professor Leikola's view was that, generally speaking, if newer, better kits were becoming available for use, the transition should have been made as soon as possible. Deciding not to introduce the old test because the new one was imminent could only really be justified if the manufacturer was very close to releasing the second generation test. If the new test would be only marginally better, there would be less urgency to introduce the second test.<sup>453</sup>

---

<sup>449</sup> Day 82, page 37

<sup>450</sup> See also Dr Follett's letter to Dr Gunson of 4 February 1991 describing a delay in sale of Abbott test kits until April 1991 [SNB.011.6960]

<sup>451</sup> Day 71, page 122 and Professor Leikola's Statement [PEN.017.1957] at 1959

<sup>452</sup> Day 71, pages 122–123

<sup>453</sup> Ibid, page 123

### The phone calls of 23–24 March 1991

**31.314** Three telephone conversations regarding the postponement of the introduction of screening featured in evidence given to the Inquiry by Professor Cash. His was the only evidence available, and it became clear that the events were highly emotionally charged. Precise recollection cannot be expected. The first of the phone calls was made by Dr Gunson to Professor Cash at his home, on Saturday 23 March. The general topic of conversation was the upcoming meeting of the ACTTD on the following Monday, in Manchester.<sup>454</sup>

**31.315** According to Professor Cash, the first phone call was ‘very acrimonious and distressing’. Professor Cash did not know that the DoH in London had decided there would be another ‘field trial’, this time on the second generation kits. He had understood from Dr Mitchell that evaluation of the second generation kits would be fitted in after the commencement of screening (using first generation kits) on 1 July, but Professor Cash then realised that another month would go by while this kit was evaluated, and he objected to the plan. Professor Cash recalled that Dr Gunson repeatedly claimed that the Scottish Office ‘were party to this decision’.<sup>455</sup> What precisely the Scottish Office was party to was explored in oral evidence with Professor Cash; he did not know if ‘on board’ meant with the carrying out of an evaluation of second generation tests, or ‘on board’ with the postponement from July to September.<sup>456</sup>

**31.316** Professor Cash was later asked in oral evidence why he did not confirm the SHHD position with them directly. He reiterated that, regrettably, ‘Harold Gunson convinced me that SHHD had been party to the decisions that were made’.<sup>457</sup>

**31.317** Professor Cash recalled in oral evidence that Dr Gunson had been instructed to make certain that a trial of the second generation tests was agreed, and plans put in place by the time of the committee meeting on the Monday morning. The change of intention was that screening would not commence in July and instead there would be another field trial. According to Professor Cash, the idea had been abandoned, that evaluation of second generation tests could be fitted in after screening commenced on 1 July.<sup>458</sup> Professor Cash added that he had initially refused to go to the ACTTD meeting on Monday and comply with Dr Gunson’s wishes. This created ‘acrimony’ between the two friends.<sup>459</sup>

**31.318** Professor Cash told the Inquiry his initial reaction was to say, ‘We don’t need to delay at all’. In his view, other first world countries were starting to screen donors for anti-HCV using the first generation kits. Professor Cash was particularly concerned that the first generation kits would soon be unavailable as the manufacturers would withdraw them.<sup>460</sup>

**31.319** Dr Gunson telephoned Professor Cash again. According to Professor Cash’s recollection of this conversation, it became increasingly clear to him that Dr Gunson was ‘under extreme pressure to deliver a second generation field study and in doing so delay the onset of testing’. Dr Gunson agreed to send documents to Professor Cash that

---

<sup>454</sup> Day 82, page 6

<sup>455</sup> *Ibid*, page 7; also Day 72, page 166

<sup>456</sup> *Ibid*, page 21

<sup>457</sup> *Ibid*, page 76

<sup>458</sup> *Ibid*, page 9

<sup>459</sup> *Ibid*, page 10

<sup>460</sup> *Ibid*, page 11

indicated the Department had signalled that this work was necessary. It was not a decision of the Advisory Committee. In Professor Cash's words: the Advisory Committee had been 'bypassed'.<sup>461</sup>

**31.320** During the second call, Dr Gunson gave Professor Cash an assurance that the NBTS directors would 'keep in line' with regard to delaying screening to allow for evaluation of the second generation tests. Apparently Dr Gunson had assured him that, 'if anyone got out of line at all, or thought about it, DoH would come down on them like a tonne of bricks'.<sup>462</sup> It emerged in the call that a fundamental problem south of the border was one of 'funding and agreeing that funding system'. This was not a problem in Scotland. The funding situation in England was a deep-seated problem that Dr Gunson communicated to Professor Cash in the second telephone call.<sup>463</sup> As already noted, the funding problem in England was not new: it had been recognised but left unresolved for over a year.

**31.321** After further reflection Professor Cash telephoned Dr Gunson that Sunday, 24 March, to say he would agree to participate and that he would support Dr Gunson at the meeting in Manchester the next morning. He added it had been 'a matter of great regret to me ever since' that he did not insist that the whole of the UK should start implementing testing with first generation kits in the way other countries had done. Dr Gunson had told him that Dr Mitchell was 'on board' with the plan.<sup>464</sup>

**31.322** Professor Cash was asked how Dr Gunson knew that Dr Mitchell was 'on board'. He answered that Dr Mitchell had been copied into the letter he had received from the Procurement Directorate dated 21 March from Dr Gunson announcing a second generation study.<sup>465</sup>

**31.323** Professor Cash told the Inquiry in oral evidence that this became a 'painful' and 'personal' issue between him and Dr Gunson. He added:

Harold insisted that this was a device to give the Department of Health more time, more space, to resolve these very difficult financial problems that they had, and secondly, he insisted – this became very heated – that SHHD knew all of this and ... this is about the second generation evaluation, and the moment you sign up to that, July has gone.<sup>466</sup>

**31.324** Dr Gunson was unable to explain to Professor Cash why they could not just absorb the second generation tests after they had started using the first generation kits. Professor Cash came to his own independent conclusion that the DoH had 'devised a way' that gave them more time to sort out the funding problems in England and Wales. Professor Cash claimed to have discussed that with Dr Gunson, who did not deny it was a possibility but did not know for certain. Dr Gunson was, on Professor Cash's account, simply carrying out instructions.<sup>467</sup>

<sup>461</sup> Ibid, pages 13–14

<sup>462</sup> Day 72, pages 179–180

<sup>463</sup> Day 82, page 18

<sup>464</sup> Ibid, page 14

<sup>465</sup> Ibid, page 16

<sup>466</sup> Day 72, page 169

<sup>467</sup> Day 82, page 19

*Device of a further study*

**31.325** There appeared to the Inquiry to be two separate issues. First, there was the matter of postponing the start date because the English centres were not going to be ready due to funding problems. The second issue was a desire to do an evaluation of second generation kits, which would inevitably cause delay. Professor Cash was adamant the two were linked. His contention was that the evaluation of the second generation tests was promoted by Department of Health civil servants to buy more time to 'cover up' the fact that English centres were not going to meet the 1 July deadline because the funding was lacking. Professor Cash suggested the evaluation of second generation kits was used as a 'device' to justify the delay.<sup>468</sup>

**31.326** Professor Cash was asked if there was any reason why it was not possible to start screening using the second generation kits and thus to assemble evidence on how they performed. He agreed that it should have been possible. He thought that 'was done readily by half the world'.<sup>469</sup>

**Meeting of the ACTTD on Monday 25 March**

**31.327** Following the three distressing telephone calls between Professor Cash and Dr Gunson on 23 and 24 March 1991, Professor Cash said they had 'fallen out badly' but 'fell in again' shortly afterwards. Professor Cash, with 'some reluctance,' agreed to attend the meeting of the ACTTD on the following Monday (25 March) and not object to the second generation kits study and the delay in the introduction of testing.<sup>470</sup>

**31.328** The meeting of the ACTTD duly took place on the Monday.<sup>471</sup> At point 4.11 the minutes record:

The proposed starting date of 1st July presented difficulties since it was considered essential that the second generation test from both Ortho [*sic*] and Abbott should be evaluated prior to the commencement of routine tests.<sup>472</sup>

**31.329** There was reference to difficulties with the availability of both Ortho and Abbott second generation test kits. There was no official date for the launch of the second generation kit from Abbott.<sup>473</sup>

**31.330** There was an acknowledgement that 1 July looked difficult as a start date, but the minutes of the meeting did not go so far as to suggest a new date. There was a reference to Dr Gunson contacting Abbott to find out their availability date and then recommending a start date for the commencement of tests. There is no reference in the minutes to funding issues in England and Professor Cash could not recall if it was discussed.<sup>474</sup> However, as noted above, when Dr Gunson wrote to Professor Cash on 28 January, and in later exchanges, it was taken as common ground between them that for England and Wales there was the matter of financial provision to be sorted out.<sup>475</sup>

<sup>468</sup> Day 72, pages 167–68

<sup>469</sup> *Ibid*, page 169

<sup>470</sup> *Ibid*, page 175

<sup>471</sup> Meeting Minutes [SNB.001.8793]

<sup>472</sup> *Ibid* [SNB.001.8793] at 8794

<sup>473</sup> *Ibid* [SNB.001.8793] at 8794

<sup>474</sup> Day 82, page 47

<sup>475</sup> Letter [SNB.004.4574]: see paragraph 31.267 above

**31.331** There is no reference in the minutes to ‘decoupling’ the second generation evaluation from the actual commencement of testing. There is also no suggestion that, given the problems with the availability of second generation kits, the UK should screen using available first generation kits and evaluate the second generation kits afterwards.<sup>476</sup>

**31.332** Professor Cash’s position in oral evidence was that he did not suggest to the ACTTD that screening should start on 1 July with second generation evaluation being fitted in later, as he had promised Dr Gunson he would not say anything about it at the meeting.<sup>477</sup> It was put to Professor Cash during his evidence that the minutes of the meeting of the ACVSB on 25 February 1991 suggest that it was the ACVSB that had decided that there should be an evaluation of the second generation kits and that that should happen before transfusion centres decided which test to adopt. Professor Cash disagreed with that proposition, however. He believed that the mechanism by which evaluation of the second generation kits would take place before transfusion centres decided which kit to use, was achieved and delivered by this meeting of the ACTTD.<sup>478</sup>

**31.333** Professor Cash wrote a letter to Mr McIntosh dated 27 March 1991<sup>479</sup> following the ACTTD meeting and copied it to Dr McIntyre at the SHHD and to the Transfusion Directors. The letter stated that it was clear the NBTS was struggling to meet the 1 July commencement date and Professor Cash believed there was a fundamental problem with financial resources. Dr Gunson was to tell the DoH that the 1 July start date should be delayed until such time as an evaluation of the second generation HCV screening tests had been completed. If that was accepted it could push the start date to September. The impression created by Professor Cash’s evidence was that this would be an indication that the recommendation to postpone had the backing of medical professionals.

**31.334** Professor Cash stated in his letter that both he and Dr Mitchell supported the proposal that the start date should be pushed back to September. He explained in oral evidence that this was what he had agreed with Dr Gunson on the telephone that he would do.<sup>480</sup>

**31.335** Mr Panton added a handwritten comment to Mr Hogg on this letter to say that this was a ‘worrying’ development: they could not go to the Scottish Minister until they knew the start date. It appears to the Inquiry that this letter was the first indication that the SHHD had received that there was a problem with the proposed start date and a plan to postpone the introduction of screening.<sup>481</sup>

**31.336** Mr Tucker commented in his statement that there was no doubt in his mind that the Scottish Minister would have supported what was agreed by the English Ministers: ‘This would have been the case irrespective of when our minute was submitted’.<sup>482</sup>

**31.337** With regard to NHS financial problems in England and Wales, Mr McIntosh told the Inquiry in oral testimony that he could not recall any briefings about this issue. He felt this backed up his ‘secondary theory’ that there were issues about money. Professor Cash was suggesting that he was aware at the time that the English were not implementing

<sup>476</sup> Day 82, pages 48–49

<sup>477</sup> Ibid, page 50

<sup>478</sup> Ibid, pages 38–39

<sup>479</sup> Letter [SGF.001.2026]

<sup>480</sup> Day 82, page 67

<sup>481</sup> Letter [SGF.001.2026]

<sup>482</sup> Mr Tucker’s Statement [PEN.017.2060] at 2067



testing because of financial restraints in the regions, but was still encouraging Scotland to hold back and follow the 'party line'.<sup>483</sup>

### End of March to September 1991

**31.338** Mr McIntosh described this period from late March to the end of August 1991 as including discussion of further validation and testing, but in reality creating successive delays in full implementation due to dedication to 'UK solidarity'. He commented in his statement that:

[T]he successive delays from 1<sup>st</sup> April through to 1<sup>st</sup> September were not made necessary by any considerations as to what would be best for patients in Scotland nor indeed by any Scottish issues. They were exclusively – rightly or wrongly – a direct result of the UK solidarity argument prevailing over other opinions.<sup>484</sup>

**31.339** He said that there was a group of Regional Transfusion Directors in the SNBTS who favoured implementation as soon as possible. They were opposed by people who were members of the 'UK solidarity camp', as he described them, and who were firmly of the view that all parts of the UK should implement testing at the same time. According to Mr McIntosh the 'UK solidarity camp' was 'best exemplified' by Professor Cash.<sup>485</sup>

**31.340** In Mr McIntosh's view, there was no real administrative control over the dates of commencement of testing. There was no mechanism for preventing one centre from starting to screen donors before other centres were ready and there was no mechanism for censure of a centre that proceeded before the global start date. Mr McIntosh commented that if there had been control it would have been exercised in reaction to the unilateral commencement of testing by the Newcastle centre discussed below.<sup>486</sup> The only censure that the Inquiry is aware of was the suggestion, made by Professor Cash, of the exclusion from national committees of the head of the Newcastle centre, Dr Lloyd.<sup>487</sup>

**31.341** On 3 April 1991 Dr Gunson wrote to the Regional Transfusion Directors in England and Wales (and copied in Professor Cash) to advise it would not be possible to introduce testing on 1 July.<sup>488</sup> It had not been possible to start the evaluation of the second generation Ortho and Abbott tests. One of the kits would not be available until later in April. The schedule would be too tight if the transfusion services tried to evaluate the second generation test, and commence screening on 1 July. It was difficult to give a precise date for the commencement of screening, but Dr Gunson thought they should aim to start by 1 September.

**31.342** On 3 April 1991 Mrs Falconer was asked in a handwritten memorandum by David Hogg to 'Please check with DOH if they have considered a new start date ... and if they could advise us accordingly before we go to the Minister'.<sup>489</sup> On 4 April Mrs Falconer sent a handwritten note to Mr Hogg to say the DoH was considering a new start date of 1 September 1991, but the date had not yet been finally agreed.<sup>490</sup>

<sup>483</sup> Day 70, pages 108–109

<sup>484</sup> Mr McIntosh's Statement [PEN.017.2126] at 2134

<sup>485</sup> Ibid [PEN.017.2126] at 2134

<sup>486</sup> Day 70, page 16

<sup>487</sup> Professor Cash's letter [SNB.011.8726]

<sup>488</sup> Dr Gunson's letter [SNB.004.4883]

<sup>489</sup> Memo [SGH.002.7877]

<sup>490</sup> Handwritten note [SGH.002.7876]

**31.343** On 4 April, Dr Gunson wrote to the NHS Procurement Directorate in response to their letter of 21 March (as referred to in paragraph 31.308), above. The letter bore the heading 'Comparative evaluation of hepatitis C kits – phase II' and stated:

The timing of this study has slipped because of the unavailability of test kits. The Ortho 2nd generation tests have only arrived at North London RTC within the past few days and it is unlikely that the Abbott test kits will be available until the middle of April.<sup>491</sup>

**31.344** Dr Gunson stated in his letter that Dr Metters had agreed with him that the introduction of testing could be delayed until 1 September. In his evidence to the Inquiry Mr Tucker expressed the opinion that Dr Gunson appeared to be taking the decision himself.<sup>492</sup>

**31.345** On 5 April, Professor Cash replied to Dr Gunson's letter of 3 April and confirmed that, 'My colleagues would wish you to know that this most recent development, leading to a start date in September 1991, has the SNBTS Directors' fullest support'.<sup>493</sup>

**31.346** When pressed on the first occasion he gave oral testimony on this matter, Professor Cash conceded it was 'very probable' that he had written and recorded the support of his fellow directors without having specifically asked them.<sup>494</sup> On the second occasion he gave oral evidence, Professor Cash was adamant: 'I cannot imagine ... that I hadn't in some way consulted with my colleagues'.<sup>495</sup> He added later in oral evidence, 'I can't imagine I would have written it without ringing ... just to find out their views'.<sup>496</sup> The Inquiry notes that Professor Cash's letter of 5 April was not copied to the SNBTS Directors.

**31.347** On 11 April the DOH faxed Mrs Falconer (SHHD) the draft of a proposed letter, EL(91), to the Regional Health Authorities in England and Wales.<sup>497</sup> It stated:

Ministers have agreed that screening of blood and plasma for HCV should be introduced as a public health measure now that suitable tests are available .... No date for the introduction of routine testing has yet been fixed but this is unlikely to be before 1 September 1991. You will be informed as soon as a date has been agreed .... No additional [funding] allocation will be made for the cost of testing in the HCHS budget for 1991-92 and Regions will have to meet the increased blood handling charges from their general allocation. The Department is negotiating a national maximum contract price for testing kits. Further details of this will be made known as they become available.<sup>498</sup>

**31.348** On 15 April, Mrs Falconer sent a note to Mr Hogg: 'Please see para 11 of draft DOH EL(91) which shows proposed date for introduction of HEP C screening not yet fixed but unlikely to be before 1 Sept 1991. Can we now put forward submission?'.<sup>499</sup>

---

<sup>491</sup> Letter [PEN.016.0166]

<sup>492</sup> Day 69, page 126

<sup>493</sup> Professor Cash's letter [SNB.006.3958]

<sup>494</sup> Day 72, pages 174-175

<sup>495</sup> Day 82, page 68

<sup>496</sup> Ibid, pages 142-143

<sup>497</sup> Fax [SGH.002.7867]; Draft letter [SGH.002.7869] at 7872

<sup>498</sup> Draft letter [SGH.002.7869] at 7872

<sup>499</sup> Note [SGH.002.7864]

***Newcastle starts screening***

**31.349** On 30 April there was an SNBTS/NBTS Liaison Committee meeting.<sup>500</sup> It was suggested that a commencement date of 1 September would be appropriate. Dr Gunson reported that the general manager at the Newcastle Transfusion Centre, Dr Huw Lloyd, had commenced testing in the last week. There was no confirmatory testing being carried out and it was not clear whether positive donors were being counselled. Mr McIntosh immediately informed SHHD officials about these events. Dr Gunson had already advised the DoH of the same and 'advice was awaited'. Dr Gunson hoped to establish multi-centre evaluation of second generation kits with Newcastle as a participating centre. He expected an SNBTS centre would contribute to the evaluation.

**31.350** The minutes of the Liaison Committee meeting go on to note that '[i]t was agreed that a firm clarification of policy was urgently required from DoH/SHHD within 7-10 days'.<sup>501</sup> It is not clear on the face of the minutes whose responsibility it was to carry out that task as no initials appear next to that section of the minutes.<sup>502</sup> When questioned later in oral evidence, Professor Cash commented that 'Harold would have gone back to [the DoH] .... David would go to the Scottish Office. Looking at seven to ten days, that's miraculous timing'.<sup>503</sup>

**31.351** Professor Cash could not recall if there was an attempt within that limited period of time to get clarification of a policy from the SHHD. He did not know if Mr McIntosh had gone to the Scottish Office to request clarification.<sup>504</sup>

**31.352** Dr Lloyd of the Newcastle centre wrote to all Directors of the transfusion services on 2 May 1991 and copied his letter to Dr Gunson and Professor Cash.<sup>505</sup> In his letter Dr Lloyd stated that as Newcastle was already set up for testing, he had decided to keep to the July implementation date. His personal view was that to not test when there was the ability to test would be 'indefensible under the current Product Liability Legislation'. He commented: 'By 1st July all units of blood for transfusion in the Northern Region will be negative for Hepatitis C antibody'. There was a lead-in time to ensure all products were tested by 1 July, which Dr McClelland pointed out in oral evidence related to the shelf life of these products.<sup>506</sup>

**31.353** Dr Lloyd's letter generated a number of responses from other Transfusion Directors. On 7 May, Dr Mitchell wrote to Dr Lloyd with a hint of concern that screening had commenced so far ahead of the results of the evaluation tests. Dr Mitchell added that he presumed Dr Lloyd had 'started using the most appropriate test which you have validated on the results of the current three Centre evaluation of the 2nd Generation tests'.<sup>507</sup>

**31.354** Professor Cash wrote a letter about 'solidarity'<sup>508</sup> to Dr Lloyd on 7 May to express his 'profound dismay' at this turn of events.<sup>509</sup> The letter stated that Dr Lloyd's unilateral introduction of testing was both 'disgraceful and mischievous'. Professor Cash stated,

<sup>500</sup> Meeting Minutes [SNB.010.1108]

<sup>501</sup> Ibid [SNB.010.1108] at 1110

<sup>502</sup> Day 82, page 90

<sup>503</sup> Ibid, page 148

<sup>504</sup> Ibid, page 149

<sup>505</sup> Letter [SNB.004.5129]

<sup>506</sup> Day 69, page 48

<sup>507</sup> Dr Mitchell's letter [SNB.006.4010]

<sup>508</sup> Day 82, page 74

<sup>509</sup> Professor Cash's letter [SNB.011.8726]

whilst giving oral evidence, that he now regretted writing his letter to Dr Lloyd.<sup>510</sup> He added that, looking back, he 'shouldn't have sent it, period, full stop'.<sup>511</sup> Professor Cash did not ever believe Dr Lloyd's actions had been correct however.<sup>512</sup>

**31.355** Dr Lloyd wrote back to Professor Cash on 9 May. He personally believed that to start HCV testing according to the original schedule was the correct decision, even if others found it unpalatable.<sup>513</sup> He went on:

To suggest that my action was ... "mischievous", is to impart motives to this action that were not mine. If you wish to question motives, then perhaps you should be asking why a vague September start date has replaced with little explanation, a firm date in July.

**31.356** On 9 May 1991 J C Dobson, DoH, sent an internal memorandum by fax to a DoH official with copies to Dr Metters and others:

1. You will wish to be aware of a potential difficulty over screening for hepatitis C in blood donations, which may be picked up by the press.
2. Ministers decided earlier this year to authorise the routine screening of all donated blood for the hepatitis C antibody. After discussion within the NBTS a start date of 1 July was agreed but this was later delayed to allow evaluation of the "second generation" test kits. Despite this, the Northern Regional Transfusion Centre made a unilateral decision to start screening from late April.
3. Press interest is likely to focus on the prospect of the other Regions using untested blood, and may attempt to link it with the current interest in the settlement for haemophiliacs who were infected with the AIDS virus and the recent claims for compensation by people infected with HIV through blood transfusion.
4. I attach a background note and a line to take.<sup>514</sup>

**31.357** The memo by J C Dobson was also sent by fax to the SHHD, and in a handwritten note dated 8 May Mr Panton advised Mr Hogg: 'I have discussed this with Mr Tucker. We should put our submission forward about the 1 Sept start date and incorporate this: – Northern jumped the gun etc. Line to take for media enquiries'.<sup>515</sup>

**31.358** Dr Lloyd wrote a conciliatory letter in response to Professor Cash on 4 July. The two had met and mended their differences. Dr Lloyd expressed his concern that the UK was dragging its feet with regard to testing. Some of his staff had been concerned at the tone of the initial letter Professor Cash had written on 7 May and how it affected them.<sup>516</sup>

**31.359** Professor Cash wrote to Dr Lloyd for the last time on this topic, on 19 July.<sup>517</sup> He emphasised the importance of the 'team approach' and the risk of exclusion if Dr Lloyd did not adhere to the team mentality. Professor Cash expressed his concern at the

---

<sup>510</sup> Day 72, page 178

<sup>511</sup> Ibid, page 180

<sup>512</sup> Ibid, pages 182–183

<sup>513</sup> Dr Lloyd's letter [SNB.004.5142]

<sup>514</sup> Memo [SGH.002.7855]

<sup>515</sup> Handwritten note [SGH.002.7854]

<sup>516</sup> Dr Lloyd's letter [SNB.004.5732]

<sup>517</sup> Professor Cash's letter [SNB.011.7806]

'continued Balkanised mentality of BTS in England and Wales'. Dr Lloyd intended to be in Edinburgh the next month and Professor Cash invited him to take the 'opportunity of apologising ... to the SNBTS Directors'.<sup>518</sup> Professor Cash, in oral evidence, admitted to some regrets about this letter. He added that Dr Lloyd did not accept the invitation to apologise personally to the SNBTS directors.<sup>519</sup>

### *Consideration of earlier start in Scotland*

**31.360** Dr McClelland was asked about the position in Scotland, and the possibility of similarly going ahead with screening more quickly. He was uneasy about the delay in commencement and said in his statement that there 'certainly was consideration of an earlier start'. He recalled that the introduction of screening had been at the meeting of the SNBTS directors on 11 and 12 June 1991.<sup>520</sup>

**31.361** On the same theme, Dr Perry commented in oral evidence that in a practical sense it would have been possible for different parts of the UK services to have commenced testing at different times. He thought 'it would have been possible ... for the SNBTS to have gone ... on the original date of April'. He added: 'But underpinning the whole exercise was this UK common start date'.<sup>521</sup> From a 'practical and political perspective' it would have been impossible; the SNBTS would not have had the authority from the SHHD or the Department of Health.<sup>522</sup>

### *Public presentation of the further study*

**31.362** On 8 May 1991 Professor Cash faxed a letter to Dr Gunson in the immediate aftermath of the Newcastle decision. He suggested a national large-scale validation study, and added, 'We should make every effort to maximise this disaster to our corporate advantage'. It appears from the letter that it follows a previous discussion between the two on how to move on from the Newcastle events. The commencement of testing in Newcastle would be portrayed as a further, continued, study. Phase I would run until 15 July and it would be an exercise to assess the efficacy of the two different second generation kits. Phase II would run from 15 July to 31 August, in order to collect more screen test positives to assist in more extensive studies. This was described by Professor Cash in his letter as the 'public reason' for Phase II. It would allow the centres participating in the extended trial to continue to screen through to 1 September, and not have a break in between.<sup>523</sup>

**31.363** Professor Cash suggested the Glasgow centre might enter this national study. Glasgow and Newcastle would be the centres testing the Abbott kits and there would be two English centres testing Ortho kits. Professor Cash commented in his letter that Dundee and Inverness would be happy to 'pitch in' using the Ortho tests, but that their donation collections were relatively small and could be a disadvantage to Ortho. Funding was going to be a problem as it was becoming a larger exercise. Professor Cash was going to be on leave, and copied the letter to Dr Mitchell to ensure continuing SNBTS managerial support for Dr Gunson. It was also 'silent copied' to Mr McIntosh for reference.<sup>524</sup>

<sup>518</sup> Ibid [SNB.011.7806] at 7807

<sup>519</sup> Day 72, page 185

<sup>520</sup> Dr McClelland's Statement [PEN.017.2491] at 2502. The meeting at Stirling is considered further at paragraph 31.384 below.

<sup>521</sup> Day 68, page 127

<sup>522</sup> Ibid, pages 127-128

<sup>523</sup> Dr Cash's letter [SNB.005.1723]

<sup>524</sup> Ibid [SNB.005.1723] at 1724-25

**31.364** In his oral testimony, Mr McIntosh considered whether or not Professor Cash had sought the Board's consent to offer the Glasgow centre into this study. He said:

It's inconceivable that we would have done this in Glasgow without the whole of the SNBTS management board having agreed it and the other RTCs being comfortable. So one has to assume that Edinburgh, Aberdeen, Inverness, Glasgow, Dundee would have known and were content at this time.<sup>525</sup>

**31.365** Despite extensive examination of documents from this short period of time in May 1991 when Professor Cash and Dr Gunson corresponded about which centres should evaluate the second generation kit, it has not been possible to find any documentary evidence that the matter was put before the SNBTS board for consent. It appears that the two National Directors decided together that Glasgow RTC would be one of the centres to take part in the evaluation.

**31.366** There is a reference in Professor Cash's letter of 8 May 1991 to a 'public' reason for Phase II of the study. Professor Cash agreed in oral evidence it could be described as '[A] device. There is no doubt whatsoever'. He did not disagree that this suggested a degree of deception.<sup>526</sup> He claimed his preferred option, in response to the Newcastle events, was for testing to commence in an orderly fashion without sticking rigidly to September as the start date and that Scottish centres could be in the first wave of the introduction.<sup>527</sup> He wanted the Scottish Office to review the situation and give guidance on the next steps: 'it was a policy decision that had to be made by Ministers'.<sup>528</sup> He had no recollection of putting this in writing to the SHHD and the Inquiry has found no evidence of written communication to decision makers at the SHHD from the SNBTS on this particular question.<sup>529</sup>

#### *Arrangements for the further study*

**31.367** On 13 May 1991 Dr Gunson produced a draft protocol including two new English RTCs, entitled 'Extended pilot trial of 2nd generation anti-HCV tests'.<sup>530</sup> The protocol stated:

It is proposed to ask three RTCs in England and one in Scotland to undertake an extended trial of 2nd generation Ortho and Abbott anti-HCV tests. The RTCs using the Ortho tests are Liverpool and Leeds and those using Abbott tests are Newcastle and Glasgow.<sup>531</sup>

**31.368** Also on 13 May 1991, Professor Cash wrote to Dr Gunson (copied to Dr Calman and Dr Metters), in the week following the unilateral commencement of HCV screening in Newcastle. He stated:

It has always been the view in Scotland, both in the Scottish Office and throughout the SNBTS, that the introduction of additional microbiology donation screening tests would be subject to Ministerial approval. Our understanding of this issue goes back many years .... In recent times, evidence

---

<sup>525</sup> Day 70, page 48

<sup>526</sup> Day 82, page 82

<sup>527</sup> Ibid, page 83

<sup>528</sup> Ibid, page 84

<sup>529</sup> Ibid, page 84

<sup>530</sup> Draft proposal [PEN.016.0249]

<sup>531</sup> Ibid [PEN.016.0249] at 0250

that Ministers wished to acquire a firmer grip on this activity came with the establishment of the Advisory Committee on the Virological Safety of Blood. This development, in principle, was warmly welcomed in Scotland.<sup>532</sup>

**31.369** On 14 May, Professor Cash wrote to Dr Mitchell at Glasgow Regional Transfusion Centre to 'confirm that Harold Gunson and I have agreed that West BTS should form one of the Abbott wings of the UK BTS Second Generation (HCV) donation testing study'.<sup>533</sup> This study would ensure full donation testing in that region and would continue through to the proposed date for full screening on 1 September. It had been suggested by Dr Gunson that donor counselling would not feature during the study period. It appears that funding was no longer an issue: Dr Mitchell was asked to cost the exercise and let the SNBTS and John Francis (SNBTS, Finance Officer) know the figures.

**31.370** On 14 May Professor Cash sent a long memorandum about HCV testing to the SNBTS Board members in response to an article in *The Sunday Times* of 11 May with the headline 'Victims to sue in new infected blood scandal'.<sup>534</sup> This memorandum appears to be a justification, rather than a request for consent, for evaluating the improved second generation tests as the first generation tests were withdrawn. The memorandum states that:

[R]epresentations are being made, in the light of the developments in Newcastle RTC, as to whether, in future, the SNBTS is bound to a UK BTS approach with regard to donation testing, against a background of Ministerial involvement.<sup>535</sup>

That implied an understanding on his part that the SNBTS had been obliged to adhere to a start date which was the same throughout the UK.

**31.371** On 15 May 1991 Professor Cash wrote to Dr Gunson to thank him for his proposed protocol for the extended HCV trial.<sup>536</sup> Professor Cash expressed his desire to encourage the participants in the extended trial to keep going after mid-July. He acknowledged this would certainly happen in Newcastle. He expressed concern that 'some people (notably David McIntosh!) may get very jittery'. Professor Cash balanced this with his view that the period from mid-July to 1 September would deliver a further batch of screen positive samples. This was described in his letter of 8 May as the 'public reason' for Phase II of the validation study. This would mean that, by the time full screening started, the SNBTS would be in a very strong position with regard to matching data on RIBA and PCR. This in turn would help enormously in the preparation of guidelines for future handling.<sup>537</sup>

**31.372** In oral evidence Mr McIntosh denied the description of himself as 'jittery' at the time.<sup>538</sup> He was certainly 'very concerned', but in May of 1991 the anxiety about the date of introduction of screening had not reached its later heights. The SNBTS was still hoping to proceed quite soon.

<sup>532</sup> Letter [SNB.005.1721]

<sup>533</sup> Letter [SNB.005.1711]

<sup>534</sup> Professor Cash's memo [SNB.005.1717]. *The Sunday Times* article was in fact published on 12 May [SGH.002.7853]

<sup>535</sup> Professor Cash's memo [SNB.005.1717] at 1719

<sup>536</sup> Professor Cash's letter [SNB.005.1707]

<sup>537</sup> Ibid [SNB.005.1707]

<sup>538</sup> Day 70, page 53

**31.373** Mr McIntosh said later in oral evidence that his recollection was:

[N]ot that I got jittery when the news of Dr Lloyd's action became known; I got jittery, and increasingly so, from April onwards because we [SNBTS] were not doing what we ... were encouraged to do, which was to introduce screening as soon as reasonably practicable.<sup>539</sup>

**31.374** On 15 May 1991 Drs Hughes and Macvarish (Glasgow and West of Scotland BTS), reported on their evaluation of the second generation Abbott anti-HCV ELISA.<sup>540</sup>

**31.375** At the meeting of the SNBTS Medical and Scientific Committee on 16 May 1991 it was noted that the best estimate for the commencement of routine anti-HCV screening was 1 September 1991. The minutes confirm that Professor Cash had told Dr Gunson the SNBTS could 'self-fund' the second generation study in Glasgow.<sup>541</sup>

**31.376** Mr McIntosh suggested in oral evidence that the extended trial was a delaying tactic and a 'cover' for the fact that funding was not available throughout the UK. Funding was available in Scotland from April 1991, but not in England. In his opinion England could not afford it so pressure was put on Scotland not to proceed.<sup>542</sup>

**31.377** In practice, as a result of including Glasgow and West of Scotland in the UK Phase II study of anti-HCV testing, nearly half of all SNBTS blood donors were already being screened and would continue to be screened as part of the continuing evaluation exercise, until the commencement of UK-wide routine screening superseded the evaluation. In other words, from some point in May 1991, around 50% of Scottish blood donations was screened for anti HCV due to the West of Scotland Transfusion Centre taking part in the pilot trial of second generation Abbott and Ortho test kits. Anti-HCV positive donations would have been set aside. Dr Perry was not sure what happened to the donors, whether they were simply screened out or told and counselled. He thought that, as the months progressed through 1991, the policy of a common UK start date was becoming harder to reconcile and sustain.<sup>543</sup>

**31.378** The period in 1991 leading up to the introduction of screening was a confused time, according to Dr Perry. There was a confirmatory test in place and the FDA had granted a licence for the Ortho kit. The date for commencement slipped from April to July and then to September, despite a policy decision having been taken by the ACVSB in November 1990 that the UK should introduce HCV screening as soon as practicable, with individual RTCs deciding whether to use the Ortho or Abbott test. The appearance of the second generation tests in early 1991 did not assist. There were rumours of funding difficulties during this time. In his oral evidence Dr Perry commented that the process 'could have been tighter'.<sup>544</sup> He thought that issues were considered and decisions taken by the ACVSB on an incremental basis. Long-term issues such as counselling and follow-up were not considered until the initial policy decision was taken to introduce screening.<sup>545</sup>

---

<sup>539</sup> Ibid, page 104

<sup>540</sup> Evaluation of the Abbott HCV EIA 2nd Generation [SNB.006.4037]

<sup>541</sup> Meeting Minutes [SNB.009.5766] at 5768

<sup>542</sup> Day 70, pages 50–51

<sup>543</sup> Day 68, pages 128–129

<sup>544</sup> Ibid, page 134

<sup>545</sup> Ibid, page 139



**31.379** Dr Perry thought the delay in mid-1991 was caused partially by attention being given to the introduction of the second generation test. As a result first generation kits were dismissed, whereas other countries had been content to introduce them.<sup>546</sup>

**31.380** Dr Perry said in his statement that ‘the actions of Newcastle Transfusion Centre ... whilst widely deprecated, were seen to potentially undermine the rigidity of a common UK starting date, or indeed the enforceability/validity of a “DOH policy”’.<sup>547</sup>

**31.381** Mr McIntosh recalled that he and Dr McClelland had, by May/June 1991, become concerned about the lack of progress regarding the implementation of testing. The SNBTS was able to introduce it, but was held back by waiting for the common UK start date.<sup>548</sup>

**31.382** The ACVSB held a meeting on 21 May 1991.<sup>549</sup> The Chairman referred (under ‘AOB’) to the existence of ‘the policy for a uniform starting date ... endorsed by all UK Health Ministers’ and noted that, despite Northern region’s action, ‘this policy remained firm’.<sup>550</sup> The policy appeared to have been firmed up. The trial of second generation kits had resulted in the decision that individual RTCs could decide themselves which test kit to use from Ortho 2, Abbott 2 or UBI.<sup>551</sup> Mr McIntosh made the point in oral evidence that, as the ACVSB met in confidence, he would not have been aware of the policy and it would not have affected his role in Scotland.<sup>552</sup>

**31.383** Dr Gunson presented details of the proposed extended trial to the ACVSB meeting.<sup>553</sup> This related to the extended trial of anti-HCV tests on blood donations which would now include data from the English, Northern region (Newcastle).

#### ***SNBTS Board meeting, Stirling, 11–12 June 1991 and its aftermath***

**31.384** The minutes of a two day SNBTS Management Board meeting in Stirling in June 1991 record, simply and rather tersely under the heading ‘Anti-HCV testing’, the words ‘Agreed – Routine donation testing to begin on 1<sup>st</sup> September 1991’.<sup>554</sup> Professor Cash agreed in oral evidence that the short note regarding HCV testing was not an accurate record of the discussion that led to the decision that was taken. He did not disagree that the discussion was essentially whether or not Scotland should announce ‘a UDI’ (‘unilateral declaration of independence’) which, in this context, meant Scotland introducing testing ahead of the rest of the UK, as had been done at Newcastle.<sup>555</sup>

**31.385** Dr McClelland composed a letter dated 11 June, addressed to Professor Cash, on the subject of anti-HCV testing.<sup>556</sup> He wanted the matter to be discussed at the Directors’ meeting and was concerned that the fact some centres were testing, albeit on a trial basis (in Newcastle and Glasgow), left the SNBTS very exposed. Dr McClelland wrote:

I would like to be reassured that we are taking the correct decision, both professionally and medical legally, to stay in line with the positions of the

<sup>546</sup> Ibid, pages 135–136

<sup>547</sup> Dr Perry’s Statement [PEN.017.2108] at 2117

<sup>548</sup> Mr McIntosh’s Statement [PEN.017.2126] at 2135

<sup>549</sup> Meeting Minutes [SNB.001.9054]

<sup>550</sup> Ibid [SNB.001.9054] at 9060

<sup>551</sup> Ibid [SNB.001.9054] at 9056

<sup>552</sup> Day 70, page 38

<sup>553</sup> Written details, dated 17 May 1991 [SNB.001.9108]. Dr Gunson also prepared a report, dated 3 July, summarising Phase 1 [SNB.011.7594]

<sup>554</sup> Minutes of a Meeting of the Management Board held on 11-12 June 1991 [SNB.002.7666] at 7669

<sup>555</sup> Day 82, page 152

<sup>556</sup> Dr McClelland’s letter [SNB.002.7902]

majority of English RHA's [Regional Health Authorities]; I think this is in fact what we are now doing rather than abiding by a Department of Health policy because it seems to me that de facto, [there] may no longer be a Department of Health policy in this area.

**31.386** It is not clear if Professor Cash received that letter in time for the board meeting of the same date.<sup>557</sup> The letter suggested, generally, that the issue of the introduction of screening should be discussed. Professor Cash agreed in oral evidence that it was an appropriate topic for discussion at the board meeting.<sup>558</sup> He recalled at one stage in his oral evidence that:

'[W]e [the SNBTS Board] initially got into a general debate with Brian [McClelland] ... responding to the points he was making in his letter ... it was either Brian or David McIntosh that made the move, that triggered off the sad deterioration in the meeting.'<sup>559</sup>

**31.387** Dr McClelland had no personal recollection of that meeting, or the discussion on anti-HCV screening. However, he provided the Inquiry with his own handwritten notes of the meeting,<sup>560</sup> and the section relating to anti-HCV screening was later transcribed by him at the behest of the Inquiry.<sup>561</sup>

**31.388** Dr McClelland recorded in his notes of the meeting that Professor Cash had stated at the meeting that: 'The UK pack is still a pack'.<sup>562</sup> Professor Cash commented in oral evidence that, he was 'reporting back that at that moment, with the exception of Newcastle, the position was being held'.<sup>563</sup> He added that at the time, 'the UK was operating, with the exception of our friends in Newcastle, as a single unit in respect of this topic'.<sup>564</sup>

**31.389** Dr McClelland had also recorded a further comment at the meeting: 'Can we make a strength of this by demonstrating that we have considered the early start option and rejected it in the interest of support/buttressing a coordinated national service'.<sup>565</sup> Professor Cash was unable to say whether that would have been a record of him speaking, but noted that it appeared on the same line as his initials.<sup>566</sup> Mr McIntosh agreed in oral evidence that it appeared to record the decision that was taken.<sup>567</sup>

**31.390** Dr Perry recalled in his statement that, despite Glasgow's involvement in the extended study from May 1991, 'SNBTS Directors remained supportive of a common UK start date, perhaps partly in the belief that SHHD would be unwilling or unable to countenance independent Scottish action'. He recalled further that:

[T]hese issues were considered and debated at some length at the SNBTS Board Meeting on 11<sup>th</sup>/12<sup>th</sup> June, although it was finally agreed to remain firm on the agreed date of 1st September 1991 ... as is very briefly recorded in the minute of that meeting.<sup>568</sup>

<sup>557</sup> Day 82, page 93

<sup>558</sup> Ibid, page 98

<sup>559</sup> Ibid, pages 154–155

<sup>560</sup> Handwritten notes [PEN.017.2769]

<sup>561</sup> Transcription [PEN.017.2774]

<sup>562</sup> Ibid [PEN.017.2774] at 2775

<sup>563</sup> Day 82, pages 101–102

<sup>564</sup> Ibid, pages 107–108

<sup>565</sup> Transcription [PEN.017.2774] at 2775

<sup>566</sup> Day 82, page 102

<sup>567</sup> Day 70, page 145

<sup>568</sup> Dr Perry's Statement [PEN.017.2108] at page 2117

**31.391** Dr Perry recalled that ‘very substantial discussion’ took place and that there were differing views at the Board meeting on the issue of the introduction of screening.<sup>569</sup>

**31.392** Mr McIntosh recalled that the Stirling meeting gave the SNBTS the opportunity to have a ‘serious discussion’.<sup>570</sup> He thought that in some ways it is ‘good practice’ after a ‘heated debate’ with a clear outcome and decision to simply record the decision.<sup>571</sup> In his statement to the Inquiry, Mr McIntosh set out his own memory of that debate, which he would have chaired. Funding was in place in Scotland, ministerial approval had been granted and operational matters ironed out.<sup>572</sup> Professor Cash recalled Mr McIntosh supporting Dr McClelland’s view at the Stirling meeting.<sup>573</sup>

**31.393** Mr McIntosh did not think Professor Urbaniak would have supported early implementation but he thought Dr William (Bill) Whitrow from Inverness and Dr Ewa Brookes in Dundee ‘shared concern’. Mr McIntosh also suggested that Dr Perry, although not a regional director, shared the concern of Mr McIntosh and Dr McClelland. He was doubtful that ‘sharing his concern’ amounted to a willingness to vote against the views of the medical director.<sup>574</sup> The views which Mr McIntosh expressed were described by him as ‘anecdotal and from distant memory’.<sup>575</sup> His views are disputed by some of those who attended the meeting and it is not now possible for the Inquiry to resolve the difference.

**31.394** There was no evidence, according to Mr McIntosh, that any civil servant had instructed the SNBTS to postpone until further notice the planned introduction of HCV testing on 1 April. The SNBTS was funded to introduce the test, not authorised to delay it.<sup>576</sup>

**31.395** On 17 June 1991 Professor Cash wrote again to Dr Gunson:

Picking up the pieces after last week’s near disaster up here.

Could you please:

1. Give me a date when all 2nd Generation Test Study data will be on your desk.
2. Give me the date when the Report (on the 2nd Generation Test Study) will be completed and the recommendations sent “to the Minister”.<sup>577</sup>

**31.396** The Inquiry probed the reference to ‘picking up the pieces after last week’s near disaster up here’. The majority of witnesses thought this referred to the Directors’ meeting of 11 and 12 June and the proposed early implementation of anti-HCV testing in Scotland. Mr McIntosh was adamant in oral evidence that Professor Cash was referring to his pride in having averted the disaster of Scotland going ahead, alone, to start screening for anti-HCV.<sup>578</sup>

---

<sup>569</sup> Day 68, page 131

<sup>570</sup> Mr McIntosh’s Statement [PEN.017.2126] at 2135

<sup>571</sup> Day 70, page 110

<sup>572</sup> Mr McIntosh’s Statement [PEN.017.2126] at 2135

<sup>573</sup> Day 70, page 109 and Professor Cash’s Statement [PEN.017.2779] at 2784

<sup>574</sup> Day 70, pages 118–119. It has been pointed out to the Inquiry that the Directors did not formally vote at meetings.

<sup>575</sup> Day 70, page 118

<sup>576</sup> Ibid, pages 122–123

<sup>577</sup> Letter [SNB.011.8178]

<sup>578</sup> Day 70, page 57

**31.397** Professor Cash agreed in oral evidence that ‘last week’s near disaster’ was the prospect of the SNBTS going ahead with early screening, and ‘doing a Newcastle’.<sup>579</sup> If the SNBTS had gone ahead with screening at that stage, given the declared position of the Scottish Office, it would have been a breach of trust with them. He found this to be ‘unacceptable’.<sup>580</sup> He remarked in his statement that the Stirling meeting involved a hotly contested debate on the proposed early introduction of anti-HCV screening. The proposal was defeated, but if approved he feared ‘it could have triggered a descent into chaos’, with the risk of another potential ‘disaster’: the possible fragmentation of the UK BTS and the SNBTS.<sup>581</sup>

**31.398** The minutes of the June meeting were not approved until the 21 August Board meeting, when Mr McIntosh thought they must have been approved by everyone.<sup>582</sup> He could not recall, as suggested by Professor Cash, asking for the first draft of the minutes to be amended so that a report of the anti-HCV testing debate was removed from the record.<sup>583</sup> Mr McIntosh’s evidence on this point seems preferable given that the agenda for the Board meeting of 21 August – enclosing a revised copy of the draft minutes of the June meeting – stated that the draft minutes had been revised in light of comments by Professor Cash and others, but make no mention of Mr McIntosh having commented on or having sought to revise the draft minutes.<sup>584</sup>

### *Ministerial approval in Scotland*

**31.399** On 25 June 1991 Mr Hogg sent a note to Mr Panton asking, ‘can we discuss the submission format now...’.<sup>585</sup>

**31.400** On 1 July 1991 Dr McIntyre wrote to Dr Metters asking if the paper by Tedder et al in the *British Medical Journal*,<sup>586</sup> reporting ‘strong evidence for the sexual transmission of the Hepatitis C virus’, would pose problems for counselling donors found to be Hepatitis C positive and would, in turn, be ‘likely to result in any changes in the policy decision to implement routine screening on 1 September’.<sup>587</sup>

**31.401** On 11 July 1991 Dr Metters replied to Dr McIntyre’s letter of 1 July. The UKBTS Advisory Committee on Transfusion Transmitted Diseases was preparing advice for transfusion centres about counselling donors and would have regard to all of the latest information from the various studies. Dr Metters did not anticipate that advice from that Committee would influence the date of the introduction of routine hepatitis screening.<sup>588</sup>

**31.402** On a copy of Dr Metters’ letter, a handwritten note from Mr Panton to Mr Hogg dated 17 July 1991 stated: ‘We can now proceed with the Hep C submission. We must get it up this week before Recess’.<sup>589</sup>

<sup>579</sup> Day 82, page 113

<sup>580</sup> Ibid, page 115

<sup>581</sup> Professor Cash’s Statement [PEN.017.2094] at 2105

<sup>582</sup> Day 70, page 111

<sup>583</sup> Ibid, page 111

<sup>584</sup> Agenda [SNB.002.7874]

<sup>585</sup> Handwritten note [SGH.002.7848]

<sup>586</sup> Tedder et al, ‘Hepatitis C virus: evidence for sexual transmission’, *BMJ*, 1 June 1991 [LIT.001.0274]

<sup>587</sup> Dr McIntyre’s letter [SGH.002.7835]

<sup>588</sup> Letter [SGH.002.7834]

<sup>589</sup> Ibid [SGH.002.7834]

**31.403** It appears that the submission seeking approval for the introduction of routine testing of blood donations for anti-HCV did not go to Mr Forsyth (Minister of State with responsibility for health) until 24 July 1991.<sup>590</sup> This is in contrast to the submission for England and Wales, dated 21 December 1990.<sup>591</sup> Mr Tucker explained in oral evidence that the Scottish submission was delayed because it could not go to the Minister until a date for introduction had been set.<sup>592</sup> The submission would have been worked on by other civil servants before coming to Mr Tucker for a final check, prior to being forwarded to the Minister with the start date.<sup>593</sup> Mr Tucker thought approval in principle had already been given for testing, as the Minister did not object to its inclusion in the PES. The Minister turned the submission around in two days and was content to endorse the recommendation.

**31.404** The Scottish submission noted:

In anticipation that testing would be introduced in 1991/92 a PES bid was lodged and this was successful .... The costs for 1991/92 will be in the region of £700,000 and as indicated above this has been already included in the CSA allocation.<sup>594</sup>

**31.405** A draft press release was prepared which stated: 'The annual cost of the testing is in the region of £1.2 million and the Scottish National Blood Transfusion Service has been allocated additional funds to cover this'.<sup>595</sup> A copy of the submission, and a draft press release, were sent to the DoH by fax on 25 July.<sup>596</sup>

**31.406** On 26 July Mr Forsyth's Assistant Private Secretary replied to Mr Tucker to advise that the Minister agreed to endorse the recommendation that routine testing of blood donations for Hepatitis C antibody should be introduced in Scotland from 1 September 1991.<sup>597</sup>

**31.407** The press release was issued on 2 September, in almost identical terms as the original draft produced at the end of July.<sup>598</sup>

**31.408** Mr McIntosh was convinced when he gave oral evidence that the Minister must have had some awareness of the issue of screening as it was in the Public Expenditure Survey budget from April 1991 onwards.<sup>599</sup> He thought the Minister must have signed off on it for the money to have been authorised. He assumed the SNBTS budget would have been 'built' in the autumn of the year before.

### **Screening introduced in September 1991 – retrospective views of the process**

**31.409** On 8 August 1991 Mr Panton wrote to Mr Jim Donald at the Common Services Agency.<sup>600</sup> He stated: 'I am writing to formally advise you that the Minister of State has agreed to the routine testing of blood donations for the antibody to the Hepatitis C virus

---

<sup>590</sup> Submission to Minister of State (Scotland) dated 24 July 1991 [SGH.002.7828]

<sup>591</sup> English submission dated 21 December 1990 [SGH.002.7893]

<sup>592</sup> Day 69, page 117

<sup>593</sup> Ibid, page 122

<sup>594</sup> Scottish submission [SGH.002.7828] at 7829

<sup>595</sup> Draft press release [SGH.002.7831]

<sup>596</sup> Fax cover sheet [SGH.002.7827]

<sup>597</sup> Memo [SGH.002.7817]

<sup>598</sup> Final press release [SGH.002.7783]

<sup>599</sup> Day 70, pages 72-73

<sup>600</sup> Mr Panton's letter [SGH.002.7802]

(HCV) from 1 September 1991'. Funding was already in place and there were arrangements to be made that were necessary to allow testing to commence.

**31.410** On 12 August Professor Cash wrote to Mr Donald in response to his fax of 9 August.<sup>601</sup> The communication of 8 August from Mr Panton had triggered the final phase of a programme agreed at the SNBTS board meeting in June.

**31.411** On 29 August Professor Cash wrote to Mr McIntosh regarding the Stirling meeting and the SNBTS Board decision to stick to the uniform start date. He had recently read the minutes of the 21 May 1991 meeting of the ACVSB and noted the Chairman's comments that "the policy for a uniform starting date has been endorsed by all UK Health Ministers". Professor Cash went on to say in his letter, 'I think we made the right decision at our Board Meeting on 11/12 June 1991'.<sup>602</sup>

**31.412** Mr McIntosh replied by letter the very next day.<sup>603</sup> In it he communicated his conviction that they had taken the best decision available to them and expressed, with reference to the ACVSB minute, a degree of regret that such a record of clear UK policy had only come to his attention indirectly, through unofficial channels, and at such a juncture. He conveyed his belief that in the future, policy decisions potentially affecting the SNBTS should be conveyed to them, both formally and clearly, by the relevant authorities. He concluded his letter by noting that 'I remain convinced however that we can do a lot better next time than we managed, collectively (UK wide), to achieve over HCV'.<sup>604</sup>

**31.413** On 1 September 1991 the SNBTS (and the regional transfusion centres in England and Wales) finally introduced HCV screening of all blood donors using second generation ELISA and RIBA tests.

**31.414** Professor Cash responded to Mr McIntosh on 16 December 1991.<sup>605</sup> Professor Cash commented in oral evidence that the delay in replying was a result of him trying to think of what they could do about the situation.<sup>606</sup> By contrast, Mr McIntosh wrote back immediately on 17 December.<sup>607</sup> Professor Cash had noted in his letter that he was delighted with Mr McIntosh's response. Mr McIntosh commented in oral evidence that Professor Cash was 'being very supportive'.<sup>608</sup>

### Preparation of a history of events

**31.415** An ad hoc meeting was held at the National Directorate of the NBTS on 13 September 1991 to consider the implications of the introduction of anti-HCV testing.<sup>609</sup> The group comprised Dr Gunson, Professor Cash, Dr Mitchell and Professor Tedder. It was agreed that, in order to answer questions which might arise in the future with respect to the timing of the introduction of HCV antibody testing, the facts and decisions taken should be set out in chronological order. The minute of this meeting (revised on 5 February 1992) set out an account of Ortho's progress with their test systems, including their approaches to UK transfusion interests; Abbott's correspondence about their test; and the proceedings of the advisory committees.

<sup>601</sup> Letter [SNB.008.3956]

<sup>602</sup> Letter [SNB.002.0457] emphasis in original

<sup>603</sup> Letter [SNB.005.4822]

<sup>604</sup> Ibid [SNB.005.4822] at 4823

<sup>605</sup> Letter [SNB.014.0418]

<sup>606</sup> Day 82, page 132

<sup>607</sup> Letter [SNB.004.7207]

<sup>608</sup> Day 70, page 87

<sup>609</sup> Minutes of Meeting of UK Advisory Committee on Transfusion Transmitted Diseases [SNB.001.8919]

**31.416** This history of events may have been prepared in case, at a later date, questions were to arise as to whether there had been a delay in introducing HCV screening of blood donors in the UK. The minute did not refer to the following:

- The weight given to the lack of FDA approval of the Chiron/Ortho and anti-HCV ELISA test for use in the USA which was a factor down to 2 May 1990 when licensing of the test was announced (paragraph 31.209).
- The major concerns about funding in England and Wales that were explicit from at least 7 January 1991 (paragraph 31.258), underlined by Dr Pickles' memorandum of 5 February 1991 (paragraph 31.271) and which led to the DoH supporting Dr Gunson's suggestion of a start date of 1 July 1991.
- The ACTTD meeting of 25 March 1991 at which the difficulties in meeting the start date of 1 July were discussed (paragraph 31.330).
- The Newcastle initiative and its impact on the planned uniform start date.

### **Witnesses' views on the process**

**31.417** In an attempt to understand how more than two years passed between the launch of kits to test for the Hepatitis C virus and the introduction in the UK of screening of donated blood using such kits, the Inquiry included in the list of questions for witnesses a request for their individual opinions on the matter. The request was framed with reference to Mr McIntosh's letter of 30 August 1991 to Professor Cash.<sup>610</sup> This letter appeared to recognise that there had been failings in the process leading to the introduction of screening. In providing their statements, witnesses were asked to say whether they agreed with Mr McIntosh's views. Views which witnesses expressed in answering this question were then explored in oral evidence.

### **Dr Perry**

**31.418** As previously explained, Dr Perry was a member of the ACVSB. In the statement he provided to the Inquiry, he set out a considered response to the question seeking his views on possible failings in the process leading to the introduction of screening. His response was as follows:

My personal view is that the early decision to introduce new blood safety measures on a UK wide basis and on a common start date was correct. However I believe there were a number of shortcomings in the overall UK management process ultimately leading to a late delivery of that outcome. These included:

- Unnecessary secrecy and confidentiality associated with the considerations of ACVSB and other 'behind the scenes' discussions.
- Absent or confused processes for communication of ACVSB decisions to operational managers.
- A late recommendation in principle ... by ACVSB and DOH for the introduction of HCV testing. This appeared to be driven primarily by scientific rigour rather than urgent public health considerations.

---

<sup>610</sup> Letter [SNB.005.4822]. See discussion of this letter at paragraph 31.412

- The apparent absence of a clear plan, timescale, strategy or policy guidance (from either DOH or SHHD) for the introduction of testing following the decision in principle by ACVSB in July 1990 to introduce testing.
- The progressive (and largely unexplained) deferral of the UK start date from April to July to September 1991 believed to have been caused at least in part by administrative and funding issues between the English services and DOH rather than operational readiness.
- With hindsight, and given its readiness (both operational and financial) to introduce testing in early 1991, the failure of SNBTS to robustly argue a case for earlier introduction of testing in Scotland with SHHD/Scottish Ministers including the public health consequences of delays. Equally an SHHD apparent reluctance to consider such an option preferring instead to be guided exclusively by timescales determined by DOH.<sup>611</sup>

**31.419** In oral evidence, Dr Perry adhered to the views expressed in his statement. He also agreed that insofar as operational matters were being left to the ACTTD, the gap in meetings of that committee between March 1990 and January 1991 did not assist.<sup>612</sup> He described the period following the meeting of the ACVSB in November 1990 as ‘particularly confused’.<sup>613</sup> In relation to the implementation of a decision to introduce screening, it would have helped if there had been ‘scenario planning’, addressing in advance what practical steps would be required should a decision be taken to introduce screening.<sup>614</sup> Part of the reason for the lack of such planning was the limited communication of the deliberations of the ACVSB. This was due both to the insistence on confidentiality and to there being no structured approach to communication by the officials who attended the meetings; these officials were there to communicate back to operational bodies such as the SNBTS matters which were important for planning and policy purposes, but such communication appeared to Dr Perry to have happened only on a sporadic basis.<sup>615</sup>

**31.420** In relation to the composition of the ACVSB, Dr Perry’s view was that the membership could have been more broadly based.<sup>616</sup> By that he meant that there could have been people, ‘with a slightly greater public health perspective on it’,<sup>617</sup> although he did pay tribute to Dr Mortimer, who was an expert virologist who brought a useful public health perspective to discussions.<sup>618</sup> Dr Perry observed that this was not a process failure, as the membership was determined at the outset of the process.<sup>619</sup> In this regard, however, the Inquiry notes that the membership did change during the period 1989 to 1991 and an additional member or members with a public health background could have been added.

<sup>611</sup> Dr Perry’s Statement [PEN.017.2108] at 2118

<sup>612</sup> Day 68, page 133

<sup>613</sup> Ibid, page 133

<sup>614</sup> Ibid, page 139

<sup>615</sup> Ibid, page 143

<sup>616</sup> Ibid, page 144

<sup>617</sup> Ibid, page 137

<sup>618</sup> Ibid, page 13

<sup>619</sup> Ibid, page 144



## Dr McClelland

**31.421** Dr McClelland had noted in his statement that he agreed there were ‘failings in the process’ leading to the introduction of HCV screening<sup>620</sup> and expanded on this during his oral evidence. In his view, ‘something about the nature and the functioning of the institutions concerned in the UK, was profoundly different [from other countries] and led it to actually being one of the last countries to institute Hepatitis C testing’.<sup>621</sup>

**31.422** In focusing on the implications of the policy for a common UK start date, Dr McClelland observed that those involved in trying to implement screening ‘should have been much more open to recognising that there were problems in certain parts of the country and looked for a way of managing a phased introduction’.<sup>622</sup> He considered that the perception that non-A non-B Hepatitis was a US problem was relevant to the perceived ‘lack of urgency’.<sup>623</sup> The composition and chairmanship of the committee was also relevant. The focus was ‘very virological, very transfusion process-orientated and there wasn’t a loud enough voice ... saying: what about the patients?’.<sup>624</sup>

**31.423** Dr McClelland suggested that the SNBTS could have worked harder on ‘influencing, through Scottish Home and Health Department, civil servants and medical officers... through influencing them, influencing the Minister to make a decision that on this issue Scotland needed to get on with it and go it alone’.<sup>625</sup>

## Mr McIntosh

**31.424** In providing his views to the Inquiry, Mr McIntosh drew a distinction between his impression at the time, according to his recollection in 2011, and opinions he had formed in hindsight. He concentrated on the period after 21 November 1990, when the ACVSB had agreed at its meeting that the UK should introduce Hepatitis C screening of blood donations as soon as practicable.<sup>626</sup>

**31.425** In Mr McIntosh’s view, the policy at the beginning of 1991 was that there should be coordination between Scotland, on the one hand, and England and Wales on the other, and that the start date for screening should be 1 April 1991 across the UK.<sup>627</sup> Funding was in place for screening in Scotland; the target date of 1 April 1991 was, and remains in hindsight, ‘a highly appropriate date for full implementation throughout Scotland’.<sup>628</sup> Had a comprehensive brief been sent to the SHHD in May 1991 and had the up-to-date position and consequences been explained to Ministers, they ‘would surely have decided to authorise the immediate introduction of testing throughout Scotland’.<sup>629</sup> Instead the revised SNBTS position was not put to the SHHD or Ministers until the end of July 1991,<sup>630</sup> at which point the SHHD formally asked Ministers to endorse the commencement of testing on 1 September 1991. The timing of the submission to Ministers in Scotland made it clear that the department ‘was not leading but following’.<sup>631</sup> The most important reason

<sup>620</sup> Dr McClelland’s Statement [PEN.017.2491] at 2503

<sup>621</sup> Day 69, pages 63–64

<sup>622</sup> *Ibid*, page 66

<sup>623</sup> *Ibid*, page 67

<sup>624</sup> *Ibid*, page 74. Dr McClelland instanced Dr Philip Mortimer as having fulfilled this role, but having been a slightly lone voice

<sup>625</sup> Day 69, page 76

<sup>626</sup> Meeting Minutes [SNF.001.1777]

<sup>627</sup> Statement [PEN.017.2126] at 2139 paragraph 7.4. No date is recorded in minutes of ACVSB meeting of 21 November 1990

<sup>628</sup> *Ibid* [PEN.017.2126] at 2140 paragraph 7.8

<sup>629</sup> *Ibid* [PEN.017.2126] at 2140 paragraph 7.10

<sup>630</sup> Although Mr McIntosh had thought that the submission was not sent till August, he accepted that it was sent at the end of July 1991. Day 70, page 91

<sup>631</sup> Statement [PEN.017.2126] at 2144, paragraph 7.15

that Ministers in Scotland did not grant approval for the implementation of testing in the first six months of 1991 was that they were not asked or advised to do so.<sup>632</sup>

**31.426** In Mr McIntosh's opinion, it should have become clear from the first quarter of 1991 that an unsatisfactory outcome was on the cards; more should have been done to have policies and a strategy properly determined and committed to paper, with ministerial approval in place before the end of March 1991.<sup>633</sup> If there had been a formal departmental brief issued at the beginning of 1991, the SNBTS could have been working towards implementation in Scotland in April or perhaps May 1991. Mr McIntosh made the point that different starting dates between Scotland and England/Wales would not have meant a lack of coordination and cooperation.<sup>634</sup> In the absence of an instruction from the SHHD, there should have been, in Mr McIntosh's view, a strategy document from the SNBTS to set out for the CSA, for the SHHD and for Ministers 'the shape and size ... of the problem'.<sup>635</sup> He set out an example of what such a memorandum might have said.<sup>636</sup>

**31.427** What occurred in practice however was that all guidance was coming to the SNBTS via second-hand reporting of advice, recommendations and pronouncements from bodies not part of the SNBTS chain of command. The roles and authority of the ACVSB and the ACTTD over the SNBTS were not clear.<sup>637</sup>

**31.428** Mr McIntosh saw as the key lesson that:

When faced with an ambiguous policy background and a lack of clear leadership from above on an issue as important as this one was, the Service itself must take the lead, on its own responsibility and focusing firmly on its key patient care responsibilities.<sup>638</sup>

### Professor Cash

**31.429** In his statement, Professor Cash told the Inquiry that he agreed with Mr McIntosh's view that there had been failings in the process, and added that he thought there had been 'a good deal more than failings!'.<sup>639</sup> In elaborating this answer in oral evidence, Professor Cash referred to the difficulty for the SNBTS in having input to the meetings of the ACVSB.<sup>640</sup> There were also, he thought, failures of communication and of transparency.<sup>641</sup>

**31.430** Professor Cash also expressed the view that, had an approach been made to the SHHD in the summer of 1991 to propose the introduction of screening in Scotland ahead of the rest of the UK, it would not have been successful.<sup>642</sup>

---

<sup>632</sup> Ibid [PEN.017.2126] at 2144, paragraph 7.17.2

<sup>633</sup> Ibid [PEN.017.2126] at 2140, paragraph 7.12

<sup>634</sup> Ibid [PEN.017.2126] at 2141, paragraph 7.13.1.1

<sup>635</sup> Ibid [PEN.017.2126] at 2141, paragraph 7.13.2.2

<sup>636</sup> Ibid [PEN.017.2126] at 2142, paragraph 7.13.3

<sup>637</sup> Ibid [PEN.017.2126] at 2141, paragraph 7.13.1.2 and at 2142 section 7.13.5

<sup>638</sup> Ibid [PEN.017.2126] at 2145, paragraph 7.20

<sup>639</sup> Statement [PEN.017.2094] at 2105

<sup>640</sup> Day 82, page 129

<sup>641</sup> Ibid, page 130

<sup>642</sup> Ibid, page 161

## Discussion

**31.431** In closing submissions, Counsel to the Inquiry advanced eight questions in this area.<sup>643</sup> They were:

1. When it became apparent in 1988 that tests for the hepatitis C virus were shortly to become available, was there a satisfactory mechanism for determining whether these tests should be introduced for the screening of donated blood in Scotland?
2. When it became apparent that the introduction of screening for hepatitis C might be recommended, was there a satisfactory mechanism for determining when and how the introduction of screening in Scotland would be effected?
3. Whether the existence of two groups with similar remits (the ACVSB and the ACTTD) impeded decision-making.
4. The factors which contributed to there being no decision until November 1990 to recommend to Ministers that screening should start as soon as practicable until November 1990.
5. Why was there a delay of almost ten months between the decision by the ACVSB on 21 November 1990 to recommend the introduction of screening as soon as practicable and the introduction of screening in Scotland on 1 September 1991?
6. Whether, during this period, the involvement of the Health Minister earlier than July 1991 would have led to earlier introduction of screening.
7. The formulation of policy regarding the coordination of the start date for the introduction of screening in Scotland, with the start date for England and Wales, the flexibility of such policy and whether such policy as existed resulted in delay in the introduction of screening in Scotland.
8. The relevance to the decision-making process of the Consumer Protection Act 1987, and the relevance for the consideration of this Inquiry of the decision in *A v National Blood Authority* [2001] 3 All E R 289.<sup>644</sup>

The last question raises matters of law. It is convenient to address it first.

**31.432** In the litigation referred to in question 8, 114 claimants who were infected with the Hepatitis C virus from treatment with blood or blood products raised proceedings under the Consumer Protection Act 1987. These claimants were all infected after 1 March 1988, the date when the provisions of the Act came into effect, but before screening was introduced in 1991. The defendants were the National Blood Authority and others, essentially all those who were, or had become, responsible for the production and supply of blood and blood products in England and Wales. During the course of the litigation, it was agreed that the claims of those infected after 1 April 1991 would no longer be opposed (on the basis that these claimants would receive 90% of the damages to which they were entitled). Thus, the judgement does not scrutinise in detail the course of events after that date.

---

<sup>643</sup> Closing submission – list of issues – Inquiry Counsel [PEN.019.0843] at 0855

<sup>644</sup> A copy of the judgment is at [PEN.017.0302]

**31.433** When before that date testing of donated blood should have been introduced in England and Wales was considered by Burton J in great detail, based on an analysis of the factual and legal position, almost all of which involved examination of the same events as were discussed before the Inquiry. There were arguments in relation to surrogate testing, which was never introduced, and in relation to the delay in starting to test all donated blood for antibodies to the virus.<sup>645</sup> To a minor extent, some evidence emerged at the hearings of the Inquiry which was not before Burton J and, of course, he did not consider any circumstances specific to Scotland.

**31.434** This exercise – that is, determining questions of liability under the Consumer Protection Act 1987 for the non-introduction of Hepatitis C testing, – did not involve the law of negligence, but a matter of statutory liability, based on underlying European legislation. As Burton J expressed it:

What is to be done is, as against what did occur, to set out what I may be persuaded should have occurred, in the round. This involves my looking realistically as to how much time it is legitimately to be expected that the producer should have taken to introduce the precaution which he did rightly introduce but, as the Claimants allege, later than he ought to have done had he taken all legitimately expectable steps.<sup>646</sup>

**31.435** In the part of his judgement dealing with the delay in introducing what Burton J refers to as ‘the assay’, a table is set out to illustrate the position in the 25 countries referred to by the parties to the case.<sup>647</sup> These countries are in Europe, with the addition of the USA, Canada, Australia and Japan. The table shows that of those 25 countries, the last two to introduce screening for Hepatitis C were the UK and Ireland, in September and October 1991. Burton J concluded that the basic requirements which had to be satisfied before screening could be introduced were the carrying out of pilot studies and evaluations, the planning for counselling and implementation and the execution of that implementation in respect of equipment, staff and building works. In light of his assessment of how long these steps should have taken, he concluded that, as a matter of fact, routine screening ought to have been introduced by 1 March 1990.<sup>648</sup>

**31.436** This Inquiry is not bound by the decision of Burton J. It was reached in a different jurisdiction and it addressed a different question, namely that of legal liability to a group of claimants. But, as already observed, the case involved examination of the same factual material as did the investigation of this topic by the Inquiry. The decision (that after 1 March 1988, by which time surrogate testing should have been in place, blood and blood products infected with the Hepatitis C virus did not provide the safety which persons generally were entitled to expect) was not appealed. Before the Inquiry, there was no attempt to argue that the delay in introducing anti-HCV screening until September 1991 was justified, or even reasonable. The Inquiry has therefore started from the proposition that there was unjustified delay in introducing screening, and has tried to analyse how it occurred.

---

<sup>645</sup> Issues relating to surrogate testing are considered in Chapter 27, *Surrogate Testing of Donated Blood for non-A, non-B Hepatitis*

<sup>646</sup> Judgement [PEN.017.0302] at 0388, paragraph 145

<sup>647</sup> Ibid [PEN.017.0302] at 0387, paragraph 143

<sup>648</sup> Ibid [PEN.017.0302] at 0405, paragraph 172 ii)

**31.437** The issues which are highlighted in the remaining questions set out above at paragraph 31.431 are all relevant to the task of trying to identify the factors which led to the delay. These issues are addressed in the discussion which follows. It is appropriate to comment first on the two main advisory bodies, the ACVSB and the ACTTD.

### **The ACVSB and the ACTTD**

#### *Was a new body required?*

**31.438** When it became apparent in 1988 that tests for the Hepatitis C virus were shortly to become available, there was no satisfactory mechanism for determining whether these tests should be introduced for the screening of donated blood in the UK as a whole, and in Scotland in particular.

**31.439** To some extent the constitutions of the two committees that emerged reflected two distinct needs. The constitution of the ACVSB had to meet a need for scientific expertise. The main qualities required of its members would relate to the range of relevant real expertise and acknowledged authority drawn upon. Geographical representation might be uneven. In particular, office holders in territorial BTS organisations would not have been considered for selection in that capacity. Such advisory committees frequently, if not invariably, operate on a UK-wide basis, drawing on expertise from all parts of the UK where that is possible. In contrast, the ACTTD had a more practical focus and had to reflect practices in the constituent parts of the service as a whole. It would be expected that there would be representation of the territorial organisations.

**31.440** The ACTTD could not, at its own hand, establish the relationships necessary to ensure the level of collaboration that would have been required to provide fully informed advice to government, taking account of science and the practical transfusion issues that would emerge. As already commented; unfortunately, the terms of reference adopted by the ACTTD at its first meeting cut across the remit of the ACVSB.<sup>649</sup> The qualification to the ACVSB terms of reference, which was adopted on 4 April 1989, appeared to subject all changes in transfusion practices that would have major implications for other related bodies, to the ACVSB for prior oversight.

**31.441** As a practical matter, the potential for discord was real in Scotland, but it appears that it did not have practical effect in England and Wales. Dr Gunson, National Director of the NBTS in England and Wales, was a member of the ACVSB and of the ACTTD, and was in direct contact with the DoH. He also coordinated the work of Regional Transfusion Directors in England in instructing tests on behalf of the ACVSB. In contrast, Professor Cash, National Medical and Scientific Director of the SNBTS and Dr Gunson's equivalent in Scotland, was not a member of the ACVSB. Further, the policy of confidentiality pursued meant that Professor Cash was not fully informed of the thinking of the ACVSB, even when it dealt with transfusion issues relating or potentially relating to Scotland.

**31.442** In 1988, the UK Government did not have in place suitable advisory bodies to deal with emerging knowledge of HCV as the means of addressing the risk of infection with the disease in the course of NHS treatment and management. That was the view of Dr Gunson, Dr McClelland and Dr Pickles in the early part of the year. It was also the view of Dr Harris when he addressed the issue in July 1988. His opinion may have involved a particularly narrow view of the skill sets of the members of the EAGA in the context of

---

<sup>649</sup> See paragraph 31.44

transfusion medicine. Professor Cash and Dr McClelland especially thought that the EAGA might explore infection-related matters other than AIDS.<sup>650</sup> Even their view, however, serves to emphasise the lack of an appropriate vehicle for the provision of advice on viral diseases more widely. In the context envisaged by Dr Harris, the view that a new body was required was clearly correct. In principle, the need for a new advisory body was never challenged once it had been articulated by him. Professor Cash's response to the proposal, in July 1988, was to welcome the establishment of a UK group and to comment that he would appreciate, in due course, the opportunity to provide an input with regard to its membership.<sup>651</sup>

**31.443** While departmental responsibility for implementing government policy in relation to health was allocated to the Secretary of State for Scotland, it would not have been an appropriate use of resources to equip the Scottish Office generally, and the Scottish Home and Health Department in particular, with all of the skills required, first to assimilate the advice of advisory and other external bodies and then to advise Scottish Office Ministers independently of the advice available to their colleagues in United Kingdom Departments. The team of Scottish Office officials, medical and administrative, was small, and could not have been expected to act without reference to counterpart teams in the DoH. So far as obtaining advice to inform policy decisions is concerned – ultimately a facet of Cabinet government, collaboration and joint consultation – recognising the superior resources of the DoH is not open to criticism.

**31.444** It appears that to avoid budgetary issues and to avoid referring the proposals to Ministers, Dr Harris originally envisaged that the new group would be a working group of the existing NBTS Advisory Committee. What emerged was a properly constituted Advisory Committee, appointed by Ministers to advise Ministers.

**31.445** The evidence does not disclose the process by which the change was brought about nor why so much time passed between the new committee first being proposed by Dr Harris in July 1988<sup>652</sup> and the first meeting of the ACVSB on 4 April 1989. No explanation has been found for the time taken in bringing forward the proposal for Ministers' approval.

**31.446** The ACVSB interpreted its remit as relating to matters of major policy. That was reinforced by the committee at its meeting on 24 April 1990. As established, the ACVSB conformed to a well-understood model of an advisory committee, providing government with advice related to policy issues which would in turn be resolved by Ministers. Typically, it was composed of a small core of experts with relevant specialist knowledge and experience, and was attended by representatives of the government departments as observers. It was chaired by the Deputy Chief Medical Officer for England.

**31.447** In practical terms, that was reflected in Dr Perry's evidence. He said that the ACVSB was established by UK Ministers to provide expert advice and ensure a uniform approach on blood safety throughout the UK.<sup>653</sup> The group was considered to be the authoritative source of advice for Health Departments and Ministers.<sup>654</sup> Representatives of the Health Departments from Scotland, Wales and Northern Ireland attended meetings as observers.<sup>655</sup>

<sup>650</sup> See paragraph 31.47

<sup>651</sup> Letter from Professor Cash to Dr Pickles dated 19 July 1988 [SNB.006.1010]

<sup>652</sup> Dr Harris' memo [SGH.003.1265]

<sup>653</sup> Dr Perry's Statement [PEN.017.2108]

<sup>654</sup> Ibid [PEN.017.2108] at 2109

<sup>655</sup> Ibid [PEN.017.2108] at 2113

**31.448** There is no reason to doubt that the ACVSB was set up to fill a gap in the advice available to the UK Health Departments on measures required to ensure the virological safety of blood. It has to be noted that a factor contributing to the lack of expert advice on NANB Hepatitis was the premature disbandment of the MRC Working Party on Post Transfusion Hepatitis (of which Dr McClelland was a member) following its second meeting on 25 June 1981.<sup>656</sup> For a time, the EAGA masked the gap, certainly whilst AIDS was the more pressing problem. There had been a lack of structure in the arrangements for ensuring that the government had properly informed advice in making policy decisions. Establishment of a committee dedicated to consideration of the risk of transmission of viruses by blood and blood products was objectively required.

**31.449** The origins of the ACTTD were significantly different. It was not a government sponsored committee. It probably arose from an initiative of Dr Gunson, agreed by SNBTS Directors on 13 December 1988, to form a UK blood transfusion services group on microbiological testing.

**31.450** From the outset, Dr McIntyre appears to have seen the establishment of a committee by the Transfusion Directors as a negative development. In his letter of 9 January 1989 to Dr Pickles, he indicated that the Directors' proposals for a committee would be unsatisfactory since 'decisions reached might be influenced to a considerable extent by the views of the Transfusion Directors'. It is not easy to understand what Dr McIntyre meant in expressing his concern that the SHHD might be 'forced into a course of action which might have repercussions for the UK as a whole', though it did emphasise his view that the ACTTD would be a threat to the SHHD and the DoH.<sup>657</sup>

**31.451** Dr Perry had no direct knowledge of the evolution of the two separate groups, but his understanding was that:

[T]he ACTTD was established by the UK Transfusion Services, in the absence of any other suitable mechanism at the time, to coordinate its professional view on the need for additional measures concerning the virological safety of blood and any ... new or revised safety interventions. The original intention ... was that it would provide advice to the Departments of Health either on request or at its own instigation.<sup>658</sup>

**31.452** He commented further in oral evidence that:

[T]ransfusion directors in the UK felt that it would be better if there was a formal process or a committee that could primarily bring together all the expert views on various subjects, but also expecting there to be quite serious and important discussions around surrogate testing.<sup>659</sup>

### *The committees' roles in practice*

**31.453** Hindsight suggests that some of the difficulties that arose between the two committees might have been avoided had the ACVSB been established with a sub-committee, consisting mainly of members with transfusion experience, addressing implementation of policy. Due to their different origins, the terms of reference adopted by the ACTTD at its first meeting on 24 February 1989 cut across the concerns of the

---

<sup>656</sup> See Chapter 15, *Knowledge of Viral Hepatitis 2 – 1975-1985*, paragraphs 15.74–15.76

<sup>657</sup> Letter [SGH.003.1251]

<sup>658</sup> Dr Perry's Statement [PEN.017.2108]

<sup>659</sup> Day 68, page 4

ACVSB as they were to emerge. In specifying a role in advising the Departments of Health on policy to be implemented by the UK blood transfusion services for the control of transfusion-transmitted diseases, the terms of reference had the potential to give rise to demarcation disputes. At the first meeting of the ACVSB on 4 April 1989,<sup>660</sup> the role of the ACTTD was interpreted as covering many of the same issues as the ACVSB, 'but only from a transfusion standpoint', a qualification that in itself had considerable potential for dispute. The second branch of the ACVSB remit was closely related to the operation of the Blood Transfusion Services, and the remit could not be fulfilled without knowledge of the practical implications of advice on scientific matters.

**31.454** The respective roles of the two bodies were specifically addressed at the meeting of the ACVSB on 24 April 1990.<sup>661</sup> As discussed below, while Dr Metters emphasised at that meeting that the ACVSB was concerned with policy and the ACTTD was concerned with operational matters arising from the implementation of policy, the ACVSB does not appear to have always borne that distinction in mind in their deliberations. Dr Gunson's view that there was no conflict between the committees was over-optimistic.

**31.455** Dr Perry commented that the ACVSB could not have functioned 'without the ACTTD, without creating an operational group to explore some of the details that it needed to make its decisions'.<sup>662</sup> From his perspective as a member of the ACVSB, and his knowledge of the workings of the ACTTD, Dr Perry suggested that the ACTTD was more 'action centred' and was more likely to generate work from its meetings. By contrast, if the ACVSB required additional work to be done, it would, in his view commission that through Dr Gunson and the ACTTD.<sup>663</sup>

**31.456** Dr Perry added that the ACTTD brought a 'collegiate expert view from transfusion experts ... with a view ... to advis[ing] departments of health on issues that they thought the Department of Health should be acting on'.<sup>664</sup> The ACTTD provided Dr Gunson with expert views to transmit to the Department of Health. Dr Gunson was the National Director of the Blood Transfusion Service in England and Wales, and in addition Dr Perry thought Dr Gunson was the expert adviser to the Department of Health.<sup>665</sup>

**31.457** Dr McClelland, who generally had a clear insight into the functioning of the transfusion service, said that it was never clear to him why it was necessary to have two committees. He suspected two groups eventuated because both the DoH and Dr Gunson, the NBTS National Director, wanted to influence decision making.<sup>666</sup> However, Dr McClelland commented that it was consistent with the remit of the ACVSB to 'cover all the territories' and include observers or participants from the other health departments.<sup>667</sup>

**31.458** Professor Cash commented in his statement that he thought the ACTTD was the 'brain-child' of Dr Gunson who believed it would help him to take the views of a wide group of UK BTS experts to the ACVSB.<sup>668</sup> Professor Cash commented that Dr Gunson was at times in a difficult position when he thought advice generated by the ACTTD would not be acceptable to the Department of Health.<sup>669</sup>

<sup>660</sup> Minutes [SNF.001.1219]

<sup>661</sup> Meeting Minutes [SNB.001.9761] at 9765. See discussion in paragraphs 31.202–31.204

<sup>662</sup> Day 68, page 8

<sup>663</sup> Ibid, page 22

<sup>664</sup> Ibid, page 4

<sup>665</sup> Ibid, page 5

<sup>666</sup> Dr McClelland's Statement [PEN.017.2491]

<sup>667</sup> Day 69, page 2

<sup>668</sup> Professor Cash's Statement [PEN.017.2094] at 2095

<sup>669</sup> Ibid [PEN.017.2094] at 2095



**31.459** Mr McIntosh commented in oral evidence that it would be too simplistic to classify the ACVSB as dealing with ‘policy’, and the ACTTD as dealing with ‘operations’.<sup>670</sup> In reality he thought there was some overlap in their work, and there were tensions and some unhappiness between the two committees.

**31.460** The ACVSB did not, however, restrict its work to providing independent expert advice to government to assist in formulating policy. It discussed, and took decisions on, operational matters that impacted on the transfusion services. Specific examples have been highlighted in the narrative of the evidence, in particular the instruction of the three-centre comparative trial of the first generation Abbott and Ortho tests, in which the ACVSB appears clearly to have been entering into the ‘operational implications of policy’ (the function of the ACTTD).<sup>671</sup> The committee also took account of the implications of funding in its deliberations, instructed by Dr Metters and influenced by Dr Gunson. Dr Metters’ understanding of UK Government policy, that there would be no new money for screening and that health boards (at least in England and Wales) would have to find the necessary funds within their existing budgets, was an important consideration for government. But it is not obvious that it should have been a consideration for the experts on the ACVSB. One would have expected them to give independent, objective and scientific advice, and to have left it to the health departments to weigh that advice against its financial implications in the broader context of health policy.

### *Locus of ACVSB in Scotland*

**31.461** In the view of Mr Tucker, the SHHD was content to leave the ACVSB to assess whether introducing screening was the right thing to do: it was an expert committee. The SHHD would get a report-back of ACVSB meetings from their observer, Dr McIntyre.<sup>672</sup> Mr Tucker had been given the opportunity of examining the relevant SHHD file from the time in question and noted that the Minister of State, Mr Forsyth, appeared to be content for action to be taken in Scotland in line with England. He thought all Ministers at that time were part of the same government and would have no desire to break ranks and embarrass other colleagues by taking contradictory action without due cause.<sup>673</sup> They would want to present a ‘united government on an issue like this’.<sup>674</sup>

**31.462** In the opinion of Mr Tucker, as expressed in his statement, it was not unusual for the SHHD to follow the DoH lead on national issues if it was sensible to do so, as the Department of Health had greater resources. He felt that the introduction of national testing was a good example, as it was clear from the expert advice of the ACVSB that bringing in screening was the right thing to do and there was no disagreement in the committee. He said that the SHHD would not necessarily have followed the DoH if England had decided not to introduce screening, but the advice in Scotland had been that testing was worthwhile.<sup>675</sup>

**31.463** This perception within the SHHD that matters could be left in the hands of the DoH, as advised by the ACVSB, implied that the SHHD was not itself required to promote discussion or investigation of an issue such as the introduction of screening, and could

---

<sup>670</sup> Day 70, page 14

<sup>671</sup> See paragraphs 31.220 and 31.223

<sup>672</sup> Day 69, page 106

<sup>673</sup> Mr Tucker’s Statement [PEN.017.2060] at 2063–64

<sup>674</sup> Day 69, page 107

<sup>675</sup> Mr Tucker’s Statement [PEN.017.2060] at 2063

await advice from England, with a degree of assurance that it would have the backing of a ministerial decision that the Health Services should stay in line. The SHHD had the advantage, meantime, of information from its observer of the proceedings at the ACVSB, Dr McIntyre. He produced a note of the first ACVSB meeting, which was discussed with Dr Perry in oral evidence.<sup>676</sup> It was understood that, as an observer, Dr McIntyre could formally provide information from the Department of Health to colleagues in the SHHD. The transfusion services did not have the advantage of direct reporting other than through Dr Mitchell and Dr Perry, but relied on the information being further passed to them by the SHHD.

**31.464** Mr McIntosh also said that no-one involved in the management of the SNBTS felt that the ACVSB had any locus in Scotland. The activities of the Advisory Committee in London did not have any effect on his role as general manager of the SNBTS.<sup>677</sup> He remarked later that the SNBTS had a duty to formulate policy for itself and take it forward, rather than relying on bodies like the ACVSB and the ACTTD with no executive or medico-legal responsibility for the activities of the SNBTS in Scotland.<sup>678</sup>

#### *Confidentiality of the proceedings of the ACVSB*

**31.465** Having regard to the whole of the evidence as it developed, it appeared that the most substantial cause of dissatisfaction in Scotland with the ACVSB was not that its role was opaque or difficult to understand. It was that its business was confidential and was not reported in detail to the SNBTS or to the ACTTD. Due to the requirement of confidentiality, as perceived by its Scottish members, the SNBTS general manager and its Medical and Scientific Director were not always informed of the content of debates or decisions at the ACVSB meetings.

**31.466** At the first meeting of the ACVSB, the position was made clear by Dr Harris. Members' advice could be publicly sensitive and should not be discussed outside the committee, unless specifically authorised.<sup>679</sup>

**31.467** The perception, therefore, was that confidentiality had to be maintained. Dr Perry told the Inquiry that it was not appropriate for him or Dr Mitchell to return from the committee and brief SNBTS colleagues on the activities of the committee as they were prevented from doing so by confidentiality agreements.<sup>680</sup>

**31.468** Dr McIntyre could formally provide information from the Department of Health to colleagues in the SHHD: the SHHD was among the bodies entitled to receive the advice of the ACVSB. The SHHD could pass information to the SNBTS when it was necessary for individuals to be briefed.<sup>681</sup> Dr Perry believed that Dr McIntyre was able to relay information to his own department in Scotland, provided that information remained within the Government.<sup>682</sup>

<sup>676</sup> Note of Meeting of the Advisory Committee on the Virological Safety of Blood, 4 April 1989 [SGH.003.1228] and Day 68, pages 17–18

<sup>677</sup> Day 70, page 11

<sup>678</sup> Ibid, page 86

<sup>679</sup> Paragraph 31.51

<sup>680</sup> Day 68, page 18

<sup>681</sup> Ibid, page 18

<sup>682</sup> Ibid, page 21

**31.469** As already noted, at its inception, the ACVSB conformed to a well-understood model of an advisory committee providing government with advice related to policy issues. Confidentiality of its proceedings reflected that. Information that Ministers were entitled to accept or reject in formulating policy, in relation to which technical information was one only among a wide range of possible considerations, was inherently sensitive.

**31.470** It followed that, as Dr Perry recognised, he and Dr Mitchell were unable to brief colleagues in the SNBTS about ACVSB business.<sup>683</sup> It followed also, that SNBTS Directors would not have a role in suggesting items for the agenda of the ACVSB, and could not submit briefing papers or have access to minutes of the meetings. Professor Cash's comment to that effect reflected the formal reality of the status of the ACVSB, though he saw it as a deficiency in the arrangements.<sup>684</sup>

**31.471** Dr Perry's view was that the issue of confidentiality was a difficulty for the SNBTS, as policy discussed at the ACVSB often became operational practice and there was concern the SNBTS might be left behind.<sup>685</sup> He commented that there was '[u]nnecessary secrecy and confidentiality associated with the considerations of the ACVSB and other 'behind the scenes' discussions'.<sup>686</sup>

**31.472** With Dr Perry and Dr Mitchell bound by an obligation of confidentiality and the SNBTS general manager and its Medical and Scientific Director otherwise dependent on the SHHD as an additional source of information, there was some dissatisfaction within the SNBTS about the extent of the information coming from the ACVSB. This was remedied, to some degree, in February 1990 when it was confirmed by Mr Rab Panton of the SHHD that Drs Mitchell and Perry could report the committee's discussions and recommendations to the SNBTS Directors and the ACVSB minutes could be scrutinised and discussed, on an informal basis, at the directors' meetings.

**31.473** Professor Cash, as Medical and Scientific Director, remained dissatisfied with the provision of information. He considered it to be patchy and inconsistent. He commented that Dr McIntyre, as the SHHD observer on the ACVSB, told him that he would advise him when he believed there were things he, Professor Cash, should know. He complained about lack of regular briefings and said that the SNBTS Directors got to see the ACVSB minutes only on 'rare occasions'.

## **How the policy decision on screening was reached – a chronological review**

### **1989**

**31.474** From the starting point of the UK Ministers' decision on a uniform start date for the introduction of screening, all relevant agencies subscribed to the view that UK blood transfusion services should act in unison. Dr Perry thought it was the accepted view of the ACVSB that testing would be implemented in a coordinated manner across the UK. Professor Cash strongly supported the idea of a common start date.

**31.475** In the course of 1989, the NBTS and the SNBTS proceeded with the evaluation of test kits received from Ortho. By the end of August 1989, UK commentators appear to have formed a generally favourable view of the first generation Ortho test. There were still

---

<sup>683</sup> Ibid, page 18

<sup>684</sup> Professor Cash's Statement [PEN.017.2094]

<sup>685</sup> Day 68, page 19

<sup>686</sup> Dr Perry's Statement [PEN.017.2108] at 2118

reservations related, for example, to the predictive value of the test in low HCV prevalence populations, such as UK blood donors. Several commentators thought that without a confirmatory test, using an antibody distinct from that used in the initial screening test, there would be serious problems for the blood transfusion services in differentiating between true and false positives. The issues around the specificity and sensitivity of the first generation Ortho HCV ELISA test could not be addressed definitively as part of the evaluations carried out. There were no samples with well established links to NANB Hepatitis available to be tested.

**31.476** In September 1989, Dr Gunson and Dr Mitchell had acquired better knowledge of the international scene from the Rome symposium organised by Ortho. In their respective reports for the ACTTD, each expressed concerns about the lack of a confirmatory test.

**31.477** At the end of his report,<sup>687</sup> Dr Gunson asked the ACTTD to approve in principle the routine testing of blood donations for anti-HCV, and to request the National Directors in England and Scotland to arrange for the simultaneous introduction of the tests at an appropriate time when a policy for handling the seropositive donors had been defined. Dr Gunson's report was amended for submission to the fourth meeting of the ACVSB on 6 November 1989.<sup>688</sup> So far as procedure is concerned, the ACVSB had asked for advice and the ACTTD had approved a report for submission. The ACVSB was asked to approve routine testing for anti-HCV in principle, subject to conditions relating to counselling and management, the availability of a confirmatory test, an FDA licence, and pilot studies of routine use of the test on freshly collected blood.

**31.478** At this stage, the blood transfusion services, through the ACTTD, had played their part in recommending the introduction of routine screening in principle. The initiative now lay squarely with the ACVSB. On 6 November 1989, the ACVSB stopped short of approving the introduction of routine testing, in principle or otherwise.<sup>689</sup> It was decided that three English centres should conduct pilot studies of the feasibility of adding the kits to routine practice. There was no firm intention to recommend screening once the conditions outlined in Dr Gunson's report had been met. The ACVSB appeared unwilling to go further than to offer support for 'general introduction' if the three conditions were met. At this point, that position was not open to objection. The conditions were substantial, and hesitation in recommending positive action was understandable.

## 1990

**31.479** By the time the ACVSB next met, on 17 January 1990,<sup>690</sup> the FDA had licensed the Ortho product for export,<sup>691</sup> and the pilot studies had been completed, showing satisfactory test sensitivity and specificity. The emphasis changed. Discussion became more specific in relation to FDA approval for domestic use. The committee had a letter from Professor Zuckerman pointing out that 'considering the overall morbidity of chronic non-A non-B hepatitis ... and litigation which would be indefensible, the introduction of screening could not be delayed much beyond FDA approval'.<sup>692</sup> So far as the minutes disclose, there was no clear recommendation in favour of testing, even once any remaining

<sup>687</sup> Dr Gunson's report [SNB.006.1456] at 1460

<sup>688</sup> The report is part of the papers relating to the ACVSB meeting [SNF.001.1383] at 1401-06

<sup>689</sup> ACVSB Minutes [SNB.001.9563]

<sup>690</sup> ACVSB Minutes [SNB.001.9657]

<sup>691</sup> Professor Cash was so informed by Ortho on 27 November 1989, see [SNB.006.1560]. Dr Gunson was informed at the same time – see [SNB.001.8919]. The information does not appear to have reached ACVSB.

<sup>692</sup> Meeting Minutes & Associated Documents [SNF.001.1491] at 1511

regulatory obstacle was removed.<sup>693</sup> It is also noteworthy that the committee concluded that routine testing should not yet be introduced, whilst also recording an estimate that the annual incidence of NANB Hepatitis in the UK following blood transfusion could be 10,000 cases.<sup>694</sup>

**31.480** It has already been observed (paragraph 31.416, above) that the minute prepared as a result of the ad hoc meeting on 13 September 1991 did not reflect, among other matters, the major concerns about funding in England and Wales that were explicit from at least 7 January 1991<sup>695</sup> and underlined by Dr Pickles' memorandum of 5 February 1991 (paragraph 31.271, above).<sup>696</sup>

**31.481** Dr Perry's note adds to a general sense of unease that the ACVSB was, at this stage, beginning to be less a helpful provider of relevant and well-directed expert scientific advice to government, and was becoming involved in wider policy issues. However, there was some force in Professor Zuckerman's point that it would be difficult for the ACVSB to approve for use a test that had not passed the regulatory criteria for use in its country of origin.

**31.482** There were significant events between 17 January 1990 and the next meeting of the ACVSB on 24 April 1990.<sup>697</sup> In February, Ortho distributed RIBA test kits for evaluation in the United Kingdom. On 8 February the AABB, the American Red Cross and the Council of Community Blood Centres issued joint guidelines in preparation for the introduction of anti-HCV testing of donations, a clear indication that licensing for domestic use in the near future was anticipated.<sup>698</sup> Intimation of the guidelines to the DoH 'stirred up a hornet's nest'. Mr Angus' comment that the expression reflected the unexpectedness of the US guidelines appears to be a reasonable interpretation. Professor Zuckerman and Dr Rotblat had both relied heavily on the likelihood of delay at the meeting of the ACVSB in January and Professor Zuckerman had written that the introduction of screening could not be delayed much beyond FDA approval. The unexpected progress towards introduction of screening in the USA went to the roots of ACVSB advice on policy.

**31.483** At the ACVSB meeting of 24 April, Dr Mitchell reported on the Abbott symposium he had attended in Chicago and the actions of the AABB immediately following the symposium in directing that anti-HCV testing should be introduced as soon as the FDA approved the test. It was reported that as at 24 April the FDA had not approved the test. The discussion moved to other matters. The idea that the UK could not delay the introduction of screening much beyond FDA approval was not articulated, so far as the minutes disclose. Rather the discussion focused on perceived shortcomings in the test systems available, all of which had been identified in one way or another before January 1990.

**31.484** It is appropriate to look at another significant event that had occurred before the meeting of the ACVSB in April: the Ortho symposium held in London in February. There were differing views of it. Professor Zuckerman and Dr Rejman presented adverse reports to the ACVSB. Dr Boulton's report of the symposium to Professor Cash recognised that

---

<sup>693</sup> See paragraph 31.173

<sup>694</sup> Meeting Minutes & Associated Documents [SNF.001.1491] at 1497

<sup>695</sup> Notes of NBTS-SNBTS Management Meeting, 7 January 1991 [SNB.011.7258]

<sup>696</sup> Memorandum [PEN.016.0236]

<sup>697</sup> ACVSB Minutes [SNB.001.9761]

<sup>698</sup> Guidelines [SNB.001.9825]

there were defects in the Ortho test system, but he nevertheless felt strongly that it should be introduced at the earliest opportunity. He was concerned that the SNBTS would face future litigation from people infected with HCV in blood that could have been screened.<sup>699</sup> At the ACVSB meeting the risk of litigation was mentioned by Dr Mitchell as a factor he had noted at the Abbott symposium, but the minutes do not record any reaction to that.

**31.485** A further issue debated on 24 April was the advice to be given to donors.<sup>700</sup> Since this was a problem inherent in screening from the outset, widely acknowledged and obviously requiring a solution as soon as the possibility of any form of screening was first suggested, it is difficult to understand how it could take on such prominence in ACVSB deliberations at this stage. A solution along those lines did not depend on any insights that could only have been obtained by new information emerging between January and April 1990.

**31.486** In reality, the advice of Professor Zuckerman and Dr Rejman, possibly supplemented by the reservations of Dr Mitchell, prevailed. There was no commitment to introducing screening, even subject to FDA approval of the test systems for use in the USA.

**31.487** Looking at the record of the proceedings on 24 April, there are several reasons for concern. Papers from the London symposium were produced.<sup>701</sup> Dr Rejman's notes were brief and one can assume that members of the committee would have informed themselves fully. Professor Thomas had reported on the epidemiology of NANB Hepatitis. In particular, he had reported that most anti-HCV positive patients had mild, frequently sub-clinical, hepatitis after an initial incubation period, but half then made a complete recovery and half progressed to chronic liver disease. A proportion of NANB Hepatitis patients progressed to cirrhosis.

**31.488** While the minutes may have provided a less than comprehensive account of discussion, the impression left is that the meeting on 24 April 1990 failed to reflect an appreciation of the seriousness of infection for patients receiving blood, blood components, or products. There was no reference in discussion to Dr Lee's abstract, for example. She had reported that the use of Ortho kits had confirmed anti-HCV sero-positivity in *all* haemophilia patients with well documented NANB Hepatitis. While there were legitimate reservations about the sensitivity and specificity of the ELISA test at that stage, a balance was necessary that recognised the interests of recipients of human blood in whatever form. The minutes do not provide any comfort that the members of the committee had this in mind or gave it sufficient weight on 24 April 1990.

**31.489** Professor Leikola's comment in response to Dr Rejman's observation that the Ortho test was not sensitive or specific enough for reliable testing<sup>702</sup> was apposite: the tests were considered good enough by the Finnish authorities for screening to have been introduced there in early 1990. Dr Metters had noted at the meeting in April 1990 that France, Belgium, Luxembourg and Italy had all introduced anti-HCV testing. There is a distinct sense that a determination to pursue the best was becoming detrimental to finding a practical and acceptable solution to a real problem affecting the health of significant

<sup>699</sup> See Dr Boulton's letter to Professor Cash dated 21 February 1990 [SNB.014.1644] and his enclosed notes [SNB.014.1645]

<sup>700</sup> Note of 6th Meeting of the Advisory Committee on the Virological Safety of Blood – Hannibal House, 24 April 1990 [SGH.002.7947] at 7949

<sup>701</sup> Report on Ortho HCV symposium [SNF.001.1628]

<sup>702</sup> See paragraph 31.208

numbers of NHS patients. Professor Leikola's assessment of the position is accepted. That position can be summarised as follows:

- The Ortho test was not a perfect test at this time.
- The experts contributing to the symposium in London would rightly take a critical approach to the tests, and emphasise what they had found.
- But to conclude on the basis of the information before the symposium that the test should not be introduced was a view he could not take.<sup>703</sup>

**31.490** Professor Leikola found the change of attitude in the ACVSB between January and late April 1990 'remarkable'.<sup>704</sup> While other countries were largely moving towards a policy of introducing the new tests, the ACVSB's reservations on routine screening had grown in that period. Dr Rejman, a DoH medical officer, had emerged as a contributor to the case against introduction. The next meeting of the committee was scheduled for 24 July, three months later. There was no sense of urgency. The study proposed would require a protocol to be prepared by the sub-committee nominated and then a considerable period to carry it out, whether the target number to be tested was 25,000, 50,000 or 100,000 individuals.

**31.491** The contrast between the negative tone of Dr Rejman's comments and Dr Boulton's observations is clear. The evidence concerning the Ortho symposium raises the issue, reflected in Dr Perry's evidence, whether consideration at this meeting of the topic of screening was dominated by reports and discussion from academic virologists.<sup>705</sup> Dr Perry's view at this time in the process was that the best was becoming the enemy of the good.<sup>706</sup> In his note to Professor Cash about the meeting he concluded:

[Gunson] and [Perry] felt there was sufficient data to justify testing now (based on U.S data suggesting 50% reduction in PTH) but the majority and the D.O.H. preferred more cautious approach.<sup>707</sup>

**31.492** Drs Gunson, Mitchell, Mortimer and Tedder constituted the study protocol sub-committee to organise the trial. It met on 23 May 1990. By letter dated 5 June 1990, Dr Metters brought forward the meeting of the ACVSB previously scheduled for 24 July.<sup>708</sup> In the light of 'subsequent events,' namely FDA approval of the ELISA test for use in the USA and 'some additional scientific information' that had become available, an extended study of RIBA and PCR techniques might not be appropriate. The next meeting of the ACVSB would be brought forward to 2 July. The questions to be addressed are set out in paragraph 31.215. They provided for a wide-ranging re-assessment of the approach to screening.

**31.493** At the meeting of the ACVSB on 2 July,<sup>709</sup> the committee concluded that it should recommend to Ministers that testing should be introduced, but that first there should be a pilot study comparing the first generation Ortho and Abbott tests to decide which test was better for RTCs to introduce.

<sup>703</sup> Day 71, pages 135–137

<sup>704</sup> Professor Leikola's Statement [PEN.017.1961] at 1962

<sup>705</sup> Dr Perry's report [SNF.001.1710] at 1711

<sup>706</sup> Day 68, page 136

<sup>707</sup> Dr Perry's report [SNF.001.1710] at 1712. As was observed in the submissions from the patient representatives, this was not cautious from the perspective of prospective recipients of HCV positive blood.

<sup>708</sup> Letter [SNB.002.0245]

<sup>709</sup> ACVSB Meeting Minutes 2 July 1990 [SNF.001.1705]

**31.494** The papers disclose that there had been additional information on the effectiveness of screening to reduce transmission of HCV infection. The extensive discussion at the previous meeting was not dealt with, and the resolution of the scientific issues then set out – if it occurred – is obscure. The most obvious substantial change was that the FDA had in fact approved the ELISA tests.

**31.495** While the decision of the ACVSB in July 1990 to recommend to Ministers that HCV screening should be introduced was policy advice of the kind properly within the remit of that committee, it is less easy to understand why the ACVSB appears to have sought to retain responsibility for deciding which test kit should be used by RTCs. On the face of it, that was very much an operational decision which could have been left to the ACTTD, members of which had long standing practical experience and expertise in evaluating and introducing new screening tests. At that point, however, there does not appear to have been a meeting of the ACTTD scheduled to take place in the then foreseeable future: it did not meet between 16 March 1990 and 8 January 1991.

**31.496** It was forecast that four months would be required for the pilot study, after finance had been agreed. At the meeting it was anticipated that the next meeting of the ACVSB would be in October. The date was later amended to 21 November, a date which appears to have allowed for completion of the pilot study. As noted at paragraph 31.233, Dr Gunson reported to the November 1990 meeting of the ACVSB that both the Ortho and Abbott first generation screening tests could be deemed to be satisfactory for routine use within RTCs from an operational viewpoint, and that the results of the supplementary testing would be the decisive factor when considering whether one test was better than the other. In the event, the final report was not available until February 1991.<sup>710</sup> Had the introduction of screening truly been dependent on the completion of this pilot study, the result of the decision of 2 July would have been that until its completion no decision would have been possible on advice to be given to Ministers as to the preferable test until its completion.

**31.497** There were conflicting views before the Inquiry on whether a completed pilot study was required before screening was introduced. Dr Mitchell and Dr Perry, for different reasons, thought that it was. Professor Leikola thought that comparative studies could have been carried out after introduction of screening. Professor Leikola's view appears correct. As it transpired, the study did not add much to the process apart from delay.

### *Eighth Meeting of the ACVSB*

**31.498** By the date of the November 1990 meeting of the ACVSB<sup>711</sup> enough information was available about the pilot study for Dr Gunson to give the information already noted. Equipment would be a factor, but the results of supplementary testing would be decisive in making the choice. After hearing Professor Tedder and Dr Mortimer, the Committee concluded that a combination of RIBA and PCR would provide a useful confirmatory service. Professor Zuckerman observed that, on the results available, it was impossible to choose between the tests. The Committee agreed that it was important to start screening as soon as possible.

---

<sup>710</sup> An Investigation of the Use of the First Generation Ortho and Abbott Anti-HCV EIA Screening Tests [SNB.001.9032]

<sup>711</sup> ACVSB Minutes 21 November 1990 [SNF.001.1777]



**31.499** Although there is no reference to a particular date in the minutes, there clearly was discussion of a start date for screening. Dr McIntyre's note<sup>712</sup> that Dr Metters had proposed 1 April 1991 is accepted as factually correct. Mr Canavan's note to Ministers dated 21 December 1990 indicated that routine screening was unlikely to be possible before 1 April 1991.<sup>713</sup> That was consistent with discussion of that date by the committee. Dr Mitchell's letter to Professor Cash dated 23 November<sup>714</sup> was in line with paragraph 10 of the minute. It was on that basis, rather than a precise set date, that Professor Cash contacted RTDs in Scotland to find out when they could begin routine testing. So far as the Inquiry has been able to discover, those who replied could all have commenced screening before 1 April 1991. Subject to the problems that arose later with the Gulf War, meeting that date would not have been a practical problem for RTDs in Scotland. At the November meeting, Dr Metters once more stressed the importance of a common date of introduction of screening throughout the United Kingdom. Since there was no technical or scientific basis for this view, it appears simply to have represented a re-assertion of the continuing policy position of Ministers as understood by the committee.

**31.500** In November the ACVSB discussed the counselling of HCV-positive donors. Dr Mitchell advised the committee that the issue had been discussed in Scotland and that a draft document was available which could form the basis of discussion at the meeting of the ACTTD which was to consider the matter. Since the ACTTD was at all times the committee likely to have the responsibility for resolving the practical issues relating to counselling, it is clear that this was a decision that could have been taken at any time over the long period during which the introduction of screening had been discussed by the ACVSB. Had the ACTTD been asked for advice on counselling and failed or delayed in providing it, matters might have been different. But on the evidence available, there was no such failure or delay, and consideration of arrangements for counselling was never a legitimate reason for the ACVSB to delay the provision of scientific advice to Ministers.

### **The policy of a uniform start date – implementation of screening**

**31.501** Items 7 and 5 of the series of issues identified by Inquiry Counsel noted at paragraph 31.431, can conveniently be taken together:

The formulation of policy regarding the co-ordination of the starting date for the introduction of screening in Scotland with the starting date for England and Wales, the flexibility of such policy and whether such policy as existed resulted in delay in the introduction of screening in Scotland;

and

Why was there a delay of almost ten months between the decision by ACVSB on 21 November 1990 to recommend the introduction of screening as soon as practicable and the introduction of screening in Scotland on 1 September 1991?<sup>715</sup>

<sup>712</sup> Dr McIntyre's note of the ACVSB Meeting held on 21 November 1990 [SGH.002.8501] at 8502. Dr Perry thought the proposed date might have been edited out of the minutes: Day 68, page 124.

<sup>713</sup> Note [SGH.002.7893] at 7896

<sup>714</sup> Letter [SNB.005.3696]

<sup>715</sup> Closing Submission – list of issues – Inquiry counsel [PEN.019.0843] at 0855 – questions 7 and 5.

*Uniform start date*

**31.502** As emerges from the discussion of November 1990, UK Government policy appears to have been static from its earliest articulation down to the end of 1990. Commitment to a unitary start date became almost an article of faith. There is no evidence that the Scottish Office Minister of State with responsibility for Health, or the Secretary of State were ever minuted by officials with a proposal that there should be a different, earlier, start date in Scotland than in the rest of the UK, or that this possibility was ever raised with Scottish Ministers. Without such a step, there was no mechanism by which the political implications of a suggested change of policy could have been addressed and resolved. While that may have been understandable during much of 1990, when it became clear in late 1990/early 1991 that the introduction of testing would be delayed in England, it is a matter of concern, given the public health issues involved, that the matter was not brought to the attention of Ministers in Scotland to consider the earlier introduction of screening.

**31.503** There was evidence that the consent of the Secretary of State to a start date of 1 April 1991 was implicit in the approval of the PES for 1991–92. In terms of accountability for public expenditure that was clearly so: the public accounts auditor would have found an appropriate vote authorising the expenditure on screening had it been commenced at any date after the beginning of the financial year. It would, however, be a total fiction to infer detailed knowledge on the part of Scottish Office Ministers of the practical implications and policy background to every line of the PES.

**31.504** What is clear is that there was marked reluctance on the part of Scottish officials to bring the question of implementation of screening to the notice of Ministers at all. A full submission was sent to UK Ministers on 21 December 1990.<sup>716</sup> Mr Canavan's note identified 1 April 1991 as the earliest practicable date. It is not obvious that there was any obstacle to a parallel course being taken in Scotland. Dr McIntyre understood the date to be 1 April 1991. It would have been appropriate for Scottish Office Ministers to have been informed. They were not. If there were good reasons for the delays in presenting a 'Hep C submission' to Scottish Office Ministers during the first half of 1991, they have not become clear in the course of the Inquiry. In the result Mr Forsyth, Minister of State with responsibility for health from September 1990, did not receive a submission until 24 July 1991,<sup>717</sup> by which time the commencement date of 1 September had been set in stone.

**31.505** Scotland's policy had been subordinated to the requirements of England and Wales, effectively the DoH. When Mr Panton wrote to the CSA on 8 August 1991 formally communicating the Minister of State's agreement to testing,<sup>718</sup> it was too late for any other course to be put to Mr Forsyth. It would, of course, be a matter of pure speculation to suggest any course of action that might have followed an earlier submission that Scotland should commence screening at an earlier date.

*Implementation of screening*

**31.506** The more substantial question is the second: why was there delay from November 1990 to 1 September 1991?

<sup>716</sup> Note [SGH.002.7893]

<sup>717</sup> Submission to the Minister on HCV Screening [SGH.002.7828]

<sup>718</sup> Letter [SGH.002.7802]

**31.507** Dr McIntyre had the impression that the ACVSB had reached a decision that screening should be introduced with effect from 1 April 1991. Dr Mitchell, who had been at the same meeting, thought that the exact date would be 'the earliest practical moment'. That discrepancy is, in itself, indicative of a lack of clarity about implementation. It is also noteworthy that the only steps Dr McIntyre appears to have taken on his return were to report orally to Mr Panton and to prepare a note of the meeting, which was sent to Mr Tucker and copied to the CMO, Mr Panton and Dr Skinner.<sup>719</sup> According to Professor Cash, Dr McIntyre had previously made the position very clear to him in relation to the ACVSB meetings. Dr McIntyre's position was that he would advise Professor Cash when he believed that there were things Professor Cash should be told.<sup>720</sup> A decision such as that reported by Dr McIntyre, namely that screening should be introduced from 1 April 1991, would fall within that description.

**31.508** As it happened, however, Dr Mitchell informed Professor Cash of the position, although without the specification of 1 April as the date. One could not be critical of the SNBTS response to this news: Professor Cash responded quickly to Dr Mitchell's letter of 23 November 1990<sup>721</sup> by writing to Directors on 27 November.<sup>722</sup> There was some uncertainty over the meaning of 'start date', but in the event that had no bearing on any relevant decision required in Scotland. Preparation for donor counselling was put in hand and instructed the ACTTD's thinking on the subject. Again, work in Scotland was ahead of the rest of the United Kingdom and did not adversely affect UK-wide progress towards testing.

**31.509** External events affected progress. The Gulf War changed the pattern of demand for blood components, generated a surge in blood donation and for a period into 1991 was an understandable block on progress towards routine screening. But in the early months of 1991, the CSA was on track to deliver funding which would have enabled commencement of screening on 1 April 1991.

**31.510** From the beginning of 1991, Professor Cash knew that funding for screening in England and Wales was a problem. He was present at the meeting of the NBTS/SNBTS liaison committee on 7 January 1991, where Dr Gunson explained his concerns about the failure of the DoH to decide on a start date, and indicated that funding was the major problem.<sup>723</sup> Uncertainty about dates persisted: on 16 January 1991, government commitment was limited to introducing screening 'as soon as is practicable', without a date being indicated.<sup>724</sup> Lack of funding was related to the UK Government policy position, noted by Dr Metters on 17 January 1990, that 'funding would have to be found from the existing health vote allocation'. The position in Scotland regarding funding was materially different.

**31.511** On 21 January 1991, Mr Tucker in the SHHD reported to Mr Panton a conversation he had held with Mr Canavan in the DoH. Mr Tucker had accurately foreseen slippage in timing, and had suggested setting a date of 1 April to prevent all parts of the UK being required to wait for the last area to be ready.<sup>725</sup> But he viewed this as a suggestion he made

---

<sup>719</sup> See Minute [SGH.002.8501] and covering Memorandum [SGH.002.8500]

<sup>720</sup> Day 72, pages 104-105

<sup>721</sup> Letter [SNB.005.3696]

<sup>722</sup> Professor Cash's letter [SNB.005.2555]

<sup>723</sup> Professor Cash's notes on the NBTS-SNBTS Management Meeting on 7 January 1991 [SNB.011.7258] at 7259

<sup>724</sup> Policy memo [PEN.016.0259]

<sup>725</sup> Memo [SGH.002.7890]

to the DoH, rather than as a basis for action by the SHHD to set a date for Scotland.<sup>726</sup> He regarded the policy of a uniform start date as firmly established; the Scottish Minister 'would not have taken a different course'.<sup>727</sup>

**31.512** Dr Pickles' memorandum dated 5 February 1991,<sup>728</sup> which was copied only to Dr Metters, Dr Rejman and another official, paints a telling picture of the stage reached at the DoH. It emphasised the practical problems in the way of implementation, and the 'real concern about how the necessary money will get into the system'. Against this background, Dr Gunson's suggestion of a start date of 1 July seemed 'OK', though it would result in some stragglers being left behind. The memorandum was not copied to anyone in the SHHD. It suggests a distinct lack of urgency given the public health issues at stake.

**31.513** In Scotland, Professor Cash maintained the commitment to the commencement of screening at the same time in both Scotland and England. On 24 January 1991, he repeated the commitment of the SNBTS to a uniform start date; if pressed he would suggest 'a May/June date'. On 13 February, the SHHD learned from the DoH that it was hoped that screening would commence on 1 July. The SNBTS was specifically identified as a body not to be informed of this.<sup>729</sup> On 15 February 1991, Professor Cash wrote to Dr Gunson reiterating the SNBTS wish to stay in line with the NBTS/BPL. On the same day, Dr Gunson wrote to regional transfusion directors in England and Wales advising that screening would commence on 1 July 1991.

**31.514** The ACVSB met on 25 February 1991.<sup>730</sup> The need for 'proper' evaluation of the second generation Abbott and Ortho tests was emphasised. It was thought that the kits would 'in principle' be available from 1 July. It was noted that patent rights 'had not yet been determined'. There was no discussion of the problems anticipated. In particular there is no record that members were told that finance was a real concern. So far as the Minute discloses, that remained an internal issue for the DoH, as did the selection of a start date. Those were by this stage properly in the hands of the DoH (at least in so far as England and Wales were concerned).

**31.515** In the course of the 'difficult' telephone conversations on 23–24 March, Professor Cash learned from Dr Gunson that there was to be a further postponement. As he described it, only with great difficulty did he support Dr Gunson at the meeting of the ACTTD on 25 March 1991, where the ACTTD accepted the postponement.<sup>731</sup>

**31.516** On 27 March 1991, Professor Cash wrote to Mr McIntosh<sup>732</sup> and stated that it was clear the NBTS was struggling to meet the 1 July commencement date and that he believed there was a fundamental problem with financial resources. He copied the letter to Dr McIntyre (SHHD), causing concern among the civil servants who had access to it. Why he did not personally speak to the SHHD became an issue for the Inquiry. Professor Cash was asked in oral evidence why he did not confirm the SHHD policy position with them directly. He reiterated that, regrettably, 'Harold Gunson convinced me that SHHD had been party to the decisions that were made'.<sup>733</sup>

<sup>726</sup> Day 69, pages 117–120

<sup>727</sup> Day 69, page 121

<sup>728</sup> Memo [PEN.016.0236] The name of the recipient has been redacted.

<sup>729</sup> Memo [SGH.002.7886]

<sup>730</sup> Meeting Minutes [SNB.001.8934]

<sup>731</sup> Paragraphs 31.314–31.327

<sup>732</sup> Letter [SGF.001.2026]

<sup>733</sup> Day 82, page 76

**31.517** Professor Cash said that following his letter he spoke to Mr McIntosh, urging him to approach the SHHD and ask whether Scotland needed to continue to ‘hang in’ with the English dates.<sup>734</sup> He maintained that at this point he was firmly of the view that an approach needed to be made to the SHHD to consider decoupling the plans for Scotland from those for England and Wales, and expected Mr McIntosh to make the approach, which he would support as National Medical and Scientific Director.<sup>735</sup> Mr McIntosh did not accept Professor Cash’s account of briefing him on the current position in 1991 regarding the introduction of testing and suggesting to Mr McIntosh that he rather than Professor Cash should contact the SHHD.<sup>736</sup> Professor Cash’s account of wanting to see the plans for Scotland proceeding separately from those for England at this point was difficult to reconcile with his evidence that he did not confirm the SHHD position directly because he had been convinced by Dr Gunson that the SHHD was ‘party’ to the decisions made.

**31.518** On his return to complete his evidence, Professor Cash explained that as National Medical and Scientific Director he had to report ‘exclusively’ to David McIntosh. Mr McIntosh had ‘insisted that all communications from the SNBTS ... into the Scottish Office was his job’. Mr McIntosh had support from Jim Donald for this.<sup>737</sup> He said that he had no direct access, in terms of management line access, into the Scottish Office.

**31.519** This was not an entirely convincing explanation: Professor Cash had a long track record of direct communication with the SHHD when he considered that there were issues to address. The conflict in evidence between him and Mr McIntosh – whether Mr McIntosh was asked to take the initiative – casts doubt over the sequence of events. But it appears to be clear that no approach was made to the SHHD to re-consider a phased introduction of testing across the United Kingdom, rather than the existing ministerial commitment to unified action, in order to avoid the further postponement of screening beyond 1 July 1991.

**31.520** If issues concerning the introduction of screening were indeed matters of management, it would be difficult to reconcile that with Professor Cash’s communications with Dr Gunson over the issue. The question concerns Professor Cash’s role as National Medical and Scientific Director. From at least 5 June 1990 he had special responsibility for operational quality, and for research and development, and he was charged with convening and chairing the Medical and Scientific Committee of the SNBTS (MSC).<sup>738</sup> The MSC remit was professional and scientific matters. In contrast, the SNBTS Management Board was the body through which all key policy and strategic decisions were to be channelled.<sup>739</sup>

**31.521** The introduction of screening clearly involved professional and scientific matters within the remit of the MSC, as well as policy and strategic matters within the remit of the SNBTS Management Board. The selection of a start date would have required advice on technical feasibility. Funding would have been a matter of policy on which the SNBTS Management Board might offer views, but it would then have been for the SHHD and Ministers to take a policy decision. On no view of Professor Cash’s role as National Medical and Scientific Director was he entitled to negotiate and conclude an agreement with Dr

---

<sup>734</sup> Day 72, page 171

<sup>735</sup> *Ibid*, page 172

<sup>736</sup> Day 70, page 103

<sup>737</sup> Day 82, pages 58–59

<sup>738</sup> Management of the SNBTS in the ‘90s – Part 1 – The Skeletal Structure [SNB.002.4674] at 4675-76

<sup>739</sup> *Ibid* [SNB.002.4674] at 4674

Gunson as to Scottish, much less UK, policy on the date for the introduction of screening, without reference to the MSC and the SHHD. That this is what happened is supported by the contemporaneous documentation; as the submission for the Scottish Government observed, there is no evidence from 1991 to support the suggestion that Professor Cash was in favour of a reconsideration of the policy of a common UK start date, and much that is against it.<sup>740</sup>

**31.522** Even on Professor Cash's account of events, direct discussions between him and Dr Gunson (who did not, in the opinion of Mr McIntosh, have executive authority for the NBTS)<sup>741</sup> had illustrated the vague nature of policy making for Scotland in relation to the introduction of screening. The manuscript note on the SHHD copy of Professor Cash's letter to Mr McIntosh dated 27 March 1991, implies that officials did not know until that point of the further postponement of the introduction of screening.<sup>742</sup>

**31.523** Formally, it was open to Scottish Office officials at any time to make a submission to the appropriate Minister, and onwards to the Secretary of State for Scotland, that the commitment to a uniform UK start date for the introduction of any form of screening, but specifically anti-HCV, should be withdrawn and that screening should be introduced in Scotland when the SNBTS regions were equipped, funded and fully prepared to implement the decision. It would have become a political issue for Scottish Office Ministers in the first instance, and no doubt thereafter for discussion with UK Departments, whether to make a change of direction.

**31.524** This is precisely what was to happen at the end of 1994 in respect of Hepatitis C look-back. Lord Fraser of Carmyllie, then Minister for Home Affairs and Health at the Scottish Office, was advised that the SNBTS was ready to proceed with look-back and that, on medical and legal advice, the Secretary of State and he had a duty to initiate the process notwithstanding earlier UK policy.<sup>743</sup> In the result, UK policy was changed. However, the obligation of Scottish Ministers to act independently of UK colleagues where Scottish health issues were concerned, was asserted unequivocally.

**31.525** In the end, problems of funding the NBTS in England and Wales to start screening pushed the start date for the UK back to 1 September 1991. Mr McIntosh's assessment of the position is accepted. The successive delays over the period March to September 1991 were exclusively a direct result of giving priority to the UK solidarity argument. That was underlined by the financial problems in England and Wales.

**31.526** The 'device' of presenting the implementation in Glasgow – along with Newcastle and two other centres – as a further study, was related to Newcastle's decision to take unilateral action. As a practical matter, the result was that for half of Scotland agreement on a UK-wide start date ceased to matter. In Edinburgh, testing began on 30 July 1991.<sup>744</sup> For the remaining parts of Scotland, UK solidarity may have been a significant disadvantage. In this regard, however, it has been pointed out to the Inquiry that in Dundee, contemporaneous documents suggest that assessment of, and familiarisation with, testing kits began in the middle of July, with all units producing other than negative results being withheld from issue.

<sup>740</sup> Submissions on behalf of the Scottish Government [PEN.019.0274] at 0343

<sup>741</sup> Day 70, page 83

<sup>742</sup> Letter [SGF.001.2026]

<sup>743</sup> Letter from Lord Fraser to Tom Sackville, MP, dated 22 December 1994 [SNB.008.4848]

<sup>744</sup> See paragraph 31.248

## Summary and conclusions

**31.527** It is now necessary to try to draw the material together. The topic addressed in this chapter is conveniently viewed in two parts. First, there is the period between the summer of 1988 when the establishment of the ACVSB was first mooted, until the committee decided to recommend the introduction of screening for Hepatitis C on 21 November 1990. Secondly, there is the period after that decision when implementation was arranged, with screening finally starting across the UK on 1 September 1991. The Inquiry does not have enough information to be critical of the composition of the ACVSB, or to assess the dynamics of particular meetings. All those appointed were experts in their respective fields and there is nothing to suggest that they acted other than in good faith at all times. There is therefore no basis on which individual members of the committee or officials in attendance can be criticised in relation to the workings of the committee, and no observation made or conclusion reached by the Inquiry should be understood as making any such criticism.

**31.528** Reverting to the questions posed at the conclusion of the Inquiry,<sup>745</sup> the first three of those questions concern the construction of processes for reaching a decision about introducing screening, and implementing any decision to proceed. It is therefore appropriate to consider these matters together.

1. Until the establishment of the ACVSB, the UK did not have in place an appropriate mechanism for providing Ministers with independent scientific advice on the risks presented to NHS patients by transmission of viruses in blood, blood components and blood products. The decision to establish the ACVSB was therefore well founded.
2. The emergence of two committees – one established by the DoH in consultation with the other health departments of the UK and one established by the transfusion services – created a risk of confusion as to the respective remits of each and the relationship between them. The formation of the ACTTD appears to have been due to a perception on the part of Dr Gunson and Professor Cash that nothing had happened to progress matters, after the creation of a government committee had been mooted by Dr Harris in July 1988.
3. In retrospect, a better model would have provided for advice as to policy and arrangements for implementation to be coordinated, for example by the establishment of an ACVSB with a sub-committee, consisting mainly of members with transfusion expertise, to address the implementation of policy. Thus, what Dr Perry termed 'scenario planning' could have been addressed in a dedicated forum whilst policy was being finalised by the ACVSB.
4. There was a lack of clarity as to how there was to be implementation in Scotland of decisions reached by the committees. There was asymmetry in that the Director of the NBTS, Dr Gunson, served on the ACVSB whereas his equivalent in Scotland, Professor Cash, did not. The requirement of confidentiality relating to the proceedings of the ACVSB, coupled with a lack of routine communication back to the SNBTS, contributed to the perception in Scotland that there was little direct involvement in decision making. That said, it is not clear that the deliberations of the committee would have been influenced by additional Scottish representation, and it is clear that when the decision to recommend the introduction of screening was finally made by the

---

<sup>745</sup> See paragraph 31.431

ACVSB in November 1990, Scottish centres were well placed promptly to implement the decision.

**31.529** The fourth question posed related to factors which contributed to there being no decision until November 1990 to recommend to Ministers that screening should start as soon as practicable:

5. From around the end of 1989, the ACVSB became involved in more than expert scientific advice; the committee was considering wider policy issues and addressing the practical implementation of policy.
6. In retrospect, the meetings of the ACVSB on 24 April and 2 July 1990 were missed opportunities to recommend the earlier implementation of screening.
  - a) At the meeting on 24 April 1990, the committee was presented with a particular impression of the symposium held by Ortho in London in February. That impression appears to have influenced the committee against the test. Dr Boulton, Deputy Director of Edinburgh and South East Scotland BTS, had also attended the seminar, and reported on it to Professor Cash. The Inquiry considers that Dr Boulton more accurately identified and weighed the relevant considerations in suggesting to Professor Cash that screening should be introduced at the earliest opportunity than did the members of the ACVSB at their meeting of 24 April.
  - b) It had been pointed out by Professor Zuckerman at the beginning of 1990 that the introduction of screening could not be delayed much beyond FDA approval of the test, but it appears that the committee was taken by surprise by news that approval had been granted on 2 May 1990. When that occurred, as Burton J pointed out in *A v National Blood Authority*, it completed the three requirements set out in the minutes of the ACVSB meeting of 6 November 1989: successful pilot trials in the UK, the grant of FDA approval and the existence of a RIBA supplementary test (albeit not strictly a confirmatory test).<sup>746</sup> An inference that FDA approval was imminent could have been drawn: an export permit had been granted in the USA in November 1989 and guidelines for testing had been issued there in February 1990.
  - c) The decision at the meeting on 2 July 1990 to delay implementation until the completion of a further trial – this time to compare the Ortho and Abbott tests – was not warranted in the circumstances; local centres could have made their own choices and comparisons of the kits could have been made once screening had started.
7. In all the circumstances, a decision to recommend to Ministers the introduction of routine screening of blood donations for anti-HCV could and should have been taken by the middle of May 1990. It appears unlikely; however, that screening in any centre could have started much before the autumn of 1990. Having regard to the supplies of test kits available.

**31.530** The remaining questions concern the period after the decision to recommend the introduction of screening. The Inquiry has endeavoured to assess why there was a delay of almost 10 months between the decision by the ACVSB on 21 November 1990 to recommend the introduction of screening as soon as practicable and 1 September

---

<sup>746</sup> Judgment [PEN.017.0302] at 0393, paragraph 154



1991, the point from which donations across Scotland were all being screened. It has also analysed the original policy that introduction of screening should take place at the same time across the UK, and considered if involvement of the Scottish Health Minister earlier than July 1991 would have led to earlier introduction of screening.

8. It is relatively straightforward to explain as a matter of fact why the time elapsed. There was a delay of almost ten months because a policy set at the outset – that the introduction of screening across the UK should take place at the same time – was maintained despite some areas being ready to begin considerably earlier than others.
9. It is much less straightforward to explain why there was no deviation from this policy. The period 21 November 1990 to 12 June 1991 included a number of missed opportunities for more prompt introduction of screening in Scotland.
  - In the first place, if Dr McIntyre had communicated to Professor Cash his understanding that the date for introduction of screening was to be 1 April 1991, the efforts of the SNBTS would have been directed towards achieving that implementation date.
  - In the second place, if Mr Tucker had been less diffident in communicating his perception in January 1991 that ‘to delay for the slowest could mean a long wait’, there would have been an opportunity for the date of 1 April to be confirmed as the date for introduction of screening in Scotland.
  - In the third place, if Dr Pickles had copied her memorandum of 5 February 1991 to any officials in the SHHD, it would have been appreciated more clearly that the funding problems in England and Wales were delaying the introduction of screening in Scotland.
  - In the fourth place, if the SNBTS, especially Professor Cash, and Mr McIntosh had explained the situation fully to the SHHD at the end of March 1991, and had put to them the suggestion that Scotland was in a position to move ahead with the introduction of screening in July 1991 as previously intended, a decision to adhere to that start date could have been taken. Instead, Professor Cash in effect determined the policy for Scotland, by agreeing with Dr Gunson a postponement of the introduction of screening to 1 September 1991, to be ascribed to the need for evaluation of second generation test kits.
10. Any suggestion that taking one or more of these steps would have led to earlier introduction of screening involves a determination that the position of the responsible Minister in Scotland would have permitted different dates for the introduction of screening in Scotland and in England/Wales. It is not possible to make such a determination. Viewed now, the reluctance to bring the issue of when screening was to start in Scotland to the attention of Ministers seems odd; the proposition that authorisation of the setting of a date could not be sought until a date had been determined elsewhere appears surprisingly passive. It may be that officials took for granted that there would be no change in direction. But within Scotland, the ultimate responsibility for the safety of patients undergoing NHS treatment with blood and blood products was that of the Secretary of State and his Ministers. Serious problems in relation to the introduction of a measure which would improve that safety should have been communicated to them, in order that they could decide what should be done.

© Crown copyright 2015

An online version of the report is available at [www.penroseinquiry.org.uk](http://www.penroseinquiry.org.uk)

**ISBN: 978-0-85759-022-0 (Volume 4 of 5)**

**This Inquiry Report comprises an Executive Summary (ISBN: 978-0-85759-023-7), five volumes and a DVD**

Published on behalf of The Penrose Inquiry by APS Group Scotland, 21 Tennant Street, Edinburgh EH6 5NA  
DPPAS43828 (03/15)

THE  
PENROSE  
INQUIRY

# Final Report

**Volume 5:  
Information to Patients**

THE  
PENROSE  
INQUIRY

# Final Report

**Volume 5:  
Information to Patients**

Laid before the Scottish Parliament by the Scottish Ministers  
under section 26 of the Inquiries Act 2005.

March 2015  
SG/2015/15

© Crown Copyright 2015



This publication is licensed under the terms of the Open Government Licence v3.0 except where otherwise stated. To view this licence, visit [nationalarchives.gov.uk/doc/open-government-licence/version/3](http://nationalarchives.gov.uk/doc/open-government-licence/version/3) or write to the Information Policy Team, The National Archives, Kew, London TW9 4DU, or email: [psi@nationalarchives.gsi.gov.uk](mailto:psi@nationalarchives.gsi.gov.uk).

Where we have identified any third party copyright information you will need to obtain permission from the copyright holders concerned.

This publication is available at [www.penroseinquiry.org.uk](http://www.penroseinquiry.org.uk).

ISBN: 978-0-85759-022-0  
(Volume 5 of 5)

Published on behalf of The Penrose Inquiry by APS Group Scotland, 21 Tennant Street, Edinburgh EH6 5NA  
DPPAS43828 (03/15)

# CONTENTS

<b>Volume 5: Information to Patients</b>	Page
32 An Investigation into the Systems in Place for Informing Patients about the Risks – Ethical Context	1489
33 An Investigation into the Systems in Place for Informing the Patients about the Risks – HIV/AIDS	1537
34 An Investigation into the Systems in Place for Informing the Patients about the Risks – Hepatitis C	1639
35 An Investigation into the Steps Taken to Identify the Individuals who were Infected (Look-back)	1689
 <b>Appendices</b>	
Appendix 1: Inquiry Procedures	1749
Appendix 2: Inquiry Organisation and Administration	1763
Appendix 3: Core Participants	1769
Appendix 4: Inquiry Witnesses	1771
Appendix 5: Inquiry Procedure Directions, Guidance Notes and Restriction Orders	1779

## CHAPTER 32

### AN INVESTIGATION INTO THE SYSTEMS IN PLACE FOR INFORMING PATIENTS ABOUT THE RISKS – ETHICAL CONTEXT

#### Introduction

#### *Scope of this part of the Report*

**32.1** This part of the Report comprises four chapters. They explore the issues raised by Terms of Reference 2 and 3 for the Inquiry:

2. To investigate the systems in place for informing patients treated by the NHS in Scotland of the risks associated with the use in their treatment of blood or blood products with particular reference to the risks of infection with the Hepatitis C virus and HIV.

3. To investigate the systems in place in Scotland for obtaining consent from, and testing for infection with Hepatitis C and HIV, patients treated with blood or blood products, and informing patients found to be so infected.

**32.2** This chapter looks at the development of the relationship between clinician and patient during the reference period. Chapter 33 deals with various aspects of the information provided to patients on HIV/AIDS and at the testing of patients for HIV. Chapter 34 deals with the same matters in respect of NANB Hepatitis/Hepatitis C. Chapter 35, *An Investigation into the Steps Taken to Identify the Individuals who were Infected (Look-back)*, deals with the methods available to identify patients put at risk of HCV transmission by treatment with blood or blood products, and the steps taken in that regard.

#### *Background to this part of the Report*

**32.3** As stated in Chapter 4 of the Preliminary Report, it was a recurring theme in the witness statements which the Inquiry obtained from patients and their relatives that many patients felt that they were given little or no information from their treating clinicians about the risk of infection to which they were exposed as a result of their treatment with blood or blood products. Many of the patient witnesses who received blood transfusions in the 1970s, 1980s and in the 1990s stated that they were not warned of the risk of transmission of infection. The reasons for patients receiving blood transfusions varied, as did the circumstances in which they required medical care. In some cases the circumstances surrounding a surgical procedure will hardly have been conducive to a rational discussion of the long-term risks potentially associated with transfusion, but in others, such as planned medical procedures, there would have been more ample opportunity for discussion of risks. Most patients with a blood disorder who provided statements commented that they were not warned of the risk of infection with HTLV-III/HIV or non-A non-B Hepatitis from the blood products they received, including cryoprecipitate and factor concentrates.

**32.4** The investigations discussed in this part of the Report arose against this background, and reflected the questions that the experiences of many patients and their relatives naturally and understandably prompted. At the most general level, there was a need to know how it came about that materials subsequently found to be infectious were used in treatment without the patient being made aware that there was a risk of transmission of viral infection. Questions expressing that need have ranged from simple, but sometimes desperate, pleas for information to enable people to understand how they, or their relatives, came to be infected with HCV or HIV, to accusations, sometimes angry, against clinicians

responsible for prescribing therapeutic materials capable of transmitting infection. Some patients felt that, as a result of not being warned of the risks of infection from their treatment, they were denied the opportunity to make an informed choice about the treatment they received.

**32.5** Furthermore, many patients complained that they were tested for HIV and/or Hepatitis C without their consent and knowledge. A large number of the witnesses expressed dissatisfaction about the manner in which their diagnosis with HIV and/or Hepatitis C was conveyed to them and about the information which they were given about these viruses. Many witnesses felt that the health implications of the viruses and other matters, such as secondary infection, were not adequately explained to them.

**32.6** In very general terms, the clinicians' position, set out in submissions on behalf of the NHS in Scotland, was that: 'In their interactions with patients, clinicians made every effort to communicate effectively in unprecedented circumstances'.<sup>1</sup> Further it was noted that testing blood samples without express consent was commonplace and acceptable by the ethical standard of the time.<sup>2</sup> With regard to advising patients of the results of their test results, it was stated on behalf of the NHS for Scotland that: 'the preponderance of evidence strongly suggests that patients were told of their diagnosis'.<sup>3</sup> They highlighted evidence which indicated the difficulties for patients of absorbing information, particularly bad news.

**32.7** The Scottish Government recognised, in its closing submissions, that communication between doctor and patient: 'is an important and sensitive topic. Good communication is fundamental to the clinical relationship, and a critical factor in obtaining informed consent to medical treatment or surgical procedures'.<sup>4</sup> It also recognised and welcomed the fact that attitudes to communication and consent had 'progressed significantly' in the last 25 years.

**32.8** These brief comments reflect differences in the evidence of fact: what actually happened in the course of clinical procedures over long periods of time; what protocols were in place for communication between clinician and patient; and whether the differences in recollection and report can be resolved. In this chapter, evidence relating to the development of generally recognised ethical rules and practices will be discussed. Controversial issues emerged and some of them have to be discussed at length in an attempt to define the professional standards in place from time to time. In later chapters these standards inform discussion of the evidence of what probably did happen as between clinician and patient in the particular cases reported. This chapter explores the issues more generally. Resolving the competing evidence of experts proved to be difficult.

### *Evidence*

**32.9** For the purpose of exploring the range of issues discussed in the four chapters of this part of the Report at the Oral Hearings of the Inquiry, the following topics were defined:

#### **HIV/AIDS**

- The information given to patients (or their parents) about the risk of AIDS before their treatment with blood or blood products.

---

<sup>1</sup> Closing submission by NHSScotland on information given about the risk of AIDS [PEN.019.0428] at 0436

<sup>2</sup> Ibid [PEN.019.0428] at 0432

<sup>3</sup> Ibid [PEN.019.0428] at 0436

<sup>4</sup> Submissions on behalf of the Scottish Government [PEN.019.0274] at 0309



- The tracing and testing of patients who might have been exposed to the virus through their treatment with blood or blood products.
- The information given to patients who might have been infected, or who were found to be infected, and their families.

### **Hepatitis C**

- The information given to patients (or their parents) about the risk of non-A non-B Hepatitis before their treatment with blood or blood products.
- The tracing and testing of patients who might have been exposed to the virus through their treatment with blood or blood products.
- The information given to patients who might have been infected, or who were found to be infected, and their families.

Evidence on these topics was taken from the written and oral evidence of patients and their relatives, doctors, nurses, other professionals, and officials.

### ***Expert guidance***

**32.10** It was recognised that the Inquiry would require expert guidance on medical ethics and Professor Vivienne Nathanson and Dr Charles Hay were asked to assist in this respect. Professor Nathanson had been the Director of Professional Activities at the British Medical Association (BMA) for 16 years before coming to give evidence. Before working for the BMA she qualified and practised as a specialist registrar in general medicine. Dr Hay was Chairman of the United Kingdom Haemophilia Centre Doctors Organisation (UKHCDO). He was an experienced haemophilia clinician with a long and distinguished career in haemophilia care.

**32.11** Professor Nathanson attended the Inquiry twice to give evidence on ethical issues and provided two reports in which she answered a series of questions posed by the Inquiry team. The first report<sup>5</sup> dealt with HIV and AIDS. The second report<sup>6</sup> dealt with NANB Hepatitis and Hepatitis C. Dr Hay prepared a report<sup>7</sup> on the communication of information to patients about hepatitis in which he explained his opinion of the information patients should have been given about NANB Hepatitis/HCV against the background of the changing scientific knowledge of the condition in the period 1974–1995. In addition, Dr Hay set his evidence on the relationships between haemophilia patients and their doctors squarely in the context of his clinical experience. He gave oral evidence, based on his experience in practice in haematology medicine from mid-1977 to the present day, on the information and advice he personally gave to patients, or their parents, of the risks of contracting, and the severity of, NANB Hepatitis/HCV.

### ***Scope of this chapter***

**32.12** Although the separation between the two viruses, HIV/AIDS and NANB Hepatitis/HCV, will be maintained in discussion in the following chapters, it is appropriate to set the scene for particular discussion of the questions that have arisen from the evidence by a more general discussion. It is necessary to understand the nature of the doctor-patient relationship at the beginning of the reference period and to follow some of the

---

<sup>5</sup> Professor Nathanson's first report to the Inquiry [PEN.012.0330]

<sup>6</sup> Professor Nathanson's supplementary statement [PEN.018.0419]

<sup>7</sup> Dr Hay's report on communication to patients about hepatitis [PEN.018.0961]

developments thereafter as background to the discussion of the provision of information to patients.

**32.13** The accepted understanding of the way in which doctors should interact with their patients developed during the reference period, as knowledge of the viruses emerged and changed, and clinical practice was adapted to reflect that understanding. In her written reports and in oral evidence, Professor Nathanson commented on the development of the core elements of the ethical practice of medicine during the reference period, as she saw them, such as consent to treatment and testing and communication with patients. In oral evidence she expanded on the interaction of developing medical knowledge and ethical practice:

I think the important issue here is that when you look at ethics, not only has ethics changed during the period in question, or at least the practice of ethics, what we would regard as best practice and what we would expect as the minimum standard but that that has also had to reflect the change in scientific understanding during that period, and the two things have to come together.<sup>8</sup>

**32.14** In considering the response of clinicians to the needs of patients for information it is necessary to bear in mind these two distinct, if interrelated, factors.

**32.15** The clinical settings confronted by medical practitioners vary widely. Most of the discussion in this chapter will relate to the treatment of patients with coagulation disorders, typically Haemophilia A or B, managed over long periods of time. Monitoring patients at regular hospital attendances in that context afforded opportunities for discussion and the informed selection of materials for therapy that would not exist in many other situations involving transfusion, such as surgery or general medical procedures. The treatment of general medical and surgical patients may involve single or multiple sessions with more or less opportunity for discussion, depending on the circumstances. Transfusion in a surgical setting may be elective, providing an opportunity for discussion, or in an emergency setting in which prolonged discussion of options could threaten the life the surgeon is anxious to save. Sometimes a patient is unconscious before the need to give a blood transfusion, possibly to save his or her life, becomes apparent. It is necessary to bear in mind that issues raised by urgency or the immediate demand for relief of suffering may be very different from those that arise from care of patients with chronic conditions. In the first place, however, the focus will be on therapy in relief of blood coagulation disorders.

**32.16** It was to become apparent that, while there was a very substantial overlap between the underlying ethical principles and rules applicable as they developed from time to time, their application to the doctor-patient relationship varied in relation to the specific viruses to which the Terms of Reference relate, HIV/AIDS and NANB Hepatitis/Hepatitis C. Patients were exposed to the risk of transmission of these viruses over very different periods (see Chapter 2, *Patients at Risk*) and the factors driving changes in professional standards varied as between them, both in terms of chronology and in the context of developing medical knowledge.

**32.17** This chapter will therefore deal with what the Inquiry has learned and been told about the history of the doctor-patient relationship from the 1970s to the present day and then more specifically with the development of the ethical background to information

---

<sup>8</sup> Professor Nathanson – Day 84, pages 1–2

given to patients about the tests they were undergoing, the illnesses from which they suffered and about relevant treatment, again from the 1970s onwards. It deals principally with the evidence on those aspects of medical ethics that are of specific importance for the purposes of the Report. It is not a history of medical ethics generally. Nor does it provide a critique of the witnesses' general evidence. Differences between Professor Nathanson and Dr Hay are examined where they are material to the Terms of Reference.

**32.18** In general, it cannot be emphasised too strongly that, as the history of events in Scotland and elsewhere unfolded, in relation to information to patients and the way doctors were expected to interact with patients, the changes that occurred were sometimes dramatic. In relation to knowledge of the relevant diseases, not only were there significant changes over time in the understanding among clinicians of their respective aetiologies and natural histories, developments in knowledge were not consistent across all relevant disciplines. Knowledge among many clinicians inevitably lagged behind cutting-edge research to some degree at any particular point in time. The scientific and clinical developments are fully dealt with in Chapters 8 to 10 (HIV/AIDS) and Chapters 13 to 16 (viral Hepatitis). In this context it is particularly important to avoid being wise after the event and to avoid viewing events and developments in the light of later insights – applying up-to-date clinical knowledge and ethical standards to periods when such rules as applied were at best inchoate versions of later statements of principle and developments in practice.

## Sources of ethical guidance

### *Pre-1980s*

**32.19** There is no central UK committee on healthcare ethics. Clinical advice to practising doctors is provided by the BMA and the General Medical Council (GMC).<sup>9</sup> The BMA has had a committee looking at medical ethics since 1849.<sup>10</sup> The committee provides general advice to doctors in the form of guidance notes and leaflets. In the course of the reference period there were a number of landmark stages, reflected in published guidance documents, which help trace developments. Less formal means of providing guidance to doctors were also adopted. As Director of Professional Activities at the BMA, part of Professor Nathanson's job consisted of answering questions from doctors in practice about ethical dilemmas – advising doctors on what they should do in the specific circumstances brought to her attention.<sup>11</sup> Contemporaneous published guidance from the BMA and the GMC was not the only means of providing advice and was therefore not the exclusive test available of what was considered to be ethical practice. However, published guidance provides an accessible measure of the formal steps taken by representative medical authorities to inform doctors of their ethical duties and assists in setting a chronological framework for discussing other issues.

**32.20** Professor Nathanson recounted the history of medical ethics over the last 40 years in her first report to the Inquiry. It is not necessary to trace all developments in this field for present purposes as the nature and extent of the developments that are relevant can be demonstrated more briefly.

<sup>9</sup> The General Medical Council registers doctors to practise in the UK. Its purpose is to protect, promote and maintain the health and safety of the public by ensuring proper standards in the practice of medicine.

<sup>10</sup> British Medical Association, *Medical Ethics Today: Its Practice and Philosophy*, 1993, BMJ Publishing Group, London XXV.

<sup>11</sup> Professor Nathanson – Day 37, pages 1–3

**32.21** At one level, the requirement for patients to have necessary information relating to their treatment was referred to in documents from as early as the 18th century. Professor Nathanson referred to a quotation from the case of *Slater v. Baker and Stapleton* in 1767 which stated in the context of surgery (before the advent of anaesthesia) that it was 'reasonable that a patient should be told what is about to be done to him, that he may take courage and put himself in such a situation as to enable him to undergo the operation'.<sup>12</sup> This case was referred to in the BMA publication *Medical Ethics Today: Its Practice and Philosophy (1993)* in which it was observed that the comment:

[P]erhaps foreshadows current thinking that most people fare best when they have a clear view of what is being proposed and its implications.<sup>13</sup>

**32.22** Professor Nathanson also referred to the rules on medical research promulgated in 1949 after the Nuremberg trials, stating that they were the first explicit modern statement of the right of every patient to consent to and therefore refuse any medical treatment. Rule 1 of the Nuremberg Code provided:

[T]he person involved should have the legal capacity to give consent; should be so situated as to be able to exercise free power of choice, without the intervention of any element of force, fraud, deceit, duress, over-reaching, or other ulterior form of constraint or coercion; and should have sufficient knowledge and comprehension of the elements of the subject matter involved, as to enable him to make an understanding and enlightened decision.<sup>14</sup>

**32.23** The context for the Rule was medical research and, in particular, experimentation on human subjects. Professor Nathanson commented:

Following the Nuremberg trials legal rules on medical research were put in place. While these were not then well known to doctors throughout the world [Rule 1] was the first explicit modern statement of the right of every patient to consent to, and hence to refuse, any medical treatment.<sup>15</sup>

**32.24** Until 1949, the BMA and its ethics committee resisted preparation of an ethical code.<sup>16</sup> In 1949, the BMA Council produced a 16-page booklet mainly concerned with relationships between doctors and members of other professions.<sup>17</sup> In 1974 it produced a booklet of 50 pages, including a full reprint of the current GMC rules, the Hippocratic Oath and relevant ethical codes, including the Declaration of Helsinki.<sup>18</sup> Professor Nathanson suggested that, at a very basic level, the change in the approach to ethics could be illustrated in the difference in scale between the 50-page 1974 booklet and the current edition which is produced on a CD-ROM and is just under 1000 pages.<sup>19</sup>

---

<sup>12</sup> Quoted in Professor Nathanson's first report to the Inquiry [PEN.012.0330] at 0332

<sup>13</sup> British Medical Association, *Medical Ethics Today: Its Practice and Philosophy*, 1993, BMJ Publishing Group, London, xxv.

<sup>14</sup> *Trials of War Criminals before the Nuremberg Military Tribunals under Control Council Law No. 10*. Washington, D.C. (1949): U.S. Government Printing Office. Vol. 2, 181–182. Available online at <http://history.nih.gov/research/downloads/nuremberg.pdf> [last accessed 23/12/2014]

<sup>15</sup> Professor Nathanson's first report to the Inquiry [PEN.012.0330] at 0334

<sup>16</sup> British Medical Association, *Medical Ethics Today: Its Practice and Philosophy* 1993, BMJ Publishing Group, London, xxv.

<sup>17</sup> Ibid

<sup>18</sup> Professor Nathanson's first report to the Inquiry [PEN.012.0330] at 0330. The Declaration of Helsinki is a set of ethical principles regarding human experimentation developed by the World Medical Association and adopted by the WMA General Assembly in June 1964. It has undergone six revisions since then. The current, sixth revision was adopted by the General Assembly in Korea in October 2008. It was addressed primarily to physicians, and emphasised the physician's duty to promote and safeguard the health of patients, including those involved in medical research. It provided that in medical research involving human subjects the well-being of the individual research subject must take precedence over all other interests.

<sup>19</sup> Professor Nathanson – Day 37, pages 15–17

While superficially attractive, that could only be a sufficient measure of change if the publications were the sole source of guidance on ethical practice. However, as stated in paragraph 32.19 above, the BMA also produced specific advice sheets and guidance notes to its practitioners on a variety of areas and gave advice to doctors who contacted its ethics advice services. The proliferation of less formal advice suggests that the scale of change was even greater. However, on any view, the change in scale of the handbook reflects an appreciation of a growing need for formal written advice over the period that is relevant to this Report.

**32.25** More fundamentally, the nature of the advice given by the BMA to members has varied widely, reflecting the ethical mores and standards of the times. A reviewer of the 2003 edition of *Medical Ethics Today*, perhaps cynically, captured the flavour of the BMA's 1974 booklet from a modern medical perspective:

The 1974 edition ... provided guidance on important matters such as whether a consultant or a GP should enter the room first when both visited a patient.<sup>20</sup>

**32.26** Both the hierarchical structure of the profession and the paternalistic attitude towards patients were reflected in the 1974 guide. The culture of the time was summed up in a quotation from Dr CO Hawthorne who was the Chairman of the BMA Central Ethical Committee for many years. He was reported to have written between the wars that:

In the relations of the practitioner to his fellows, while certain established customs and even rules are written and must be written, the principal influence to be cultivated is that of good fellowship. Most men know what is meant by 'cricket' and the spirit of the game. Difficulties and differences will arise, but most of them can be successfully met by mutual goodwill and recognition of the other fellow's point of view.<sup>21</sup>

**32.27** As Professor Nathanson noted, this statement seemed to envisage a practitioner who already knew what the ethical rules were. At that time there was little in the way of specific guidance. She noted that the only reference to patient consent in the first edition of this guide related to the particular issue of organ donation. Academic texts discussed consent but it was rare for patients to question doctors' advice and consent was seen as a non-contentious issue.<sup>22</sup>

**32.28** In her evidence, Professor Nathanson undermined the notion that it could be assumed that practitioners would know the ethical rules. By way of background, she said that, in reality, the teaching of ethics lacked consistency and was of variable quality. In the 1970s, for more general ethics teaching, most medical students in London were educated by attending voluntary lectures given by the London Medical Group, an informal group of practitioners. Studies by the Institute of Medical Ethics in 1987 and 2006 demonstrated a continuing deficiency in ethics teaching of medical students and noted that, although the topic was a course requirement, it was rarely part of the final examination. The subject was taught in every medical school but there was, and remains, concern at the BMA about the consistency and quality of teaching. Although the teaching of medical ethics

---

<sup>20</sup> Barratt, 'Medical ethics today', *Triple Helix*, Spring 2005; 20–21. Available at <http://www.cmf.org.uk/publications/content.asp?context=article&id=1595> [last accessed 8/1/15]

<sup>21</sup> Quoted in Professor Nathanson's first report to the Inquiry [PEN.012.0330] at 0330

<sup>22</sup> Professor Nathanson's first report to the Inquiry [PEN.012.0330] at 0330

could be an independent part of the course structure, often it has rather depended on interested and knowledgeable clinicians teaching ethics as an additional element within a clinical discipline.<sup>23</sup>

**32.29** The publication of Ian Kennedy's 1980 Reith lectures, 'The Unmasking of Medicine', had a profound impact.<sup>24</sup> It advocated a more patient-centred approach to medicine in which patients were seen as partners in investigation, management and treatment decisions.

**32.30** According to Professor Nathanson, there was a shift in the period between 1974 and 1980 towards more guidance on specific ethical issues in response to clusters of queries about the correct approach to take in particular clinical situations.

**32.31** With regard to blood transfusion, 'Notes on Transfusion' issued to UK hospitals by the Department of Health and Social Security in 1973 required a record of every transfusion to be made in the patient's case notes.<sup>25</sup> It emphasised that 'the main reason for accurate recording is the protection of the patient'. No mention was made in these notes or their revised version in 1984 of patient information or of consent.<sup>26</sup> According to Dr Derek Norfolk '[i]nformed consent for blood component transfusion does not appear to have been a major issue for clinicians in the 1970s although there was increasing awareness following the emergence of HIV in the 1980s'. In the UK consent for transfusion has not been formalised and, in the surgical setting, has been regarded as part of the normal process of obtaining consent for the overall procedure.<sup>27</sup>

### 1980s

**32.32** The first BMA handbook on medical ethics was published in 1980 and revised in 1981 and 1984.<sup>28</sup> The 1980 BMA handbook, which was written by a sub-committee of doctors, gave more situation-specific advice and, in addition to the handbook, the BMA continued to produce advice sheets and guidance notes (sometimes on broad issues and sometimes focused on very specific issues) for its practitioner members on a variety of areas and gave advice to doctors who contacted its ethics advice services.

**32.33** The style of the 1980s publications before 1988 was to give ethical guidance through a list of generally agreed precepts. That style was abandoned in 1988, when, according to the 1993 publication *Medical Ethics Today: Its Practice and Philosophy*, the handbook set out 'the influences which give rise to the general moral and ethical order and set out principles as a basis for studying practical problems'.<sup>29</sup> The approach adopted by the BMA in 1988 is important for the purposes of this Inquiry, having regard to the evidence of the two principal witnesses dealing with ethical issues, and in particular the use by Professor Nathanson of the 1988 texts to explain wider ethical issues. However, reviewers were not uniformly of the view that the book succeeded in its objectives, as noted below (paragraph 32.45).

**32.34** In addition to BMA guidance, the GMC also published advice. In 1980 the advice produced by the GMC took the form of a list for doctors of what might constitute poor practice and lead to allegations of professional misconduct. By way of contrast, today

<sup>23</sup> Ibid

<sup>24</sup> Available at <http://www.bbc.co.uk/programmes/p00gg1z0> [last accessed 08/01/2015]

<sup>25</sup> Dr Norfolk's statement on the use of blood and blood components in clinical medicine [PEN.010.0048] at 0065

<sup>26</sup> Ibid [PEN.010.0048] at 0068

<sup>27</sup> Ibid [PEN.010.0048] at 0070

<sup>28</sup> British Medical Association, *Medical Ethics Today: Its Practice and Philosophy*, 1993, BMJ Publishing Group, London, XXV.

<sup>29</sup> Ibid

the GMC produces detailed advice of what constitutes good practice rather than bad. The GMC advice on consent has developed the concept of patient autonomy and, in this area also, the GMC now gives advice on what builds good practice rather than listing bad practice that could result in disciplinary issues. The change in emphasis and approach is stark: over time the GMC's guidance on ethics has become more prescriptive, directing doctors as to what best practice requires.<sup>30</sup>

**32.35** If the brief BMA ethics booklet published in 1974 reflected the attitudes of doctors and patients at the time, little appears to have changed in relation to general attitudes by 1980. Professor Nathanson contrasted BMA advice in 1980 with the more developed position in 1988.<sup>31</sup> In relation to consent, in 1980, the BMA stated:

The patient's trust that his consent to treatment will not be misused is an essential part of his relationship with his doctor.<sup>32</sup>

In 1988, the equivalent passage (quoted in full at paragraph 32.44 below) stipulated for patient consent before any investigation and treatment was carried out.

**32.36** In terms of good ethical practice, as at 1980 there was no specific requirement for consent, or any related procedure. Consent to treatment was still assumed rather than prescribed. By 1988, as Professor Nathanson observed, there was 'increasing comfort in using formal ethics language and concepts in describing the basic principle'.<sup>33</sup>

**32.37** In the interval between 1980 and 1988, a significant development was the adoption by the World Medical Association in October 1981 of the Declaration of Lisbon, a statement on the rights of the patient which provided that:

A mentally competent adult patient has the right to give or withhold consent to any diagnostic procedure or therapy. The patient has the right to the information necessary to make his/her decisions. The patient should understand clearly what is the purpose of any test or treatment, what the results would imply, and what would be the implications of withholding consent.

The patient has the right to refuse to participate in research or the teaching of medicine.<sup>34</sup>

**32.38** The Declaration was the earliest significant, and relevant, general statement on patient consent drawn to the attention of the Inquiry. The rights of a mentally competent adult patient were comprehensively formulated. It was a clear indication, from the autumn of 1981, of recognition by the international medical community of the patient's right to information relevant to, and to participate in any decision on, investigation and treatment, and participation in research. However, acceptance of the statement as part of a definitive code of ethical conduct would inevitably depend on its adoption by national authorities for their own jurisdictions. In the event, the Declaration came after and was not reflected in the BMA's 1980 statement. So far as drawn to the attention of the Inquiry, BMA publications did not reflect the general Lisbon principle of explicit and informed consent until 1988.

---

<sup>30</sup> Professor Nathanson's first report to the Inquiry [PEN.012.0330] at 0331

<sup>31</sup> Ibid [PEN.012.0330] at 0334–35

<sup>32</sup> Quoted in Professor Nathanson's first report to the Inquiry [PEN.012.0330] at 0335

<sup>33</sup> Professor Nathanson's first report to the Inquiry [PEN.012.0330] at 0335

<sup>34</sup> The full text of the Declaration of Lisbon is available at <http://www.wma.net/en/30publications/10policies/14/> [last accessed 08/01/2015]

**32.39** In May 1988, the GMC set out guidance specifically in relation to HIV and AIDS in a publication entitled *HIV Infection and Aids: the Ethical Considerations* (the GMC Guidance of 1988).<sup>35</sup> It narrated the Council's expectations of doctors intending to carry out investigative procedures related to these conditions and stipulated the need for patient consent, whether explicit or implied, to the procedures being undertaken. The guidance stated that the Council believed that the same principles should apply generally. It appears from Professor Nathanson's explanation of the immediate past history of the guidance on AIDS that the guidance may have related more to what the GMC *wished* doctors to aspire to rather than to established and generally recognised rules of behaviour.

**32.40** As Head of Ethics at the BMA between 1987 and 1989, Professor Nathanson attended a GMC meeting in April 1987 as an observer, ensuring cross-representation in the discussion of ethical issues. A paper on the benefit of routine testing and testing without consent, probably written by GMC staff on the basis of debate at previous committee meetings, was discussed. One of the members, a doctor in general practice, advocated that doctors should be able to test patients for HIV infection without consent. After debate it was decided that it would be unethical to carry out such tests without consent. Professor Nathanson recollected, however, that in about 1986–87 the BMA had actually voted for a policy which allowed doctors to test without consent. As soon as the policy was agreed the BMA took legal advice and they were advised that testing without consent was illegal. The policy was reversed the next year at the BMA's annual meeting of 600 representative doctors. In fact the BMA had received conflicting advice from two QCs on the topic. The rationale of the advice which was followed was that because the HIV test was not a standard test the implied consent given for more general tests, like a full blood count, did not apply and specific consent was therefore required.<sup>36</sup> These discussions, in committee and more broadly, eventually resulted in the GMC Guidance of 1988.

**32.41** It is worthy of comment that, in the legal opinion followed by the GMC, reasons specific to the HIV test were persuasive, differentiating it from 'standard' testing. Specific consent was required for anti-HIV testing, implicitly recognising that 'standard' testing was in a different position. Professor Nathanson's anecdote demonstrated clearly that, until the BMA meeting in April 1987 and the GMC Guidance of 1988, the question of consent to investigation and treatment was capable of generating serious debate even among the members of representative bodies' ethics committees, quite apart from dividing the BMA's legal advisers.

**32.42** That debate was not reflected in the publications in 1988. (In addition to *HIV Infection and Aids: the Ethical Considerations* a BMA publication *Philosophy and Practice of Medical Ethics* was revised that year – see paragraph 32.43). In the GMC Guidance of 1988, in a section headed 'Consent to Investigation or Treatment', the GMC stated:

12. It has long been accepted, and is well understood within the profession, that a doctor should treat a patient only on the basis of the patient's informed consent.<sup>37</sup> Doctors are expected in all normal circumstances to be sure of their patient's consent to the carrying out of investigative procedures involving the removal of samples or invasive techniques, whether those investigations are performed for the purposes of routine screening, for example in pregnancy or

<sup>35</sup> *HIV Infection and Aids: the Ethical Considerations*, General Medical Council, May 1988 [PEN.016.1165]

<sup>36</sup> Professor Nathanson – Day 37, pages 31–35

<sup>37</sup> 'Informed consent' had a specific meaning in the USA, where it was a legal requirement. It was not a requirement of UK law, and the use of the expression in this context is 5 questionable.



prior to surgery, or for the more specific purpose of differential diagnosis. A patient's consent may in certain circumstances be given implicitly, for example by agreement to provide a specimen of blood for multiple analysis. In other circumstances it needs to be given explicitly, for example before undergoing a specified operative procedure or providing a specimen of blood to be tested specifically for a named condition.

....

13. The Council believes that the above principles should apply generally, but that it is particularly important in the case of testing for HIV infection, not because the condition is different in kind from other infections, but because of the possible serious social and financial consequences which may ensue for the patient from the mere fact of having been tested for the condition.<sup>38</sup>

**32.43** The BMA publication *Philosophy and Practice of Medical Ethics* (in revised format in 1988) provided BMA guidance of more general application.<sup>39</sup> It discussed for the first time the underlying philosophical basis of medical ethics.<sup>40</sup> Professor Nathanson said that this allowed doctors to make a judgment for themselves when they came across a situation which had not been specifically detailed, based on the general principles underlying specific guidance. Each subsequent edition of this book has also included a section about unresolved dilemmas where the correct approach was still held to be in the balance. The 1st edition already recognised that there were many situations where the nuancing of the particular patient's situation was so important that doctors had to be given information to help them understand how to judge different things, and to recognise that medical ethics was not fundamentally about whether one or another approach or action was correct, but was about balancing different people's rights, responsibilities and duties.

**32.44** In relation to consent, the passage in the 1988 BMA ethics guide equivalent to the brief statement in the 1980 publication quoted in paragraph 32.35 had become more specific, apparently reflecting the thinking in the Declaration of Lisbon. It stated:

The basis of any discussion about consent is that a patient gives consent before any investigation and treatment proposed by the doctor. Doctors offer advice but the patient decides whether to accept it.<sup>41</sup>

**32.45** The 1988 guide did not meet with universal approval. In a review article in the *Journal of Medicine and Philosophy*,<sup>42</sup> written from a US point of view, it was stated:

Handbooks of medical ethics serve to put a little flesh on the bare bones of a professional code that is necessarily brief. Indeed in its previous incarnations (1980 and 1984) this is just what the British Medical Association's *Handbook* sought to do. The latest edition, retitled *Philosophy and Practice of Medical Ethics*, has a more ambitious aim: "...to set out the arguments and counter-arguments which lead either to universally accepted ethical principles or to consensus views" (... emphasis added). ... Unfortunately, the B.M.A's attempt fails. "Unfortunately", because there is a real need in Britain for thoughtful

<sup>38</sup> *HIV Infection and AIDS: the Ethical Considerations*, General Medical Council, May 1988 [PEN.016.1165] at 1168

<sup>39</sup> British Medical Association, *Philosophy and Practice of Medical Ethics*, 1988, London, Chapter 4 : 'Consent to Treatment' [PEN.018.0424]

<sup>40</sup> Professor Nathanson – Day 37, pages 24–25

<sup>41</sup> Quoted in Professor Nathanson's first report to the Inquiry [PEN.012.0330] at 0335

<sup>42</sup> Kessel, 'Book Review: British Medical Association: 1988, *Philosophy & Practice of Medical Ethics*, BMA, London', *Journal of Medicine and Philosophy*, 1989; 14/6:709–710 [LIT.001.5839]

discussion of these issues, and especially for one that can reach Britain's doctors. For despite the work of the London Medical Group, and its progeny around the country, and of the efforts of the Institute of Medical Ethics and its *Journal*, doctors and their patients are very rarely exposed to principled arguments concerning issues such as ... informed consent and treatment decisions ... (all topics mentioned in the B.M.A book).

Viewed from a US perspective, the handbook failed to fill the gap in teaching of ethics already noted at paragraph 32.28 above. Perhaps of greater importance, it failed, in the reviewer's opinion, to meet its own aim of providing material for the debate required for consensus to emerge on ethical principles.

### 1990s

With effective screening of donations for anti-HCV from 1 September 1991, the cohort of patients who were carriers of the virus or its antibody as a result of previous therapy but who remained untested for anti-HCV necessarily grew smaller in a relatively short space of time. Most of them would have had a history of testing with the technology available over previous years and would have known that their medical histories reflected the results of tests for anti-Hepatitis B, other virus infections and liver function and other biometric tests. However, in large part due to the debate on testing for HIV, there was, in Professor Nathanson's words, a sea change in the approach to medical testing, and in relation to consent to treatment.<sup>43</sup>

**32.46** The BMA's *Medical Ethics Today: Its Practice and Philosophy* (1993) was the first relevant publication in the 1990s. It offered a summary of the ethical background to the advice set out, as well as the advice itself. The legal basis of the advice was said to have been set out in *Rights and Responsibilities of Doctors* published by the BMA in 1992. The 1993 text stated that, as a prerequisite to choosing treatment, 'patients have the right to receive information from doctors and to discuss the benefits and risks of appropriate treatment options'.<sup>44</sup> The clinicians assisting the patient in making their decision must offer information in an appropriate manner to ensure the patient understands its relevance and is able to ask questions. In Professor Nathanson's view, an understanding developed from the late 1980s to early 1990s that meaningful consent was important. The patient should have the opportunity to make a free and sufficiently informed decision and a doctor could not do anything to a conscious and competent patient without their agreement.

**32.47** In terms of content, and expression, the 1993 handbook reflected development of the philosophical underpinning of the doctor patient relationship. In relation to consent, now expressly twinned with refusal of consent, it stated:

The relationship between doctor and patient is based on the concept of partnership and collaborative effort. Ideally, decisions are made through frank discussion, in which the doctor's clinical experience and the patient's individual needs and preferences are shared, to select the best treatment option. The patient's consent to be examined and to receive treatment is the trigger which allows the interchange to take place .... [T]he basic premise is that treatment is undertaken as a result of patients being actively involved in deciding what is done to them.<sup>45</sup>

<sup>43</sup> Professor Nathanson's first report to the Inquiry [PEN.012.0330] at 0337

<sup>44</sup> British Medical Association, *Medical Ethics Today: Its Practice and Philosophy*, 1993, BMJ Publishing Group, London, page 3

<sup>45</sup> *Ibid* at page 1

**32.48** Professor Nathanson sought general support for her views on the doctor-patient relationship in relation to therapy from the GMC advice on *Serious Communicable Diseases* published in October 1997.<sup>46</sup> She quoted the second half of paragraph 4 from that document:

Some conditions, such as HIV, have serious social and financial, as well as medical, implications. In such cases you must make sure that the patient is given appropriate information about the implications of the test and appropriate time to consider and discuss them.<sup>47</sup>

**32.49** This paragraph was said by Professor Nathanson to be particularly important. It was the first reference (as late as 1997) by the GMC to the non-medical, as well as the medical, implications of diseases. There are conditions other than HIV with social, financial and other similar implications and, while many practitioners may well have thought that 'best practice' implied these should be discussed, this was the first time the GMC made that obligation explicit. Though the title of the booklet was *Serious Communicable Diseases*, Professor Nathanson thought that the guidance set out in this particular section applied to other conditions where there were equivalent consequences. In those cases also the consequences should be discussed. By way of example, she referred to a diagnosis of epilepsy, which would have immediate serious implications, but is not a 'serious communicable disease'. It would, in her view, nonetheless come within the scope of paragraph 4 of the *Serious Communicable Diseases* advice leaflet. She stressed that the consequences of a diagnosis (of any condition) are not solely medical and that other factors such as family circumstances, a patient's role in the community and the workplace have to be considered. In her view, paragraph 4 reflected good practice generally.<sup>48</sup>

**32.50** In 1998, long after the events that are relevant to the Terms of Reference of the Inquiry, the position on consent became more explicit and clear. The GMC produced *Seeking patients' consent: the ethical considerations*.<sup>49</sup> This highlighted the patient's right to information about their condition and the treatment options available, the complexity of the treatment and the risks associated with the treatment procedure, going into some detail about the information which patients might want to have or ought to know before reaching a decision. It provided:

Successful relationships between doctors and patients depend on trust. To establish trust you must respect patients' autonomy – their right to decide whether or not to undergo any medical intervention even where a refusal may result in harm to themselves or in their own death. Patients must be given sufficient information, in a way that they can understand, to enable them to exercise their right to make informed decisions about their care.<sup>50</sup>

**32.51** In 2001 the Department of Health produced a reference guide to consent. In reviewing some of the existing sources of advice the guide commented that the 1998 GMC publication had gone further than the case law required in stating that doctors should do their best to find out about patients' individual needs and priorities when providing information about treatment options and in emphasising the duty to provide truthful

---

<sup>46</sup> General Medical Council, *Serious Communicable Diseases*, October 1997 [PEN.018.0494]

<sup>47</sup> Ibid at 0495

<sup>48</sup> Professor Nathanson – Day 84, pages 27–28

<sup>49</sup> General Medical Council, *Seeking patients' consent: The ethical considerations*, November 1998 [PEN.019.1523]

<sup>50</sup> Ibid

answers if a patient asks specific questions about procedures and associated risks.<sup>51</sup> The reference guide noted more generally that the standards expected of health professionals by their regulatory bodies may at times be higher than the minimum required by law.

**32.52** The Scotland Act 1998 and the Human Rights Act 1998 gave direct legal effect in the United Kingdom to the rights enshrined in the European Convention on Human Rights. The Department of Health's *Reference Guide to Consent for Examination or Treatment* mentioned above, set out the Department's understanding of the English common law relating to consent and the possible implications of the Human Rights Act 1998 for English medical law.<sup>52</sup> For present purposes differences between Scots and English law are not material. Among the Articles of the Convention that were thought likely to be relevant to the law, existing and developing, were Article 2 (protection of right to life), Article 3 (prohibition of torture, inhuman or degrading treatment), and Article 5 (right to liberty and security).

**32.53** In 2003 the BMA published general ethics advice as the second edition of *Medical Ethics Today*.<sup>53</sup>

**32.54** The published texts on ethics noted thus far reflect increasing sophistication in the analysis of ethical issues and in the presentation of rules and guidance for doctors to follow in ensuring good ethical standards. Each stage in the development provides focus for discussion as to whether the progression was simply expressive of an ethical standpoint that had been reached independently and was recognised in the published text or reflected innovative thought and the introduction of ideas that would not necessarily have been recognised by doctors generally prior to adoption by the BMA or the GMC as formal statements for publication.

### **The development of relationships between doctors and patients from the 1970s**

**32.55** Medical practice up to the 1970s was described as having been 'paternalistic': doctors felt that they had the necessary knowledge to deal with patients' needs and, as Professor Nathanson put it:

[D]octors would tell patients what they thought the patient ought to know and they would tell the patient what they were going to do as doctors to the patient.<sup>54</sup>

**32.56** Many of the medical witnesses who gave evidence to the Inquiry confirmed Professor Nathanson's description of the paternalism that was endemic at the beginning of the reference period. Dr Winter, who was for most of his career a Haemophilia Director, gave as an example the fact that, when he was working as a leukaemia doctor in 1980, it was by no means standard that a patient would be told about the diagnosis of a serious condition. At that time, it would be normal to speak to the patient's family first to find out if the patient would want to know about the diagnosis. Sometimes the next of kin would say that they did not want the patient to be told. He explained that there was no culture of doctors and nurses working with patients. A patient was 'a passive vehicle with an illness'. The patient went into hospital where an 'active vehicle' – the doctor or the nurse – made the patient better. A patient was not expected to have a view about treatment;

---

<sup>51</sup> Department of Health, *Reference Guide to Consent for Examination or Treatment*, 2001 [PEN.019.1487]

<sup>52</sup> Ibid

<sup>53</sup> British Medical Association, *Medical Ethics Today: Its Practice and Philosophy*, 2003, 2nd edition, BMJ Books, London

<sup>54</sup> Professor Nathanson – Day 37, page 11

rather, they would be told their treatment and would not be offered any choices about it. Dr Winter thought that this was particularly the case with haemophilia patients who had usually been seeing the same nurse and same doctor at the same centre for years. This made patients with haemophilia very trusting of their doctors and more passive.<sup>55</sup>

**32.57** Professor Nathanson put the matter bluntly:

In the late 1970s many doctors did not tell patients the whole truth, especially where that truth was of a diagnosis of an incurable illness. This was the well-intentioned legacy of Thomas Percival's influential text on medical ethics.<sup>56</sup> The intent was to shield patients from disturbing information. The duty of beneficence was interpreted as an obligation to be reassuring rather than honest.<sup>57</sup>

**32.58** Professor Forbes acknowledged the existence of paternalism in the early days.<sup>58</sup> This position was also confirmed by the one of the patient witnesses in her written statement. She was a retired nurse who contracted HCV from a blood transfusion in the late 1980s. She captured the atmosphere of the period when she was in employment and provided an illustration of the 'paternalistic' doctor-patient relationship that persisted at the material time:

When I received the blood transfusions, nothing was discussed with me regarding the benefits and risks of a blood transfusion. This was not done in those days. When I worked as a nurse in the 1970s and the early 1980s, I gave blood to patients. You never discussed the risks or benefits of this with patients although you maybe told them to watch for a reaction. I was not informed of a risk of infection from any of the blood transfusions. I was not given an opportunity to refuse the blood transfusions. You just did what you were told.

**32.59** Professor Nathanson noted that there has been a continuing move from this essentially paternalistic, 'doctor-knows-best' culture to a working relationship where the patient is fully involved in decision-making, or 'patient-centred medicine'. The emergence of AIDS appears to have accelerated this move. Changes occurred, according to her evidence, due to improvements in doctors' education and training, including improved teaching of medical ethics and training in communication skills so that doctors could speak with patients and relatives in a sensitive manner.<sup>59</sup> Although, in general, '[t]he earlier the time frame under consideration the commoner an essentially paternalistic approach would have been'<sup>60</sup> progress has not been uniform: the attitudes and practices of individual doctors changed at different rates within a broad pattern of historical change.

**32.60** Professor Nathanson commented that many doctors had begun to depart from the historic, paternalistic, approach early in the reference period and began instead to develop a more equal relationship with patients.<sup>61</sup> From the whole evidence on this topic, it appears that the culture of paternalism subsisted beyond the end of the 1970s and characterised practice widely, if not universally, in the early 1980s when formal ethical statements began to appear. The timing of these changes, and the timing of general acceptance that ethical principles had changed, are issues in this chapter.

<sup>55</sup> Dr Winter – Day 16, pages 147–149; Dr Winter's Submission to the Archer Inquiry [PEN.015.0283] at 0291

<sup>56</sup> Leake CD ed, *Percival's Medical Ethics*, 1927, Williams and Wilkins, Baltimore

<sup>57</sup> Professor Nathanson's first report to the Inquiry [PEN.012.0330] at 0339

<sup>58</sup> Professor Forbes – Day 33, page 123

<sup>59</sup> Professor Nathanson's supplementary statement [PEN.018.0419] at 0419

<sup>60</sup> Ibid

<sup>61</sup> Professor Nathanson's first report to the Inquiry [PEN.012.0330] at 0339

**32.61** It was not suggested that the BMA handbooks published in 1980, 1981 and 1984 pointed to a significant change in or development of general principles. The advice given in these handbooks was situation-specific until 1988.

**32.62** In the period between 1980 and 1988 the AIDS epidemic struck and the advent of that disease brought about a major change in perception of the relationship between doctor and patient and in clinical practice. It is probably fair to say that the emergence of AIDS and the public and medical responses to it have had a more profound effect on relationships between doctors and patients than any other single event. Not only did it affect attitudes generally, it also impacted on a wide range of specific ethical issues, such as the need for informed consent to testing and treatment. Statements on medical ethics, published in and after 1988 after AIDS became a reality for coagulation disorder patients in the UK, reflected those changing attitudes.

**32.63** As noted above (paragraph 32.42) the statements in the GMC and the BMA 1988 publications were introduced as reflecting long accepted practice. In formulating new rules, as in 1988, it is understandable that bodies such as the BMA and the GMC should seek support in principles thought to be implicit in earlier practice. It is an important stage in the development of any system of regulation of professional behaviour when one can distil from accumulating evidence of particular instances of conduct, on one side of acceptability or the other, a principle or rule of general application. However, the formulation adopted may nevertheless understate what may be a considerable degree of innovation, especially where a regulatory or representative body is seeking clearly to express current expectations of practitioners' approaches to practice.

**32.64** When the stage is reached at which formal expression of principles and rules is appropriate, it is not unusual to find precedents cited.

**32.65** It would not, however, be appropriate to infer from the juxtaposition of the references in Professor Nathanson's evidence that there was a common basis for advice spanning two centuries. The context of the Slater case (see paragraph 32.21) conjures up an image of procedures, life-threatening in themselves, requiring the patient to prepare for all eventualities rather than a rational discussion of options: the doctor had to tell the patient what he was about to do and warn of possible outcomes. The modern approach to providing information and supporting patient choice has much more recent origins.

**32.66** Professor Nathanson's observation, that Rule 1 of the Nuremberg Code (see paragraph 32.22) was the 'first explicit modern statement' of the right of every patient to consent to and hence to refuse any medical treatment, points to a problem inherent in her approach to describing generally accepted standards of ethical conduct. She construed Rule 1 of the Nuremberg Code as expressing the right of every patient to accept or refuse medical treatment. She accepted, however, that the rules would not have been well known to doctors, not just in the United Kingdom but throughout the world. Since this was, on her approach, the first explicit modern statement of the rules, it became necessary to consider the evidence which had a bearing on a broadly based ethical obligation to recognise the patient's rights, apart from their formulation in formal statements in the 1980s.

**32.67** Given the clear evidence noted above of the 'paternalistic' attitude of doctors to patients, it is not possible, on the evidence before the Inquiry, to form a view that in the 1970s proper ethical practice depended on, or drew heavily on, the Nuremberg Rules, or historical judicial observations adapted to particular situations.

**32.68** It is perhaps not surprising that the Nuremberg Rules were not well known to doctors. It would be difficult to read them as a code intended to regulate general clinical practice, rather than specifically concerning experimentation on human subjects, the specific context for which they were drawn up. While one can see reflections of part of the language of Rule 1 in later statements of practice and while it can be accepted that those who drafted later the BMA and the GMC guidance may well have drawn on the language of the Code, it cannot be maintained as a matter of language or substance that Rule 1 was an explicit statement of the right of every patient to consent to and hence to refuse any form of medical treatment. As Professor Nathanson recognised, the modern rule on consent is not unqualified: public health requirements may over-ride individual patient interests, for example.<sup>62</sup> The Nuremberg Code was unqualified because it dealt with a particular and limited context in which more or less absolute rules were appropriate.

**32.69** In contrast to these sources, ethical principles and rules may often be influenced by judicial decisions. Decisions declaratory of the common law are, in principle, not innovative, and may support the view that a professional response, in stating or re-stating current ethical requirements, is an expression of the pre-existing position. *Medical Ethics Today: Its Practice and Philosophy* (1993) stated (in the language of English law):

In many aspects of medicine, the legal and ethical requirements are separate and ethical guidance need make no reference to law. Consent, however, is an issue which binds the two since failure to seek patient consent is not only a moral failing but leaves the doctor liable in the crime or tort of battery or in the tort of negligence.<sup>63</sup>

In Scots law, the doctor might be liable to criminal proceedings for assault or open to a claim for damages for negligence.

**32.70** Some landmark decisions were relevant to the consideration of generally accepted standards of ethical conduct:

- In *Bolam v Friern Hospital Management Group* (1957) it was noted that the test of negligence in treatment of a patient had long been whether the doctor's practice conformed to that of a responsible body of opinion among practitioners skilled in the relevant field.<sup>64</sup>
- In Scotland, similar principles had been expressed in 1955 by Lord President Clyde in *Hunter v Hanley*. The test was said to be whether the doctor has been guilty of such failure as no doctor of ordinary skill would be guilty of if acting with ordinary care.<sup>65</sup>
- The legal standard for deciding whether adequate information had been given to the patient was held in *Sidaway v Board of Governors of the Bethlehem Royal Hospital* (1985) to be the same as in negligence.<sup>66</sup>

**32.71** It is possible that there had been a professional standard relating to explicit and informed consent prior to 1988 that was higher than the standard in negligence. However, Lord Scarman's comments in the *Sidaway* case, quoted in *Medical Ethics Today* (1993), suggest that that would have been difficult. Of the test in negligence, he said:

<sup>62</sup> Professor Nathanson's first report to the Inquiry [PEN.012.0330] at 0332

<sup>63</sup> British Medical Association, *Medical Ethics Today: Its Practice and Philosophy*, 1993, BMJ Publishing Group, London, page 3.

<sup>64</sup> *Bolam v Friern Hospital Management Committee* [1957] 2 All ER 118

<sup>65</sup> *Hunter v Hanley* 1955 SC 200

<sup>66</sup> *Sidaway v Board of Governors of the Bethlehem Royal Hospital* [1985] AC 871

Ideally, the court should ask itself whether in the particular circumstances the risk was such that this particular patient would think it significant if he was told it existed. I would think that, as a matter of ethics, this is the test of the doctor's duty. The law, however, operates not in Utopia but in the world as it is: and such an inquiry would prove in practice to be frustrated by the subjectivity of its aim and purpose.<sup>67</sup>

**32.72** In *Medical Ethics Today: Its Practice and Philosophy* (1993), at page 11, it was commented:

Thus ideally, the doctor should inform the patient about any risks inherent in the treatment which might be particularly important to that patient as well as explaining the risks and benefits of alternatives and of non-treatment.<sup>68</sup>

**32.73** It is not unlikely that a doctor, also operating in the world as it is in treating a patient, might be as frustrated by the ideal question as is the law. One might think it necessary that a regulatory or advisory body stipulating that the clinician should ask 'whether in the particular circumstances the risk was such that this particular patient would think it significant if he was told it existed' should also provide guidance on how to approach the question and gather the information required for a rational analysis. The 1993 guidance attempted to do that, but that was after the material period for this Inquiry.

**32.74** The Inquiry was not provided with published evidence that there was a generally accepted rule of practice up to 1988, of sufficient specificity, that was more demanding than the test of negligence (namely, did the doctor's practice conform to that of a responsible body of opinion among UK practitioners skilled in the relevant field) and specifically a test requiring a doctor to treat a patient only on the basis of the patient's explicit and informed consent. On the best view of the publications and Professor Nathanson's evidence, the 1988, and then the 1993, publications were the first specifically to adopt that formulation.

**32.75** Professor Nathanson adopted the position that each of the BMA and the GMC 1988 publications represented the general comments on consent as reflecting long accepted practice, well understood within the profession. Though focussed on HIV infection, she considered it clear that paragraph 12 of *HIV Infection and Aids: the Ethical Considerations*, quoted above at paragraph 32.42, described the basis of treatment for all illnesses and not just HIV.<sup>69</sup>

**32.76** Professor Nathanson commented that the best practice standard in 1988 was that doctors only treated patients with their consent. Patients made the decisions and the doctor offered advice and guidance and might assist an individual in deciding between treatments but ultimately it was the patient who made the decision:

[I]t was quite clear to me from published information that we would expect that patients would be given information to make decisions for themselves, certainly about treatment.<sup>70</sup>

**32.77** In presenting her evidence, Professor Nathanson did not distinguish testing from treatment. The 1988 statement in the GMC publication *HIV Infection and Aids: the Ethical Considerations* reflected the Council's view that consent was required for treatment,

---

<sup>67</sup> British Medical Association, *Medical Ethics Today: Its Practice and Philosophy*, 1993, BMJ Publishing Group, London, pages 10–11

<sup>68</sup> Ibid page 11

<sup>69</sup> Professor Nathanson – Day 84, pages 25–26

<sup>70</sup> Ibid page 25



but spelled out specifically its view of the need for consent to investigative procedures. Professor Nathanson thought that the approach of the publication reflected more general changes in attitude among doctors during the 1980s. This led to discussion. Professor Nathanson said that it was a highly complicated issue. In the mid 1980s the BMA sought legal advice from counsel whether consent to treatment included consent for testing (specifically with regard to HIV testing). Counsel's opinion was explicit that treatment included testing, in that it was a necessary implied part of treatment.<sup>71</sup>

**32.78** Professor Nathanson commented in oral testimony:

We had expected that to be the case because you don't do testing if you are not thinking of doing something with that test result and you can't carry out treatment without having done testing, and they are so integrated that treatment is held, and I think in most of medical practice would be held, to include that process of seeing the patient, examining them, taking a history and so on, doing various tests and carrying out treatment and monitoring that treatment and modifying it, and that that is all-encompassed under that word "treatment".<sup>72</sup>

**32.79** So far as related to periods before 1988, the representation that the statements concerning consent published in 1988 were long-accepted practice became a focus for disagreement between Professor Nathanson and other experts. Having regard only to Professor Nathanson's evidence of the background circumstances in which the GMC came to adopt the guidance of 1988 relating to HIV testing, it would be difficult to accept the statements in the 1988 publications as an indication of a generally accepted standard of ethical conduct in, say, 1984, a significant year in the investigation of the prevalence of HTLV-III/HIV infection in the haemophilia population. Professor Nathanson considered that later publications such as *Medical Ethics Today: Its Practice and Philosophy* (1993) also expressed what was already accepted or established as proper ethical conduct by the time of publication.

**32.80** On the evidence available to the Inquiry, the formal documents published by the BMA and the GMC remain the best sources of evidence of when the process of development of thought crystallised into rules of general ethical practice, what those rules were, and how they were regarded by the medical profession, in the material period.

### **Testing for HIV and the communication of test results**

**32.81** As events were to prove, the risk of transmission of NANB Hepatitis/HCV was present before and continued after the AIDS period (broadly 1981 to 1985 in the case of coagulation disorder patients). However, there are questions as to whether AIDS was so significantly different from other viral diseases that the scientific and clinical response to it marked a step change in ethical practice that not only affected later ethical standards relating to hepatitis, but also innovated on previous accepted standards. If the answer to these questions is in the affirmative there is a further question as to whether one can infer from views expressed during and after the AIDS period what the direction of change in standards had been or was likely to have been in relation to NANB Hepatitis/HCV.

---

<sup>71</sup> While Professor Nathanson did not say so explicitly, it appears that this advice was sought separately from the advice referred to in paragraph 32.40.

<sup>72</sup> Professor Nathanson – Day 84, page 31

**32.82** As already noted, the statements of 1988 narrated that the guidance then set out reflected 'long accepted practice'. There is a temptation, to which those seeking to drive forward professional standards are perhaps irresistibly exposed, to make assertions to that effect. The response to an emerging problem such as AIDS may provide an opportunity for a wider and more general re-assessment of standards: anything that disturbs the equilibrium of a more or less static social group can open the way to radical change. Both factors are apparent in the 1988 documents.

**32.83** The impact of AIDS was swift and significant following the first reports in 1981. Dr Hay said 'the presentation itself was fairly dramatic and ... it was associated with death from the very beginning'.<sup>73</sup> Some patients with haemophilia died early in this period. In the mid-1980s an HIV test became available for use and it became apparent that 50% of UK patients with severe haemophilia were infected. There were patches of the UK (and in Scotland in particular) where the concentration of infection was lower.<sup>74</sup> However, under these circumstances, HIV/AIDS became the principal concern of both haemophilia clinicians and their patients. Dr Hay said:

This overshadowed hepatitis, which was considered benign and of little concern at the time to the extent that patients were not counselled to the same degree about non-A, non-B hepatitis as they had been in the immediately preceding period.<sup>75</sup>

**32.84** He also commented that:

The implications of a +ve HIV test could be perceived as a death sentence, led to loss of insurance, marriage breakdown, and even in some cases suicide.<sup>76</sup>

**32.85** Speaking about communication with patients, Dr Mark Winter stated that the culture of medicine 'was completely changed by AIDS'.<sup>77</sup> Many of the clinicians who lived through the period have also stressed that the arrival of HIV and AIDS was responsible for changing medical practice irrevocably. It is important to remember the effect of AIDS when examining the practices and decisions taken by clinicians during the reference period, and the suddenness with which they were confronted by this new disease. Even so, it was 1988 before the GMC responded with the publication of *HIV Infection and Aids: the Ethical Considerations*.

**32.86** The circumstances leading up to the publication of *HIV Infection and Aids: the Ethical Considerations* have been described in paragraph 32.40 above. HIV testing was distinguished from other conditions for which patients were tested. The question of consent to investigation first became prominent in the second half of 1984 when research assays were used to investigate the prevalence of HTLV-III/HIV in a broad range of cohorts including haemophilia patients, and then more generally in early to mid-1985 when the first diagnostic test for antibodies to the virus became available and the significance of the results began to be appreciated. It is not necessarily the case, however, that there would have been widespread appreciation of the issue throughout the medical profession.

---

<sup>73</sup> Dr Hay – Day 83, page 111

<sup>74</sup> Ibid page 112

<sup>75</sup> Dr Hay's statement on communication to patients [PEN.018.1186] at 1209

<sup>76</sup> Ibid [PEN.018.1186] at 1212

<sup>77</sup> Dr Winter – Day 16, page 148

**32.87** Professor Nathanson emphasised the small number of AIDS cases that would have been seen by non-specialist medical professionals, even by 1986 and 1987 when the BMA committee on standards and ethics was considering the topic that resulted in the guidance of 1988.<sup>78</sup> The science on AIDS was at an early stage and still evolving. The majority of doctors in the UK had never seen a patient who was HIV-positive or who had AIDS. Many doctors might have known the symptoms: they would have known the theory but they may not have been completely up to date.

**32.88** There were specialists with intimate practical experience and knowledge of HIV. Infectious diseases doctors and haemophilia clinicians were among those who did see a disproportionate number of patients with HIV and Professor Nathanson's views on the ethical requirements for testing have particular relevance in the context of the management of their patients.

**32.89** Considerable debate developed over whether those for whom a test for HIV might be considered clinically relevant needed to be asked for consent to the test. In the early days of testing many doctors believed that HTLV-III antibody tests could and should be carried out without consent and that taking blood for the test at the same time as other routine medical tests would mean that 'necessarily implied consent' had been given. In her report Professor Nathanson commented:

If patients are aware that they are routinely and regularly being tested for a panel of infections, for example blood borne viruses, it was certainly arguable that testing for hepatitis C was no different from other such routine tests. Many would then have considered testing for HIV in the same way, given that there was at the beginning of the period considerable doubt as to its nature, transmissibility and relevance to the newly emerging medical condition of acquired immune deficiency.<sup>79</sup>

**32.90** Professor Nathanson commented on what specific consent requires:

The General Medical Council's advice is that consent requires that the patient understands what you are doing, why you are doing it, what the consequences are and what you will do about it. It's a counsel of perfection. How much we all, as individual patients, remember about what we are told is always variable and arguable, but certainly all that information should be made available and should be offered to the patient and there should be no limit .... You should be prepared to tell the patient everything.<sup>80</sup>

**32.91** She also described what was meant by 'necessarily implied consent':

Necessarily implied consent really means that the patient is doing something which makes it clear that nobody would argue that they are doing anything other than consenting to that test. The interesting issue around this was, for example, if you go in to see a doctor and the doctor says, "I want to take some blood tests" and you roll up your sleeve and hold your arm out to have the blood taken, then you are clearly necessarily implying [consent] to having a needle stuck in your arm and some blood taken.<sup>81</sup>

---

<sup>78</sup> Professor Nathanson – Day 37, pages 33–35

<sup>79</sup> Professor Nathanson's first report to the Inquiry [PEN.012.0330] at 0336

<sup>80</sup> Professor Nathanson – Day 37, pages 86–87

<sup>81</sup> Ibid page 90

**32.92** In relation to HTLV-III/HIV testing, Professor Nathanson's own view was unequivocal. Put simply, testing required specific consent. The concept of necessarily implied consent could not be held to apply to testing for this virus. In principle, implied consent could only be held to apply to procedures in hand and not to new procedures.

**32.93** How that related to the general clinical environment can perhaps best be understood in the light of Professor Nathanson's observations on the steps she considered it was necessary for her to take as head of ethics at the BMA:

[O]ne of the first things I did in April 1987 – when I took over as head of ethics, I was involved ... in developing a series of videos for doctors, which Wellcome actually sponsored, and we got pharmaceutical reps to take it around the country into every GPs surgery: three films on testing for HIV, including getting consent, upon all the issues around control of blood-borne infections and particularly the kind of advice that they could give to families. We were developing a lot of advice to individuals, but also schools and churches were contacting the BMA for advice on the risks of cross-infection and there was just a lack of good solid, simple consolidated information on the science for the non-experts and the people who might be seeing a case for the first time.<sup>82</sup>

**32.94** The observations are significant. They reflect the lack of previous advice from regulatory, advisory and other official sources; they underline Professor Nathanson's own role among those driving developments in ethical practice; they provide a reference date for the provision of effective advice about HIV to the wider profession; they define the background to the publication of the BMA's advice in 1988; and they express the lack of relevant knowledge of the disease among the medical profession generally. Finally, they reflect the contemporaneous understanding among those leading the development of professional thought, that guidance on questions such as consent was required.

**32.95** At this time, the BMA was moving towards the provision of explicit advice generally. Professor Nathanson commented, specifically in relation to testing, but with wider relevance:

Throughout medicine, consent was obtained for most things that are done. The question was always about whether a test was something that was so much inherently part of the treatment, including the diagnosis, of that patient that it was covered by necessarily implied consent or whether it was something that was less common, less usual, less standard and therefore needed to be explicitly taken out of that and to be absolutely explicitly the subject of consent. We were in the process of moving towards being as explicit as possible about everything that is done and that included the HIV test, and many people who were content with the concept of necessarily implied consent for many other tests were not content for it on HIV, for example, because of other reasons, not necessarily purely medical ones but because of the consequences of the test result.<sup>83</sup>

---

<sup>82</sup> Professor Nathanson – Day 37, pages 34–35

<sup>83</sup> Professor Nathanson – Day 37, pages 154–55. The observation was made in the context of questions related to testing stored samples, but had general significance.

**32.96** Pre-test counselling for HIV raised specific issues. Professor Nathanson explained:

Pre-test counselling is a little different. When you are testing for some conditions, what you would then do is say, “In this one area of testing there are some very specific things which you need to understand about the limits of the test or the implications of the test”. With HIV we really started to discuss pre-test counselling in a very formal basis, not necessarily because of the diagnosis clinically but predominantly because of the social and economic consequences. So the inability, for example, to get life insurance, mortgages, those sorts of things, for patients. And particularly early on, when we didn’t know whether people would survive or not ....<sup>84</sup>

**32.97** The 1988 guidance highlighted the specific non-medical consequences of a positive result, such as social stigma or employment and financial consequences. Professor Nathanson noted that such consequences may emerge and develop over time; they may not be recognised when a procedure is first introduced, although HIV did quickly come to have obvious and serious non-medical consequences, essentially financial and social.

**32.98** By 1988 it was also recognised that consent was particularly important in the case of testing for HIV infection because of the possible serious social and financial consequences which might ensue for the patient from the mere fact of having been tested for the condition, irrespective of the result of that test.

**32.99** Professor Nathanson explained that the modern approach is to offer full information to a patient about the results of a test but not to oblige them to receive that information if they indicate that they do not want to know.<sup>85</sup> Where there are health benefits to a patient from knowing their diagnosis or where a third party (such as a sexual partner) could benefit from knowing about the diagnosis, a clinician can and should press harder to encourage a patient to agree to be told of their results. However, she said that she would be reluctant to ‘force’ a patient to know the results of any given test, but that a medical practitioner should use appropriate communication skills to assist the patient in understanding the implications and to agree a plan of action. She explained that in some circumstances a clinician might increase the ‘amount of weight’ that they put in to persuading a patient about the benefits to them of receiving results.<sup>86</sup> She said that most clinicians in these circumstances found that patients: ‘don’t ever say they don’t want to know something when you are telling them that there is a benefit to them in knowing’.<sup>87</sup> She acknowledged that it is ‘extraordinarily difficult’ for a doctor to approach the question of positive test results without signalling to the patient that they have bad news to impart.

**32.100** Professor Nathanson explained that it was essential for the doctor to let the patient know that s/he has information about him, that tests had been done, and that results were available, and to ask whether the patient wanted the results. She said that it became easier to communicate results as time went on because coagulation disorder patients, who had access to the literature, and were a well-informed group, knew what was happening and realised that ‘more and more of their number were being found to be positive’.<sup>88</sup>

---

<sup>84</sup> Professor Nathanson – Day 37, pages 87–88

<sup>85</sup> Ibid pages 121–127 and 155

<sup>86</sup> Ibid page 124

<sup>87</sup> Professor Nathanson – Day 37, page 125

<sup>88</sup> Ibid pages 126–127

**32.101** The GMC guidance in 1988 stated that:

The Council takes the view that any doctor who discovers that a patient is HIV positive or suffering from AIDS has a duty to discuss these matters fully with the patient.<sup>89</sup>

**32.102** In relation to the Council's view, Professor Nathanson said:

I think that that's the first time that the GMC was as explicit as this and I'm not aware in any of their earlier publications that they had been as explicit, in any condition, about informing the patient. It had been implicit in a great deal of what they have said but not explicit. So certainly at that time, in 1988, it would have been clear to all doctors on the basis that the GMC advice goes literally to all doctors on the register.

It didn't go into any more detail about it but I think that the duty to discuss these matters fully is pretty explicit and would make it clear that you had to discuss all the relevant matters.<sup>90</sup>

**32.103** She contrasted the position adopted with what had generally been the situation previously. The Council's published view of the doctor's duty to discuss with the patient, in her view:

[R]ecognised, of course, that that hadn't been the case in the past. If all doctors had always told all patients the full details, fully informed, fully discussed, then they wouldn't have needed to make the statement or the statement would have been made something like, "As with all other conditions," or something of this form.

The fact that they felt it necessary showed that they recognised that doctors didn't always tell patients everything or fully discuss and that this was essential. And certainly in the late 1970s, it would have been extremely rare to tell patients everything but this was part of this evolution towards patient-centred care that I described earlier, that this was becoming a commoner practice anyway.<sup>91</sup>

**32.104** That period, in Scotland and indeed generally, was a time of great change in coagulation disorder therapy. HTLV-III/HIV infection had been identified in haemophilia patients and widely publicised, causing great disturbance. The majority, if not all, of haemophilia patients in Scotland (at least in the two major regions with centres in Glasgow and Edinburgh) had been tested using stored samples from routine management of their primary condition. Virus inactivation processes in the manufacture of Factor VIII concentrates were quickly devised at the end of 1984 and implemented from January 1985, changing the context in which risks associated with continuing therapy might be discussed: patients newly diagnosed with Haemophilia A after January 1985 were not exposed to risk of transmission of HIV by SNBTS concentrates. The emphasis was changing from testing (in many cases a past event) to repeat testing of established patients and the communication to them of test results. While Professor Nathanson's evidence was uncompromising that patient consent to testing was necessary, in the short period when risk was at its highest (roughly from 1982 to the end of 1984) the context for providing information and advice and seeking consent to investigation was changing rapidly. Her own actions on appointment as Head of Ethics in April 1987 were clearly innovative.

---

<sup>89</sup> *HIV Infection and AIDS: the Ethical Considerations*, General Medical Council, May 1988 [PEN.016.1165] at 1169

<sup>90</sup> Professor Nathanson – Day 37, page 113

<sup>91</sup> Professor Nathanson – Day 37, page 114

**32.105** In the circumstances, it is difficult to infer from Professor Nathanson's evidence alone that there were generally accepted ethical standards relating to the management of patients actually or potentially exposed to risk of HIV infection in the critical, short, period between 1982 and the publication of the 1988 guidance.

**32.106** Other evidence on this topic indicated that there were variations in approach. Dr Winter said that in 1984 and 1985 the way that results of HIV tests were communicated to patients varied very widely. At his Centre he personally met with each of his patients to give them news of the outcome of tests.

**32.107** In a paper produced in response to Professor Nathanson's first report, Dr Hay commented on consent to testing and the communication of test results.<sup>92</sup> He said that paragraph 4 of the 1988 GMC Guidance *HIV Infection and Aids: the Ethical Considerations*, which dealt with obtaining consent to testing, reflected normal practice for HIV infection only from the late 1980s onwards. He explained that most haemophilia centres counselled patients at the time of HIV testing, from 1985, and then communicated the results in face-to-face interviews. Much of what the patients were told in those interviews turned out to be incorrect but it was the best information or opinion available at the time. Some centres took a different approach. He said that in Liverpool and Manchester HIV results were communicated to the patient by letter. He commented:

This practice was widely considered reprehensible, even at the time, and left an understandable and enduring legacy of anger and bitterness in the affected families. There was no agreed policy about this at the time, however. Counselling for HIV testing became more formalised and universal in the later eighties.<sup>93</sup>

**32.108** In that respect, the management of patients exposed or potentially exposed to risk of HIV infection was not distinguished from practice in relation to viral infection generally. It appears to be clear that Professor Nathanson's observations relating to the doctor's duty to discuss HIV with patients were equally applicable to the wider context. There was no settled ethical standard relating to NANB Hepatitis, for example, available to the BMA or the GMC as a model or point of reference for the development of standards specific to HIV.

### **Testing for NANB Hepatitis/HCV and the communication of test results**

**32.109** The evidence of Dr Hay and Professor Nathanson in respect of testing for NANB Hepatitis/HCV and the provision of information to patients is recounted below. It will become apparent that there were some differences between them.

#### *Testing for NANB Hepatitis/Hepatitis C*

##### **Dr Hay**

**32.110** So far as haemophilia and other coagulation disorder patients are concerned, Dr Hay's approach to HCV testing and the provision of information did not vary according to the therapeutic products that had been administered, though he commented on the different levels of risk to which those receiving large-pool products were exposed in comparison with those who had received single donor products, and transfusion patients.

---

<sup>92</sup> Dr Hay's commentary on Professor Nathanson's first report to the Inquiry [PEN.018.1349]

<sup>93</sup> Ibid [PEN.018.1349] at 1353

**32.111** Dr Hay's assessment of the risk of HCV transmission by way of large-pool blood products was clear: 'Patients treated with pooled blood products prior to the introduction of viral attenuation in 1985–87, will have been infected with hepatitis C'.<sup>94</sup> With donor pools for manufacturing concentrates containing 20,000–50,000 donations in the commercial sector, even with a low prevalence of infection in the donor population,<sup>95</sup> inevitably there would be a number of infected donations in each plasma pool. He reiterated the point in oral testimony: 'all the concentrates prior to viral attenuation would transmit Hepatitis C'.<sup>96</sup> Given the large number of donor units in each pool,<sup>97</sup> there was realistically no difference, in terms of HCV-infectivity, between different product brands sourced from the UK, mainland Europe or the USA or between large-pool products based on paid or voluntary donations.<sup>98</sup>

**32.112** By contrast, the risk of HCV transmission for transfusion patients (or haemophilia patients using cryoprecipitate) was considerably lower. Dr Hay described a methodology for estimating the risk of transmission of HCV from single-donor blood products:

The risk of transmission of hepatitis C from ... single-donor blood products depends on the number of units transfused, the year in which the donations were collected and the prevalence of hepatitis C in the relevant donor population at that time .... The prevalence was considered relatively high in the USA and in Southern Europe but relatively low in Northern Europe: the UK, France and Holland.<sup>99</sup>

**32.113** As applied to the UK around 1982–84, Dr Hay estimated the risk as 'probably significantly in excess of 0.4% .... This would place the risk during 1983-4 at between 0.6% and 1% per unit of single-donor blood product transfused, say 0.75%'.<sup>100</sup> On this assessment of risk, many coagulation disorder patients would have been infected with HCV before they were given concentrate, especially those with severe haemophilia who were regularly treated with cryoprecipitate.<sup>101</sup>

**32.114** The situation changed from around the mid-1980s with the introduction of donor self-exclusion for at-risk groups and HIV testing of blood donated for clinical use.<sup>102</sup> Some evidence suggested an approximately tenfold reduction in the risk of post-transfusion HCV transmission as a result. Although Dr Hay observed that this would not make much difference to the risk from concentrates derived from large donor pool plasma, for the reasons already given, the risk of transmission from single donor units such as cryoprecipitate or red cells was considerably reduced.<sup>103</sup>

<sup>94</sup> Dr Hay's statement on communication to patients [PEN.018.1186] at 1199. See Chapter 15, *Knowledge of Viral Hepatitis 2 – 1975–1985*, paragraph 15.122. Dr Craske reported in September 1983 that the risk of contacting NANBH following first exposure to large pool concentrates was 100%.

<sup>95</sup> The prevalence of Hepatitis C in the donor population during the 1970s and early 1980s was not known with certainty but was subsequently estimated to have been approximately 0.4–1.0%. Pool volumes of the order mentioned were typical of commercial production. NHS pool volumes were considerably lower but still large enough for the same general conclusion to apply.

<sup>96</sup> Dr Hay – Day 83, page 85. Whilst effective in eliminating HIV, early attempts at viral inactivation were not completely effective in eliminating the risk of Hepatitis C transmission.

<sup>97</sup> Dr Hay – Day 83, page 86

<sup>98</sup> Dr Hay's statement on communication to patients [PEN.018.1186] at 1200; Fletcher ML et al, 'Non-A non-B Hepatitis after transfusion of factor VIII in infrequently treated patients', *British Medical Journal*, 1983; 287:1754–57 [LIT.001.0239]

<sup>99</sup> Dr Hay's statement on communication to patients [PEN.018.1186] at 1200

<sup>100</sup> *Ibid* at 1204

<sup>101</sup> Dr Hay – Day 83, pages 88–89

<sup>102</sup> Dr Hay's statement on communication to patients [PEN.018.1186] at 1192

<sup>103</sup> Dr Hay – Day 83, page 82



**32.115** The mid-1980s marked the point at which there was growing appreciation of the severity of the risks associated with NANB Hepatitis. For transfusion patients that was offset to some extent by the reduced risk of transmission but the risk of transmission was not materially reduced for those receiving large-pool concentrates. For all patients, the risks of progressive liver disease became more fully understood in about 1991, when anti-HCV testing was introduced, and there was a further step change in understanding in 1995 when the link between HCV and hepatocellular carcinoma was established.

**32.116** Dr Hay said that from the mid-1970s to the early 1980s very little would have been said to patients about NANB Hepatitis because little was known about the condition and because, insofar as it was understood, it was not thought to be a serious clinical concern.<sup>104</sup>

**32.117** Although local practices varied, in Dr Hay's experience haemophilia centres had started to check liver function tests regularly in about 1980.<sup>105</sup> Patients may have had 'persistently' or 'intermittently' abnormal liver function test results. At this time, if a patient had at least two abnormal liver function tests over at least six months, the condition was described as 'chronic'. Dr Hay said:

From the late 1970s onwards, most regularly reviewed patients would have had liver function tests conducted and I would expect most of those affected to have been told that they had non-A, non-B hepatitis but that it was probably nothing to worry about.<sup>106</sup>

**32.118** Advice on NANB Hepatitis in the mid-1980s was similar to the advice given in the previous period. Dr Hay commented that in the mid-1980s patients would have been told that NANB Hepatitis was, comparatively at least, nothing much to worry about at around the same time as they were being informed of life-threatening HIV in the blood supply. The risk of HIV/AIDS had come to dominate thinking.

**32.119** Dr Hay said in oral evidence that he provided counselling for patients prior to testing for HCV. In his haemophilia centre, the staff informed patients they were testing them for Hepatitis C, discussed the result face-to-face with them when available and wrote to their GP and documented the discussion.<sup>107</sup>

**32.120** The patient would have the opportunity to refuse the test. Although some patients did not want to be tested for HIV, Dr Hay could not recall anyone refusing an HCV test. Clinicians would have had an idea of the likely results when patients were tested for HCV for the first time on the basis of a history of abnormal liver function tests. Dr Hay said that he would discuss the implications of a positive HCV test result and, if the patient had a history of abnormal liver function tests, he would have prepared them to expect a positive result.<sup>108</sup> He explained:

[I]f I was testing for hepatitis C, I would tell the patient that I was going to conduct the test. I would take the opportunity to talk to them again about

---

<sup>104</sup> Dr Hay's evidence reflects his experience, and in particular the Sheffield studies of NANBH. In other areas, such as south east Scotland, until a test for HCV was available, people found to have abnormal liver function test results would not often have a diagnosis of NANBH on that basis alone: see Chapter 16, *Knowledge of Viral Hepatitis 3 – 1986 Onwards*, paragraph 16.32. Clinical jaundice was a required diagnostic feature.

<sup>105</sup> Dr Hay – Day 83, page 104

<sup>106</sup> Dr Hay's statement on communication to patients [PEN.018.1186] at 1208

<sup>107</sup> Dr Hay went on to comment (Day 83, page 123) that what he did went beyond what a Hepatologist would have done for a patient, then and now.

<sup>108</sup> Dr Hay – Day 83, page 121

hepatitis C. I would have expected that conversation would already have taken place about liver disease. I would not take written consent for the test.<sup>109</sup>

**32.121** Dr Hay compared the national guidelines for testing patients for HIV.<sup>110</sup> The circumstances surrounding HIV testing required a much longer and more involved conversation, having regard to the wider consequences for the patient, and patients should have been given the opportunity to go away and think about it before providing a blood sample for a test.<sup>111</sup>

**32.122** The implications of a positive HCV test result were, and are, quite different from those associated with a positive test for HIV and the pre-test conversation would be different in each case. Dr Hay considered that pre-test counselling for HIV was not an appropriate model or point of useful comparison for HCV testing. The discussion with a patient prior to an HCV test would typically take five minutes, unless the patient had a great many questions.<sup>112</sup> Now, the discussion tends to be about the side-effects and relative merits of treatment. That would not have been part of the subject matter prior to the introduction of Interferon in the mid 1990s. Dr Hay was of the view that haemophilia clinicians talked more about HCV tests with their patients than hepatologists would, in part because of their experience with HIV testing. He thought this may have created an expectation of what ‘counselling’ entails in that patient group different to that in the general population. He thought that, when thinking of the HCV test, haemophilia patients tended to draw a parallel with their experience of counselling related to HIV and respond critically, in comparison, to the discussion that took place prior to HCV testing. In reality, according to Dr Hay, there were probably never any guidelines on taking consent for Hepatitis C testing.<sup>113</sup>

**32.123** Dr Hay commented on the differences in approach adopted by hepatologists and haemophilia practitioners respectively.<sup>114</sup> In his view, a hepatologist was likely to tell a patient more assertively that they intended to test for hepatitis viruses because the patient’s liver function was abnormal. A haemophilia clinician was more likely to tell a patient they thought a test for HCV was appropriate since it was a probable cause of their signs of liver disease. He acknowledged that there was a distinction between the approaches, but he did not agree that the approach of haemophilia practitioners involved asking for the patient’s consent to test. He thought it was more likely to be down to the style of the individual doctor involved.<sup>115</sup>

**32.124** He considered that haemophilia clinicians were obliged to test everyone for HCV and would be open to criticism if they did not. If a patient had said ‘no’ to a test, there would have been a further conversation and in Dr Hay’s view consent would have been obtained by persuasion. In reality, he thought that some of his colleagues may have tested for HCV without informing the patient specifically that they were testing for the virus.<sup>116</sup> They may have regarded it as just another liver function test and with this came the view that there was no need to discuss it or to request consent.<sup>117</sup>

---

<sup>109</sup> Ibid

<sup>110</sup> He referred to the current Guidelines dating from 2008.

<sup>111</sup> Dr Hay – Day 83, page 122

<sup>112</sup> This would be the case prior to the availability of treatment with Interferon.

<sup>113</sup> Dr Hay – Day 83, page 124

<sup>114</sup> Ibid page 125

<sup>115</sup> Ibid

<sup>116</sup> Ibid page 126

<sup>117</sup> Minutes of AIDS Group of Haemophilia Center Directors, 12 February 1990 [LOT.003.4450] at 4453. Professor Bloom commented that he did not see why consent was required for a HCV test as it was just another liver function test.

## Professor Nathanson

**32.125** Professor Nathanson's view was that the best practice standard of 1988, that a patient give consent to any investigation and treatment proposed by the doctor, still applied in the 1990s. In her view the best practice in the early 1990s, when an HCV test became available, would have been for the patient to be told they were being tested for Hepatitis C before a sample of blood was taken for that purpose. She said:

So it was quite clear to me from published information that we would expect that patients would be given information to make decisions for themselves, certainly about treatment. The question that always comes then is whether testing is counted as treatment, and the best practice advice, again from the 1980s, is very much that it does, that testing is the beginning of medical treatment. It is the precursor to actually offering a treatment, whether that treatment is surgery or drugs or whatever else it is, that you have to first establish a diagnosis and that testing is part of that process. So you would expect the patient to consent to that test.<sup>118</sup>

**32.126** However, she said that much would depend on the individual patient. For all but new patients introduced to testing for the first time the history of prior testing was an important factor. If the patient had already been informed on the basis of previous monitoring that it was likely that they had NANB Hepatitis, the HCV test became in effect a confirmatory test for a specific virus. Professor Nathanson explained that the preference in those circumstances would be for patients to have been told specifically that they were being tested for one of the viruses that appeared to cause NANB Hepatitis:

That didn't mean you went back to first principles every time you did a repeat test; it just meant that the patients already knew that they had non-A non-B Hepatitis. It might simply have been, "We now have a test for a particular type of non-A non-B and we are going to carry out that test for you ...."<sup>119</sup>

**32.127** However, she would expect that at that time there would be some clinicians who would not have given patients that explanation.<sup>120</sup> Some doctors embraced the new ethical imperatives more quickly than others.

**32.128** Telling a patient that they were being tested for HCV would have involved counselling the patient about the test before it was performed, a provision that left considerable scope for flexibility in dealing with individual patients. She explained that counselling prior to HCV testing was a means of giving patients the information they needed to help them make a choice on whether to have the test or not.

**32.129** Professor Nathanson was asked about the information relating to HCV that should have been given to patients before a test was carried out after 1997. She explained that much depended on the specialist carrying out the test. From 1997, a liver specialist seeing a patient on referral from another clinician would not have to explain to a patient that they had liver function problems. The aim of the liver specialist was to carry out a series of tests to ascertain what could be done to determine the cause of and to treat the abnormalities for which the patient had been referred. A clinician seeing a patient earlier in the process, when it was unclear what their medical condition was, would have

---

<sup>118</sup> Professor Nathanson – Day 84, pages 25–26

<sup>119</sup> Ibid page 35

<sup>120</sup> Ibid pages 56–57

a different approach and would discuss with the patient the need to have their liver function examined. Much of the counselling would have been done before the patient was referred to the liver specialist.<sup>121</sup>

**32.130** Professor Nathanson said that, in comparison with pre-test counselling for HIV, she would expect pre-test counselling related to HCV to be relatively brief for most patients. Some patients would require a longer time if they found the diagnosis more difficult to accept. She would expect patients to be told it was a kind of hepatitis that had a long natural history and that it could be treated. The treatment could be unpleasant but it could be successful. If the patient's HCV test proved to be positive, it would be advisable to have further tests and almost certainly treatment would be offered.

**32.131** She would not expect there to have been much of a discussion of non-medical implications unless the testing doctor was aware of something specific for a particular patient. If a patient was a healthcare worker, for example, there would be particular concerns regarding the possible risk of transmitting the virus through their work. She was uncertain about advice to patients regarding sexual transmission as her understanding was that the evidence showed that HCV was not readily transmitted that way. The very limited evidence that it could be transmitted could be mentioned to the patient so that they would have the ability to protect their partner from any risk of transmission.

### *Communication of results*

#### **Dr Hay**

**32.132** As detailed in paragraph 32.116 above, from the mid-1970s to the early 1980s very little would have been said to patients about NANB Hepatitis. The general message to a patient diagnosed with NANB Hepatitis would have been reassuring. In his report Dr Hay summarised the position relating to NANB hepatitis at this stage:

In the late 1970s and early 1980s patients should have been told what was known about this type of hepatitis at that time. This would include:-

- a. Patients were generally asymptomatic
- b. That it was benign and non-progressive
- c. There was no test [for the condition]
- d. It was thought not to be readily transmissible
- e. There was no treatment at that time
- f. Patients should minimise alcohol intake.<sup>122</sup>

**32.133** As noted above, however, understanding of the natural history and severity of NANB Hepatitis had developed by the mid 1980s and the information available to clinicians, and therefore their patients, had improved. Dr Hay set out what haemophilia patients infected with NANB Hepatitis ought to have been told in this period:

In the mid 1980s most affected patients will have been told:-

- a. That they had non-A, non-B hepatitis,
- b. But since hepatitis was still considered non-progressive they would have been told that it was benign and non-progressive in most patients

---

<sup>121</sup> Ibid pages 34–35

<sup>122</sup> Dr Hay's statement on communication to patients [PEN.018.1186] at 1208

- c. That a minority, perhaps 20%, developed cirrhosis eventually
- d. That it was generally asymptomatic.
- e. That it was slowly progressive if it did progress
- f. That there was no test or treatment
- g. But we needed to monitor the liver disease systematically
- h. That they should minimise alcohol intake<sup>123</sup>

**32.134** Most patients received their first HCV test result in 1992 or 1993, shortly after tests became available.<sup>124</sup> Dr Hay explained that many patients had gained the false impression that they *contracted* HCV in 1992 or 1993 because that was the date of their first specific positive HCV test. In fact, as discussed above, clinicians had been aware of NANB Hepatitis for some years through routine monitoring of liver function tests. Dr Hay believed that patients with intermittent or persistently abnormal liver function tests should already have had that discussed with them and been given a diagnosis of NANB Hepatitis, although they may have forgotten that earlier diagnosis. Whether or not a clinician had previously told a patient that they were infected with NANB Hepatitis, and whether or not the patient remembered any such conversation, because of a history of abnormal liver function tests<sup>125</sup> it was assumed by clinicians that these patients had hepatitis and the newly developed HCV test in 1992 acted as a confirmatory test.<sup>126</sup>

**32.135** Dr Hay said that from the early 1990s clinicians were seeing more severe liver disease in HCV-positive patients. This was particularly so in patients co-infected with HIV since HCV progresses more rapidly in an immunosuppressed patient. Conversations about liver disease became more frequent and adopted a higher profile. Dr Hay summarised what patients were being told by the mid-1990s:

- a. That the condition was benign and non-progressive in most patients
- b. That there was eventual progression to cirrhosis in up to 30% of patients
- c. That HIV was a co-factor for hepatitis C progression as was alcohol
- d. That there was a small risk of liver cancer
- e. That there was treatment available with interferon but the treatment lasted six months and response-rate was only 25%
- f. That we needed to monitor the liver disease systematically<sup>127</sup>

**32.136** The background understanding against which to consider Dr Hay's evidence of practice in relation to the provision of information to patients differed as between coagulation disorder patients treated with concentrates and cryoprecipitate users and transfusion recipients of blood components. Notwithstanding the differences in risk, Dr Hay did not describe differences in approach to patients depending on whether they had received low or high risk therapy. It appears that if the circumstances indicated the need for an HCV test the same approach was adopted.

<sup>123</sup> Ibid at 1211

<sup>124</sup> Dr Hay explained that a small number of patients, typically those with mild haemophilia who are treated infrequently, may have been tested some time after 1992–93. In general, he felt that 'no harm will have come from this delay in diagnosis, because the rate of progression of hepatitis C is slow' and because early treatment had a low success rate. Dr Hay's statement on communication to patients [PEN.018.1186] at 1199

<sup>125</sup> Dr Hay remarked in oral evidence that some of these results could be due to alcohol consumption or obesity as in the general population, but because of the patient profile it was assumed abnormal LFTs were attributable to HCV. Some patients who tested positively for anti-HCV had normal liver function tests.

<sup>126</sup> Dr Hay – Day 83, pages 83–84

<sup>127</sup> Dr Hay's statement on communication to patients [PEN.018.1186] at 1213

**32.137** Developments in the 1990s also led to a change in the advice given to patients about the risks of sexual transmission of HCV. Dr Hay explained that, until then, nothing was said to patients about the risks of sexual transmission as, without a specific test for the disease, very little was known about the possibility of sexual transmission. Clinicians were not advising patients to use barrier contraception unless they were HIV-positive.<sup>128</sup> The advice to patients in this regard did not change until a test for HCV infection became available. It then became apparent that there was a small risk of sexual transmission and the partners of HCV-positive patients were offered tests.

**32.138** The mid-1990s also saw the introduction of therapeutic treatment for HCV infection, with Interferon available from 1995–96, and this became an important part of discussions with patients. The response rate to treatment at that time was low (early literature suggested a possible 25% response rate but a lower response rate of 10% was actually experienced by clinicians). Many patients were, and continue to be, put off by side-effects of Interferon treatment, which can be particularly unpleasant and debilitating, and many patients still refuse treatment altogether. Discussions about Interferon were often delayed for patients co-infected with HIV; partly because their response rate was even lower, partly because HIV was a sufficient burden for them to carry and partly because the clinicians were waiting for improvements in treatment. In contemporary practice, all patients are offered anti-HCV treatment. Current combination therapy is much more effective than the treatment used in the late 1990s.

### Professor Nathanson

**32.139** Professor Nathanson said that, during the period between 1991 and 2000 the correct way of communicating results of a test for HCV was essentially the same as it is today. However, while the theoretical approach was the same, it had to be recognised that medical practice and ethics were still evolving from the paternalistic basis of earlier in the twentieth century to the patient-centred model embraced today. Doctors were increasingly expected to conform to best practice, but adapted to this at different rates, not always related to their own age.<sup>129</sup>

**32.140** She also explained that it was important to recognise that in the 1980s there was great uncertainty throughout the medical profession about what a diagnosis of infection with NANB Hepatitis/HCV meant. There was a slow emergence of understanding of the disease and the very long natural history of the illness. In the early period of making a diagnosis of NANB Hepatitis/HCV this natural history was still emerging and uncertain. She explained that while doctors are used to dealing with uncertainty, including risks, many patients and relatives find that very difficult.<sup>130</sup>

**32.141** Professor Nathanson and Dr Hay had a common position relating to the patient's response to information. Dr Hay noted that some patients later denied that the conversations he described as taking place in the 1970s and early 1980s occurred. There might be no physical record detailing the conversations that did happen: he said that '[m]any of these conversations will have been forgotten and may not have been documented'.<sup>131</sup> He stated that most counselling of patients in the early 1980s was completely dominated by HIV. In addition, in the case of HCV, up to 40 years may have passed from the time of the

---

<sup>128</sup> Dr Hay – Day 83, page 118

<sup>129</sup> Professor Nathanson's supplementary statement [PEN.018.0419] at 0422

<sup>130</sup> Ibid [PEN.018.0419] at 0422–23

<sup>131</sup> Dr Hay's statement on communication to patients [PEN.018.1186] at 1208

original diagnosis of NANB Hepatitis to clinically significant manifestation of the disease. It is doubtful that, in the late 1970s and early 1980s at least, a treating doctor would have reminded their patient of their NANB Hepatitis diagnosis at every appointment in the intervening period. By way of contrast, Dr Hay told the Inquiry he now discusses his patients' liver function tests with them at every meeting and reminds them of the date of their next ultrasound.<sup>132</sup>

**32.142** In his report, in discussing what he considered to be a vital distinction between pre-test counselling for HCV as compared to the equivalent process before testing for HIV, Dr Hay noted:

Some patients have complained, many years after the event, that they were tested "without their permission". In some cases they may, indeed, have been tested without being specifically informed and in other cases it is documented that they were informed both that they were being tested and of the result. The idea that a hepatitis C test should engender prolonged pre-test counselling derives from the practice adopted after 1985 by most centres of counselling prior to HIV testing. The implications of a +ve HIV test could be perceived as a death sentence, led to loss of insurance, marriage breakdown, and even in some cases suicide. There is no comparison between this and hepatitis C testing. For that reason, there has never been a specific consent process attached to hepatitis C testing even though it would be normal practice to inform the patient that they were being tested and to inform them of the result.<sup>133</sup>

**32.143** In the mid-1980s, AIDS overshadowed hepatitis. He said of his patients that:

If they were counselled about hepatitis in the context of a consultation also about AIDS they would often "deny" hepatitis C and deny that it had been discussed. Denial is a common psychological defence mechanism. I have found that patients commonly deny that they have been counselled about hepatitis C even when such counselling has been documented in the notes.<sup>134</sup>

**32.144** In the mid-1980s clinicians telling patients that NANB Hepatitis was, comparatively at least, nothing much to worry about at around the same time as they were being informed of life-threatening HIV in the blood supply may well have contributed to the phenomenon of patients forgetting their initial diagnoses with NANB Hepatitis, particularly for those co-infected with HCV and HIV. HIV would have assumed much greater importance compared to a disease about which little was known and which was suspected of being relatively benign. In the course of a single consultation a number of things would be discussed: a patient's haemophilia, the frequency and location of bleeds, as well as their hepatitis and HIV. If they had HIV, that would be the issue with immediate importance. Discussion was dominated by HIV – a condition that rapidly led to illness and then death – for which there was no test or treatment.<sup>135</sup>

**32.145** Dr Hay added that these conversations about NANB Hepatitis would have been short and not particularly memorable. Patients would have been advised that NANB

---

<sup>132</sup> Dr Hay – Day 83, page 110

<sup>133</sup> Dr Hay's statement on communication to patients [PEN.018.1186] at 1212

<sup>134</sup> Ibid [PEN.018.1186] at 1209

<sup>135</sup> Ibid

Hepatitis was not thought to be particularly infectious and that, unless they also had HIV, condoms were not required. Spouses were generally not tested at that time.<sup>136</sup> This advice differs slightly from the advice given to patients in the late 1970s to early 1980s.<sup>137</sup> The advice to patients in that earlier period of time would have been ‘relatively reassuring’.<sup>138</sup> Dr Hay added that, even if clinicians quoted the 20% risk figure, this may well have been regarded as reassuring; again, he knew of patients who could not remember these conversations at all. Even with discussion of a risk of progression to serious liver disease, he thought that many patients left with the impression that they would not themselves be amongst those who progressed to that stage.<sup>139</sup>

### ***Dr Hay’s Commentary on Professor Nathanson’s second report***

**32.146** Dr Hay was invited by the Inquiry to comment on Professor Nathanson’s report on practice relating to HCV management (discussed above) and he produced a commentary on it.<sup>140</sup> In general terms, he noted that, of the four publications she referred to, two, the GMC *Guidance on Serious Communicable Diseases* (1997) and *Consent: patients and doctors making decisions together* (2008) were not contemporaneous with the period under discussion. None of the four was specific to HCV and only the 1997 *Guidance* made a (single) mention of the disease.<sup>141</sup> Dr Hay said that there had never been any specific advice from the GMC, the BMA, or any other body relative to consent or counselling for HCV testing.

**32.147** He observed that, although Professor Nathanson acknowledged that the approach to consent to testing would be tempered by knowledge of HCV at any particular point in time, she did not develop this point in her report and offered no opinion on the way in which changing states of knowledge would have affected consent at specific times. Professor Nathanson had not offered any evidence of the extent to which the GMC 1997 *Guidance* had ever been applied to consent for HCV testing. He also questioned whether HCV was a ‘serious communicable disease’ in terms of the 1997 publication of that name.<sup>142</sup>

**32.148** Professor Ludlam also disagreed with the view that HCV was a serious communicable disease in terms of the GMC 1997 Guidelines. In his view:

HCV was known to be a slowly progressive disease in some individuals, treatment was effective in some, the chance of death was small, in the early 1990s it was not known to be sexually transmitted (and even with current information sexual and needle stick transmission is rare), it rarely affects the type of employment, it does not affect the ability of individuals to travel and does not reflect sexual orientation.<sup>143</sup>

**32.149** Dr Hay also commented on Professor Nathanson’s reliance on a comparison between testing for HIV and HCV and, in line with the comments noted above, suggested that the situation for HCV was different in a number of important respects. First, most patients with haemophilia had been monitored for liver function from the late 1970s and

<sup>136</sup> Ibid [PEN.018.1186] at 1211

<sup>137</sup> Dr Hay – Day 83, page 115

<sup>138</sup> Ibid page 116

<sup>139</sup> Ibid pages 117–118

<sup>140</sup> Dr Hay’s commentary on Professor Nathanson’s report [PEN.018.1349]

<sup>141</sup> The other texts were the GMC *Guidance on HIV Infection and AIDS* (1988) and the BMA *Philosophy and Practice of Medical Ethics* (1988).

<sup>142</sup> Dr Hay’s commentary on Professor Nathanson’s report [PEN.018.1349] at 1352

<sup>143</sup> Professor Ludlam’s commentary on the evidence of Dr Hay and Professor Nathanson [PEN.018.1246] at 1249



would (or should) have been told that they had NANB Hepatitis if their liver function tests were abnormal and other causes had been eliminated. In such cases, an HCV test would have been confirmatory and, if discussed with the patient, may well have been presented as such. Once the Hepatitis C virus had been isolated in 1989 it was assumed to be the cause of most abnormal liver chemistry in this group. Secondly, at the time routine testing was introduced in 1992-93, treatment was available and the prognosis, even without treatment, was regarded as generally very good, in marked contrast to HIV/AIDS before the introduction of HAART in 1995.<sup>144</sup>

**32.150** He commented that in most cases it was likely that HCV testing would have been mentioned in passing in the early 1990s, as a test they intended to carry out. Formal consent for testing would not necessarily have been sought and the patient would (or should) have been told the result at their next clinic visit. He again contrasted the practice of hepatologists and haematologists. He stated:

I should also point out that hepatologists have never had a policy of taking specific consent for HCV testing. I have discussed this with our current Hepatologist and his two predecessors all of whom told me that it would be just one of a battery of [perhaps 15–20] tests conducted as part of the investigation of every patient they investigated for abnormal liver function tests and that each of these tests would not be discussed with the patient individually. As our current Hepatologist said: “Everyone checks the Creatinine [test of kidney function] all the time and that is never discussed with the patient in advance and yet the prognosis of a patient with an elevated Creatinine is very much worse than the prognosis of a patient with HCV”. He re-iterated the point that HCV is potentially curable and even untreated has a generally very good prognosis and that there is no specific guidance.<sup>145</sup>

**32.151** In contrast to hepatologists, Dr Hay understood that haematologists tended to tell their patients that they were testing for HCV and discussed the condition prior to testing. That was his practice. It was influenced by experience with HIV but counselling for HCV testing was never as involved or as prolonged as for HIV testing.<sup>146</sup>

**32.152** As Dr Hay understood it, most HIV and HCV tests are currently conducted in community or STD clinics where the counselling which now always takes place can be ‘relatively perfunctory’.<sup>147</sup> It will often take the form of the patient being given an information leaflet and being asked prior to testing whether they have any questions arising from reading the leaflet. Routine testing of blood donors follows the same pattern.

**32.153** Having also considered Professor Nathanson’s first report (on HIV/AIDS), Dr Hay took up her comparison of the position in the USA. He said:

Professor Nathanson makes the very valuable point that: “In general the UK, unlike the USA, does not have a legal requirement for treatment to require fully informed consent. Ethics advice [in the UK] over three decades has been that

<sup>144</sup> Dr Hay’s commentary on Professor Nathanson’s report [PEN.018.1349] at 1353

<sup>145</sup> Ibid [PEN.018.1349] at 1354

<sup>146</sup> Professor Ludlam was critical of Professor Nathanson’s attempt to equate HCV testing with HIV testing from 1990 onwards, as he understood it. In his view this was an inappropriate comparison. He said that there are many potential causes of abnormal liver function, and to explain all of the implications of these many causes would be impossible in the everyday clinical setting. Once the cause of the abnormal liver function has been identified and HCV is the source, then the doctor can concentrate on the specific implications of the HCV infection. Professor Ludlam’s commentary on the evidence of Dr Hay and Professor Nathanson [PEN.018.1246] at 1248

<sup>147</sup> Dr Hay – Day 83, page 136

the patient must have sufficient information to understand the choice they are making and to make that choice freely.” We tell patients about common complications, not every possible thing that could possibly happen, however unlikely. By the same token, we do not go into chapter and verse about every single test we do. If we did, we would do nothing else. There are practical limitations to informed consent.<sup>148</sup>

**32.154** These practical limitations are (a) the time required to provide full information and take full consent for every test (over 20) to be conducted following a routine appointment for someone co-infected with HIV and HCV would take two or three hours for every patient and even then would be incomplete; and (b) given that first limitation, the difficulty in selecting which of those tests to explain and obtain consent for.<sup>149</sup> The definition of a life-changing result from testing was not straightforward and perceptions changed over time. He noted that the consent process for HIV infection had actually been ‘downgraded’ since 1995, when the disease became well-controlled.

### *Professor Nathanson’s views on Dr Hay’s commentary*

**32.155** Professor Nathanson was referred to Dr Hay’s commentary on her Inquiry statement.<sup>150</sup> Her analysis of Dr Hay’s comments led her to believe that her use of the word ‘counselling’ was perhaps the cause of the sticking point between their two views.

**32.156** Dr Hay’s practice was described to Professor Nathanson by counsel, namely that he would advise patients that he wanted to carry out an HCV test, give them an ‘exposition’ of the disease, and effectively secure their agreement to proceed. Professor Nathanson said that that accorded with best practice for counselling in the period relating to HCV testing.<sup>151</sup>

**32.157** Leaving aside the semantics that occupied some time at the Oral Hearing of her evidence, Professor Nathanson’s views on the appropriate approach to patients offered HCV testing emerged clearly. In the first place she distinguished the requirements for pre-test counselling from those developed for HIV testing. HIV presented a much more complex situation and a correspondingly complex level of information was necessary. Some people assumed that that level of information was necessary for every test but that was never the position in practice. Counselling had to be appropriate to the test in question. HCV and HIV/AIDS were different conditions, with very different medical and social outcomes.<sup>152</sup>

**32.158** She thought that Dr Hay had considered that she was ‘writing from an ivory tower’ without considering the practicalities and that he had missed the nuances in her report: best practice was about being sensitive to the needs of the particular patient and the elements of the medical condition in question.<sup>153</sup> She said that, because the UK does not have informed consent as a legal requirement for almost any treatment, the BMA continued to refer to ‘real or valid consent’ which means that patients must understand enough about the options to be able to make a choice, and to then make that choice. Doctors give patients information, helping them to understand what options are available to exercise their choice. She considered that pre-test counselling was, ultimately, a very

---

<sup>148</sup> Dr Hay’s commentary on Professor Nathanson’s report [PEN.018.1349] at 1355

<sup>149</sup> Ibid

<sup>150</sup> Ibid

<sup>151</sup> Professor Nathanson – Day 84, page 38

<sup>152</sup> Ibid pages 38–39

<sup>153</sup> Ibid page 39

simple concept: it was the process of giving people enough information to make an informed decision.<sup>154</sup>

**32.159** Professor Nathanson suggested that Dr Hay appeared to assume ‘full consent’ was analogous to lengthy pre-test counselling and that a practitioner was expected to give every single piece of information on testing to a patient. She stated that she was not saying in her report that patients need to be told everything about testing in order to consent but rather that information has to be adapted to their individual requirements. Professor Nathanson concluded this aspect of her evidence by stating: ‘The problem is that ... consent is not necessarily a highly complicated process. It just has to be a process that is specific and appropriate for that patient and that test’.<sup>155</sup>

**32.160** Professor Nathanson’s attention was then drawn to Dr Hay’s view that, if informed consent was required for every test that a doctor did, it could take up most of the day and normal work would not be done. In response, Professor Nathanson remarked one had to establish what was meant by ‘real consent’. A doctor may not necessarily explain to the patient all of the tests that would be done on a blood sample. The doctor’s skill would be in communicating with the patient that a series of tests will have to be done on a blood sample and tailoring further information to the individual patient. Some patients will simply want to get on with those tests and not ask for an explanation of them at this stage; others may want to know from the beginning what all of the tests are, in which case the doctor should recognise that they have to explain them and what their purpose is. The doctor should respond to the requirements of the individual patient.<sup>156</sup>

**32.161** Professor Nathanson noted that some tests are more risky or hazardous. For example there are specific risks with performing a biopsy and those risks should always be explained to the patient. However, in her view, a doctor may not necessarily go into all of the risks associated with every intervention with a patient but, rather, should explore the most common and the most serious of the risks in the first instance. If, after that, a patient wants to have more information then it should be provided. Professor Nathanson summarised her position:

[S]ome patients will want to know more and some patients will want to know very little, and that is consent, because that is valid because the patient has been offered information and the opportunity to ask questions and has said, “That satisfies my need.”<sup>157</sup>

**32.162** Professor Nathanson was asked to comment on Dr Hay’s distinction in approach taken by different specialists and, in particular, the example given of the difference between a hepatologist and a haemophilia clinician in obtaining consent to conduct tests. She agreed that patients are referred to a hepatologist because they already have abnormal liver function and the hepatologist would then carry out the appropriate investigations. It is likely that such a patient will have already been treated by another clinician who made the referral to the specialist so that the patient should have knowledge that there is something wrong with their liver and consent to further investigatory tests is implied. Professor Nathanson would consider this to be ‘necessarily implied consent’.<sup>158</sup> She would

---

<sup>154</sup> Ibid pages 40–41

<sup>155</sup> Ibid page 46

<sup>156</sup> Ibid page 44

<sup>157</sup> Ibid page 45

<sup>158</sup> Ibid page 49

expect a hepatologist to obtain specific consent for a liver biopsy, because of the specific, well-documented and occasionally serious risks associated with the procedure, but not for tests carried out on blood samples. She would expect a hepatologist to explain that blood was being taken for testing to try to identify the cause of the liver disease and also expected that the patient would acquiesce to that general statement and, in those circumstances, that in her view would constitute consent.<sup>159</sup>

**32.163** Professor Nathanson was also referred to the final section of Dr Hay's commentary where he listed the main differences between HIV and HCV that he felt were relevant to counselling:<sup>160</sup> Dr Hay's comparison is shown in Table 32.1 below.

**Table 32.1: Dr Hay's comparison of characteristics of HIV and HCV**

<u>HIV</u>	<u>HCV</u>
Incurable, even now	Curable in 40-100%
70% Mortality prior to 1995	Mortality <2% prior to 1995
Prior to 1995 expected 100% mortality	Good prognosis, slow or no progression
Treatment ineffective prior to 1995	No treatment until late eighties
Ready sexual transmission	Low infectivity
Symptomatic when advanced	Generally asymptomatic until end-stage
Causes AIDS	30% cirrhosis, eventually 5% hepatocellular carcinoma
Uninsurable	May have an adverse effect on premium

**32.164** Professor Nathanson agreed with the details Dr Hay had listed in his table and accepted the distinctions he had made between the two viruses and, in particular, their relevance to counselling. She observed this was 'an entirely appropriate background to the way in which you would talk to the patient about consent or indeed about what the diagnosis would mean to them'.<sup>161</sup>

### *Dr Alexander*

**32.165** Dr Alexander was Consultant Hepatologist at Addenbrooke's NHS Trust from August 2003 and had extensive experience in hepatology prior to that appointment. He provided the Inquiry with a report about the tracing and testing of patients who might have been infected with Hepatitis C and the information given to patients who might have been or were infected with the virus.<sup>162</sup> Dr Alexander was asked how he advised patients that they had a positive HCV test, both in the early days of testing and after 1995. He had a similarly pragmatic approach to Dr Hay. He said that the introduction of HCV testing was a major step forward, allowing him and his colleagues to separate patients into those who had probably cleared the infection from those with ongoing infection. There were, however, concerns about the quality of the tests themselves and a lack of knowledge of the natural history of Hepatitis C.<sup>163</sup>

<sup>159</sup> Ibid page 48

<sup>160</sup> Dr Hay's commentary on Professor Nathanson's report [PEN.018.1349] at 1358

<sup>161</sup> Professor Nathanson – Day 84, page 50

<sup>162</sup> Letter from Penrose Inquiry to Dr Alexander requesting a report [PEN.018.1241]

<sup>163</sup> Dr Alexander's statement on HCV testing [PEN.018.1360] at 1365

**32.166** Dr Alexander said that in the early 1990s patients with positive HCV tests were warned that the doctors did not understand fully the implications of the test and as a consequence patients underwent regular testing for HCV. In his centre in Cambridge all HCV-positive patients were also offered the opportunity of a liver biopsy. Patients with liver damage were offered close follow-up and regular liver biopsies. At this time there was no available therapy for such patients.<sup>164</sup>

**32.167** He observed that knowledge gained by physicians seeing patients with NANB Hepatitis may not have been applicable to dealing with patients when HCV tests were introduced. He commented:

It was not possible to transpose the information we gained from non-A, non-B hepatitis epidemiology studies to HCV infection because introduction of testing had identified a far greater spread and number of patients than we had imagined prior to 1991.<sup>165</sup>

**32.168** Dr Alexander also commented on changes in the information given to patients from 1995 onwards. In his statement he said that ‘issues such as the natural history were still being resolved but studies of vertical transmission and sexual transmission were allowing us to fine tune the information given to patients’.<sup>166</sup> He added in oral testimony that in this time period the clinicians could advise on the effect on HCV of co-factors such as age, gender and obesity.<sup>167</sup>

*Differences of opinion regarding the provision of information to patients about NANB/Hepatitis C*

**32.169** It appeared from the written statements of Professor Nathanson and Dr Hay that there might have been significant differences of opinion between them concerning proper ethical practice in relation to the provision of information to patients about NANB Hepatitis and HCV and about the proper approach to discussions about testing in that context. Dr Hay was concerned that Professor Nathanson, despite acknowledging changes in scientific knowledge throughout the period, had not properly taken into account the significance of those changes. Professor Nathanson thought that Dr Hay had misinterpreted her evidence as prescribing a higher level of counselling than she had intended to convey was necessary. That there were differences is obvious but, in the end, after their oral testimony is taken into account, the differences appear to be largely differences of expression rather than of substance.

**32.170** Professor Nathanson acknowledged that best practice had to reflect changes in scientific understanding over time. Dr Hay, as a haemophilia practitioner with experience of dealing with those changes, gave considerable weight to their significance and in particular emphasised the chronology of emerging knowledge as it bore on practice.

**32.171** It is consistent with Dr Hay’s evidence that by 1985, when the first diagnostic test for HTLV-III/HIV was becoming available, neither the GMC nor the BMA had published specific guidance on NANB Hepatitis in the management of patients. There was no test for any NANB Hepatitis virus and therefore no trigger for discussion of the implications of testing patients. Thereafter, as Dr Hay put it, there was ‘much discussion and a plethora of

---

<sup>164</sup> Ibid [PEN.018.1360] at 1365

<sup>165</sup> Ibid [PEN.018.1360] at 1366

<sup>166</sup> Ibid

<sup>167</sup> Dr Alexander – Day 85, page 143

guidelines issued over the years to cover HIV-testing',<sup>168</sup> culminating in the GMC publication *HIV Infection and AIDS: the Ethical Considerations* (1988). It would be impossible to hold that, before the AIDS era began, there was a generally recognised obligation on doctors to single out NANB Hepatitis as a subject for specific discussion with patients, either in the course of haemophilia therapy or more generally.

**32.172** Professor Nathanson recognised that dealing with HIV/AIDS changed the way that medicine was practised. Dr Hay emphasised that HIV/AIDS overshadowed hepatitis. In the critical period, 1982 to the mid-1980s, patients were not counselled about NANB Hepatitis to the same degree as had been common in the immediately preceding period. There was growing knowledge that a proportion of patients with NANB Hepatitis were developing severe progressive liver disease but it was still believed that the majority would have a non-progressive or very slowly-progressing disease and, as noted, HIV/AIDS assumed a position of paramount importance at this time.

**32.173** So far as formal statements of practice are concerned, the ethical position relating to NANBH/HCV remained relatively ill-defined, depending on general rather than specific guidance even in 1988. UKHCDO guidance was related primarily to the selection and use of therapeutic products. Professor Nathanson's views were largely based on the 1988 *Guidance*. That BMA publication did not refer specifically to hepatitis, however. By 1988 it was understood that NANBH/HCV was a disease with a potentially serious prognosis, as set out in Dr Hay's table (Table 32.1). If the 1988 *Guidance* had been intended to specify proper ethical practice in relation to that disease it would have required discussion and express guidance, not least to differentiate the guidance offered from that applicable to HIV/AIDS. The debate over the need for 'counselling' and what that meant in different contexts makes that clear.

**32.174** Further, Professor Nathanson's view that much would depend on the individual patient is inconsistent with the notion that there was a well-developed and understood ethical rule requiring haemophilia clinicians invariably to adopt a particular approach to procedures relating to testing patients as a matter of general practice in the early 1990s. Implementing the general guidance left much to the discretion of the clinician in managing patients.

**32.175** Examination of proper practice in the period from 1997 further undermined the case for a specific duty to advise patients before testing for HCV infection at any earlier period. Dr Hay stated that hepatologists have never had a policy of taking specific consent to HCV testing: it was just one of a battery of tests to be performed routinely on blood samples taken from patients referred to them.<sup>169</sup> Haemophilia clinicians tend always to tell the patient if they are testing for HCV and to discuss the condition prior to testing.<sup>170</sup> Professor Nathanson's explanation was that liver specialists would expect that at an earlier stage in the process another clinician would have provided the necessary information. It appears reasonable to suggest, however, that if there had been a specific ethical rule that patients required to be counselled before being tested for HCV, a hepatologist would have had to check that prior counselling had been given. On the evidence of both experts, counselling was and is perfunctory in those situations.

---

<sup>168</sup> Dr Hay's commentary on Professor Nathanson's report [PEN.018.1349] at 1355

<sup>169</sup> Ibid

<sup>170</sup> Ibid [PEN.018.1349] at 1354

**32.176** In the circumstances, Dr Hay's evidence that there has never been any specific advice from either the BMA or the GMC or any other body about consent or counselling for HCV testing is accepted.<sup>171</sup>

**32.177** Apart from express guidance, both experts in the end looked to the wider context of growing scientific knowledge and changing perceptions of the doctor/patient relationship in identifying milestones in the development of the requirements of good ethical practice. Professor Nathanson expected that as knowledge of NANB Hepatitis and later HCV developed clinicians would pass on that information to their patients. By 1985 clinicians would have been expected to advise patients clearly of the risk of contracting the disease from the use of factor concentrates. By 1991 a clinician would have been expected to advise patients clearly of the risks associated with any medical intervention, including testing. Dr Hay considered that the years 1991–92 were particularly significant because of the introduction of specific testing for anti-HCV. However, he observed that by then treatment was available and the prognosis for patients infected with HCV was regarded as generally good. Dr Hay said that in most cases HCV testing would be mentioned in passing and formal consent to testing would not have been sought.

**32.178** It is not possible to find that up until 1988 there was a well-developed and widely recognised ethical duty, of any degree of specificity, to advise patients about the nature and implications of NANB Hepatitis or (after the isolation of HCV in 1988) of Hepatitis C. Indeed, on detailed discussion, Professor Nathanson's evidence fell short of suggesting that there was.

**32.179** As far as testing was concerned, Professor Nathanson considered that the 'gold standard' of care would involve obtaining patients' consent before testing blood samples for HCV, whether they were stored or fresh. However, she acknowledged that haemophilia patients monitored for liver function throughout the 1980s could have expressly consented to a future HCV test when blood was taken or have been held to have implicitly consented on the basis that a specific HCV test was effectively a confirmatory test for a patient who had already been told that it was likely that they had NANB Hepatitis due to persistent irregular liver function tests. However, once results were obtained, as with an AIDS diagnosis, they should have been communicated to the patients.

**32.180** There are difficulties with this as a basis for a rule of practice. Professor Nathanson acknowledged that some patients had difficulty processing bad news or complex information during consultations with clinicians and she offered this as an explanation of why some patients may not have retained information that they have been given. The memories of clinicians can be similarly fallible, and, without a record, clinicians in succession would not know what consents their predecessors had obtained.

**32.181** In practice, based on general guidance from the late 1980s and influenced by the experience of HIV/AIDS, haematologists and haemophilia specialists in particular have provided information about HCV and about testing for the disease as an aspect of their care and management of their patients. Practice has been variable, reflecting the approaches of individual practitioners, including Dr Hay and Dr Alexander. In adapting general ethical principles to specific circumstances that is inevitable.

---

<sup>171</sup> Ibid [PEN.018.1349] at 1352

**32.182** However, broadly speaking, Professor Nathanson and Dr Hay agreed that, as knowledge increased, patients should have been told about the risk of infection with HCV and that patients should have been told about the changing views about the severity of the disease as they developed. They agreed that it was appropriate to obtain consent before proceeding with an HCV test although a failure to do so for a haemophilia patient who had already given consent to have their liver function monitored for the purpose of investigating, amongst other things, NANB Hepatitis was understandable. Both agreed that the extended pre-test counselling that was appropriate before an HIV test in the 1980s is not necessary today with regards to HCV and was not necessary during the earlier period either. This level of common understanding left considerable scope for variation in individual practice.

### **The current position in general**

**32.183** It is clear from the evidence that there have continued to be significant developments in the provision of information to patients. As Professor Nathanson saw it, the modern approach to the doctor/patient relationship involves the patient fully in the decision-making process: it sees medical practice as being about sharing. The doctor does not assert that he knows everything but adopts the approach that 'This is how I would interpret the information you are giving me and what I'm learning about you from tests'. There was a radical shift from 'Doctor knows everything and will give orders' to 'We will share information and my role is to help you make a decision'.<sup>172</sup>

**32.184** Professor Nathanson explained what would constitute best practice in terms of the provision of information to patients:

[T]he most important thing is about offering information to patients, not pushing information at them. It's about helping patients to come to terms with information, giving them the opportunity to think and to question, and being open to a repeated set of questions, rather than delivering a measured amount of information each time, which is identical for each patient .... It has to be what's right for that patient at that time ... and trying to test, which is where the communication skills also come in ... that they have understood sufficient to be able to make a decision based upon the information that you are offering.<sup>173</sup>

**32.185** In modern practice in the UK, in contrast to much of the reference period, this extends to providing the patient with sufficient information to allow the patient both to understand the choice they are making and to enable the patient to make that choice freely. What is 'sufficient' will vary from patient to patient and will depend on what the patient wants to know as well as what the major risks, benefits and alternatives are. In the modern situation, a doctor is trying to make sure that the patient understands enough to make an informed decision: it is more complicated than under the regime that obtained until the late 1980s and early 1990s. In addition there are many more treatment choices available. In modern practice, ethics is considered to be far more complex and nuanced than in the past and the right thing to do is not always clear.

---

<sup>172</sup> Professor Nathanson – Day 37, pages 11–12

<sup>173</sup> Professor Nathanson – Day 84, pages 4–5



**32.186** The aim of the GMC publication *Good Medical Practice* (see paragraph 32.191 below) is to give advice, supplemented by the BMA, the Medical Defence Union and other medical defence bodies, which will help doctors to be better at their job and to follow best practice. The general direction of movement in medicine after the 1970s, away from paternalism and towards patient-centred medicine, had taken a long time, however, and according to Professor Nathanson it is still ongoing.

**32.187** There was broad agreement that there had been significant change over the reference period. As with any progressive, but relatively unstructured, development in patterns of behaviour, it can be difficult to define with any precision the point reached in general understanding of the evolving scene at any given time, in the absence of specific regulation or guidance providing a reference date. It can be particularly difficult to relate general understanding to the position of a doctor trying to assess the needs of patients presenting with a particular set of circumstances. This was particularly true in the mid-1980s with the advent of AIDS. Even now, there are still unsettled or unresolved issues.

**32.188** Quite what 'patient-centred care' requires of the doctor varies with circumstances. Two patients with the same medical condition may not necessarily want the same solution. Doctors now recognise that different patients may have different views and priorities. One patient with a serious condition might prefer to be pain free and another might prefer to be more alert and aware and able to interact with their family. The underlying concept is that the patient should be comfortable with whatever is done: it is the patient's body or illness that is being treated. The doctor has the responsibility of knowing as much as possible about the patient, of looking at the patient holistically as a person and not as a physiological, anatomical specimen. The complexity in any individual case arises because the doctor is trying to give the patient the power to decide whether they want to make a decision about treatment, but not forcing them to do so. The patient's decision could be that they want the doctor to make the decision for them. The fundamental change from the 'paternalistic' approach is that power has transferred to the patient.

**32.189** Professor Nathanson did not think that responsibility had transferred to the patient as well as power. Patients do have the responsibility to tell their doctors the truth about themselves but the patient should not be forced into taking the final decision about their treatment: the patient has to be protected from taking decisions with which they are uncomfortable. It can become very uncomfortable for the doctor where a patient may say that they know that they have a fatal disease and there is a curative treatment but they do not want to accept treatment. The picture painted by Professor Nathanson of the requirements of current ethical practice is very different from that described relative to practice in the period that is of concern to the Inquiry.

**32.190** She explained that there has been a dialogue with the public on the principles of medical ethics. Half of the BMA committee are now lay people or non-doctors. The BMA commissions pieces from members of the public and involves them in conferences. For example, with topics such as consent and assisted dying the BMA has taken into account the views of the public. The aim is to produce an ethical framework that is a balance between what doctors and the public expect.<sup>174</sup>

---

<sup>174</sup> Professor Nathanson – Day 37, page 27

## Current guidance on HCV

**32.191** In terms of formal guidance, the current approach was set out in the GMC booklet, *Good Medical Practice* and the supplement from June 2008, *Consent: patients and doctors making decisions together*.<sup>175</sup> Professor Nathanson noted the GMC's current guidance on the information that should be given to patients in her first report to the Inquiry:

You must give patients the information they want or need about:

- (a) The diagnosis and prognosis
- (b) Any uncertainties about the diagnosis or prognosis, including options for further investigations
- (c) Options for treating or managing the condition, including the option not to treat
- (d) The purpose of any proposed investigation or treatment and what it will involve
- (e) The potential benefits, risks and burdens, and the likelihood of success, for each option; this should include information, if available, about whether the benefits or risks are affected by which organisation or doctor is chosen to care
- (f) Whether a proposed investigation or treatment is part of a research programme or is an innovative treatment designed specifically for their benefit
- (g) The people who will be mainly responsible for and involved in their care, what their roles are, and to what extent students may be involved
- (h) Their right to refuse to take part in teaching or research
- (i) Their right to seek a second opinion
- (j) Any bills they will have to pay
- (k) Any conflicts of interest that you, or your organisation, may have
- (l) Any treatments that you believe have greater potential benefit for the patient than those you or your organisation can offer.<sup>176</sup>

**32.192** Professor Nathanson explained that the GMC had been producing versions of *Good Medical Practice*<sup>177</sup> for some years and it became clear over time that more detail was required on the issues of both 'consent' and 'confidentiality'. The GMC therefore put together a more detailed document on consent:

[T]o help doctors in making decisions about whether or not a patient could give consent, whether it was appropriate for somebody else to consent for that patient and about how to go about the process of giving patients information so that those decisions could be made ... this is about patients and doctors making decisions together. And that's a very deliberate decision by the General Medical Council, to stress that consent is not about a doctor deciding to do something and the patient then agreeing the doctor could do it, it's about that process of decision-making together, and that is very much a change of

---

<sup>175</sup> 'Guidance for Doctors', *Consent: patients and doctors making decisions together*; General Medical Council [PEN.018.0430]

<sup>176</sup> *Ibid* [PEN.018.0430] at 0441

<sup>177</sup> The GMC's general ethical guidance.

emphasis from say, the 60s or 70s, when it would be more about a patient agreeing to what a doctor had suggested.<sup>178</sup>

**32.193** Professor Nathanson identified what she took to be the key statement on consent in the 2008 guidance:

5(b) The doctor uses specialist knowledge and experience and clinical judgement, and the patient's views and understanding of their condition, to identify which investigations or treatments are likely to result in overall benefit for the patient. The doctor explains the options to the patient, setting out the potential benefits, risks, burdens and side effects of each option, including the option to have no treatment. The doctor may recommend a particular option which they believe to be best for the patient, but they must not put pressure on the patient to accept their advice.<sup>179</sup>

**32.194** Professor Nathanson explained that the importance of this paragraph was its emphasis on setting out all medical treatments, or options for treatment, and making it clear that the role of the doctor is to use his or her knowledge, skills and experience to understand what a patient wants and using that to identify what investigations or treatments will result in overall benefit. This section is not specific to a particular condition or type of test but encompasses all conditions and all tests.<sup>180</sup>

**32.195** She said that doctors are expected to offer their patients all of the elements of information identified in the guidance. In addition she said:

Many doctors today back up their information sharing with leaflets, or web links, so that patients and relatives are better able to make sure they have all the information they want and can test their recollections of the conversation with the doctor.<sup>181</sup>

**32.196** She commented that patients have a basic right to information about themselves. This does not mean that doctors simply hand over the information, including test results, however. Information should be shared with the patient in an appropriate manner:

In practical terms this means telling the patient where this places him/her in terms of a differential diagnosis, and what further tests are necessary, or what treatment now seems to be indicated.<sup>182</sup>

**32.197** Professor Nathanson was of the view that the guidance given by the GMC was a 'counsel of perfection' but she did not accept that it was provided by a body that was out of touch with the realities of clinical practice. She stated that it was not necessary for a practitioner to set out 'every single detail of every single option'. The guidance in this paragraph concerned the offering of information, understanding the patient's views and exploring options with them. By understanding the patient's views some options could be discounted and would not need to be explained further. In her view the guidance was that a skilled doctor should prioritise the most important pieces of information for their patient. The process is often somewhat easier in the relationship between a patient and

---

<sup>178</sup> Professor Nathanson – Day 84, pages 6–7

<sup>179</sup> Guidance for Doctors', *Consent: patients and doctors making decisions together*, General Medical Council, 2008 [PEN.018.0430] at 0438

<sup>180</sup> Professor Nathanson – Day 84, page 7

<sup>181</sup> Professor Nathanson's supplementary statement [PEN.018.0419] at 0420

<sup>182</sup> Professor Nathanson's first report to the Inquiry [PEN.012.0330] at 0337

their GP, because GPs often know their patients better than specialists to whom they may be referred and a lot of decision-making is broadly similar for different conditions. She accepted that for some patients and for some tests and procedures it can take a long time to obtain valid consent but, equally, very often it takes a short time. She explained that ‘practising doctors on my committee, for example, ten people who are in everyday clinical practice, say, “This doesn’t cause a problem”’.<sup>183</sup>

**32.198** The family members of competent adult patients have no right to know a diagnosis. Doctors should work with patients to help them understand the benefits of sharing their diagnosis with others but cannot force them to share the information.

**32.199** In oral evidence Professor Nathanson expanded on the issue of what, and how much, information a doctor should offer to a patient. She explained that the BMA is aware that the amount of information a patient can take in and accurately recall from one-to-one meetings with their doctor can be very limited. This can be affected by the patient being upset and anxious about what is happening to them. Increasingly, doctors will offer brief information leaflets or links to helpful and specific websites to their patients so they can conduct their own research and find out more themselves.<sup>184</sup> It is hoped that this approach obviates the risk of patients using unreliable or inaccurate websites, which can be unsafe, in their own research. The doctor can try to steer the patient to the sites that are reputable and this should help the patient to ask the right questions of the doctor.<sup>185</sup>

**32.200** Professor Nathanson explained that, when seeking agreement to carry out a test, information should be offered to explain why it is being performed, what the test might show and what decisions will be made in respect of the results.<sup>186</sup> In oral evidence she expanded this point by explaining that the contemporary approach to ‘seeking agreement to tests’ will depend on the circumstances. For example an individual may approach their GP because they have been feeling unwell and this may lead to the GP conducting tests for possible anaemia. The doctor could explore the patient’s medical history with them in their discussion and, based on what they found out, decide which tests are appropriate. Some patients will want to know what these are and some will prefer to await the results and then have the test results explained.<sup>187</sup>

**32.201** Offering information about testing, and deciding how much information to give, depends on the patient and what the doctor thinks they might discover in the test. The test for anaemia may be routine but there are many causes of anaemia, with some being minor and some very serious, such as leukaemia. It is not necessary that the doctor should tell the patient about the most serious possibilities at the outset: ‘How much you offer, how much information really depends upon what you think is likely to come out of that test’.<sup>188</sup> If the patient asks specifically if there could be a serious reason for the anaemia, such as cancer, then the doctor should be honest that it is a possibility, but go on to explain there is a more likely less serious cause.

**32.202** The information that a clinician gives to a patient may depend on the suspicions they have about the patient’s diagnosis or likely test results; but it also depends on the implications of the test results. If a clinician thinks the result will be negative and the test is

---

<sup>183</sup> Professor Nathanson – Day 84, pages 8–9

<sup>184</sup> *Ibid* page 10

<sup>185</sup> *Ibid* page 11

<sup>186</sup> Professor Nathanson’s supplementary statement [PEN.018.0419] at 0420

<sup>187</sup> Professor Nathanson – Day 84, page 12

<sup>188</sup> *Ibid* page 12

one of exclusion, they may not give a detailed explanation of what a positive result would mean. By way of contrast, if the clinician thinks the test result will be positive they should go into more detail about the implications of such a result. Once there is a diagnosis, the amount of information given to the patient will increase and become more detailed.<sup>189</sup> As explained by Professor Nathanson, the provision of information may be a graduated process, depending on what the clinician expects to find from a test and whether it is the initial test of a possible series of tests, at which point a relatively small amount of information may be offered.<sup>190</sup> Generally speaking a clinician should modify every piece of information that is given to the patient depending on their circumstances.

**32.203** She also explained that, in the case of ongoing, routine monitoring tests, doctors may require to provide more information than that given at an earlier period as the implications of the test results may change over time. These changes may be due to emerging knowledge about the natural history of the illness or different treatment options becoming available. They may also be due to non-medical factors such as changing public perceptions of a disease:

Another element that is relevant when testing for medical conditions with specific non-medical consequences, such as social stigma, or employment and financial consequences is that these should be part of the discussion. It should again be noted that such stigma or financial consequences emerge over time.<sup>191</sup>

**32.204** Testing for HIV has had obvious non-medical consequences, financial and social, from a very early stage. Some people think HCV is also stigmatising and can have social consequences; it can also have employment consequences in some circumstances.<sup>192</sup> In 1992, when a great deal of HCV testing was first carried out, doctors conducting the tests could not have known what the non-medical implications of a positive diagnosis would be. Professor Nathanson added that doctors would also have had limited knowledge of the medical consequences as HCV was a condition that was learned about by tracking infected patients over a long period of time.<sup>193</sup>

**32.205** Professor Nathanson was asked to sum up what she considered to be best practice today in testing for Hepatitis C:

It comes back to the consent paragraph that I quoted from the General Medical Council's book. It's about giving the patient enough information to make a decision about having that test. That means a short discussion. It is not the most serious chronic illness. It is a serious chronic illness but it is not the most serious. It is not the worst diagnosis you could be faced with. You do need to give patients some information about it, not least to make sure that they are aware that this is something that, if it's positive, you are going to want to follow them up with, and that you would want, therefore, this to be potentially the beginning of quite long period of follow-up, including potentially some quite complex treatment.<sup>194</sup>

---

<sup>189</sup> Ibid page 14

<sup>190</sup> Ibid page 15

<sup>191</sup> Professor Nathanson's supplementary statement [PEN.018.0419] at 0420

<sup>192</sup> Professor Nathanson – Day 84, page 15

<sup>193</sup> Ibid page 19

<sup>194</sup> Ibid page 20

**32.206** In light of the discussion of terminology in this chapter, it is appropriate to make a general observation about the use of the word 'counselling'. It was clear from the evidence heard by the Inquiry that this term was used by different people in different ways and at different times. While the guidance given by the GMC and the BMA to doctors is a matter for them, the confusion that entered the evidence, especially of Professor Nathanson and Dr Hay, from the use of a term of uncertain meaning should encourage the responsible bodies to ensure that official guidance and rules are expressed with sufficient clarity to have an obvious meaning or are supported by clear definitions of the scope of significant terms in context, in order to avoid confusion. The written guidance that they produce is and has always been important to practitioners but perhaps increasingly it is also important to patients, who are entitled to look to these official sources as indications of what they are entitled to expect from their medical practitioners.

**32.207** In conclusion, this chapter has discussed the medical profession's views on ethical practice relating to consent for testing for HIV and HCV, and in relation to the information provided to patients on these conditions. Although the three experts featured have some differences of opinion and emphasis, they broadly agree that best practice now in relation to informed consent and even in the sharing of information differs from the practices which prevailed during the reference period, or at least up until 1988 when the influence of HIV/AIDS helped to bring about significant changes. Dr Hay and Professor Nathanson agree that there was a qualitative difference between the nature of HIV/AIDS and Hepatitis C which, they concluded, meant the requirements for informed consent and information to patients were less onerous in relation to Hepatitis C. While their evidence is accepted, it must be acknowledged this will not bring consolation to the many patients and relatives troubled by what they see as a lack of informed consent or a lack of information in their own particular circumstances. Those suffering from HCV, especially those who progress to liver cancer, may find views that compare their condition favourably with other infections unpalatable. Some people who struggle with chronic Hepatitis C may also be experiencing repeated failed treatments for the virus. Whilst HCV is perhaps, in Professor Nathanson's words, 'not the worst diagnosis you could be faced with', for such individuals it was and continues to be devastating.

## CHAPTER 33

### AN INVESTIGATION INTO THE SYSTEMS IN PLACE FOR INFORMING THE PATIENTS ABOUT THE RISKS – HIV/AIDS

#### Introduction

##### *Scope of the chapter*

**33.1** The background to the development of doctor/patient relationships during the reference period has been discussed in Chapter 32, *An Investigation into the Systems in Place for Informing Patients about the Risks – Ethical Context*. Particular matters dealt with in this chapter include: (i) the information and advice given by doctors about the risks associated with the therapeutic use of blood and blood products, (ii) the clinical information and prognosis given to patients and, where appropriate, their families in the investigation and diagnosis of HIV/AIDS and (iii) the testing of blood samples of patients in specific situations.

**33.2** The HIV/AIDS epidemic had little impact on the treatment of blood coagulation disorder patients anywhere until 1982 and in the United Kingdom few patients (and none in Scotland) were known to be infected or to have AIDS until mid-1983. In late 1984 and in 1985 testing and screening for anti-HTLV-III/HIV<sup>1</sup> disclosed a prevalence of infection, in particular in coagulation disorder patients, which had not been anticipated. The main events bearing on developing relationships between doctors and patients occurred for the most part in and after 1983.

**33.3** Changes in knowledge of the risk of transmission of HIV, and of the threat that the infection posed for patients, did not occur uniformly throughout the UK, or within Scotland. There are few landmark dates that apply generally. The publication in *The Lancet* of 1 September 1984 by Cheingsong-Popov and others of their study of the prevalence of antibody to HTLV-III in AIDS and AIDS-risk patients in a number of English Haemophilia Centres was one such event.<sup>2</sup> So far as Scotland is concerned, the first reports in late 1984 of HTLV-III/HIV infection in patients in the west of Scotland, treated with both NHS and imported products, and in the south east of Scotland, in patients treated with SNBTS factor concentrates exclusively,<sup>3</sup> demonstrated that the findings of the Cheingsong-Popov study had direct relevance in this country and shattered any continuing belief that the AIDS epidemic was confined to those treated with commercially produced coagulation products.

**33.4** The treatment of events in this chapter is largely chronological. Specific topics discussed include:

- Issues relating to tests of patients' immune functions carried out in Edinburgh and Glasgow in the period 1983–85.
- The circumstances in which testing of patients' sera stored from earlier investigations was carried out in research laboratories in Edinburgh and Glasgow following the advent of the first anti-HTLV-III tests.
- The problems which arose subsequently over obtaining informed consent for anti-HTLV-III testing and pre- and post-test counselling.

<sup>1</sup> See Chapter 29, *The Discovery of HIV and the Development of Screening Tests* for a discussion of LAV/HTLV-III, the early names for what became known as HIV.

<sup>2</sup> Cheingsong-Popov et al, 'Prevalence of antibody to human T-lymphotropic virus type III in AIDS and AIDS-risk patients in Britain', *The Lancet*, 1984; 477-480 [LIT.001.0417]

<sup>3</sup> See Chapter 10, *Knowledge of the Geographical Spread and Prevalence of HIV/AIDS 2*

The evidence of the witnesses who spoke about the effects of their own or their relative's infection with HIV and/or Hepatitis C included evidence on some of the matters discussed in this chapter.<sup>4</sup> Where appropriate the evidence of these witnesses has been referred to in order to give context to each topic. So as not to detract from the main purpose of the oral evidence of these witnesses (for the Inquiry to learn about the full effects of infection) the Inquiry did not investigate each criticism made by these witnesses but instead took account of them when considering and reaching conclusions about the practices of their treating doctors.

### **The threat of HIV transmission, haemophilia therapy in Scotland and the provision of information to patients**

**33.5** As noted in paragraph 32.3 of Chapter 32, *An Investigation into the Systems in Place for Informing Patients about the Risks – Ethical Context*, many of the patient witnesses who provided statements to the Inquiry stated that they were not warned about the risks associated with their treatment for haemophilia.

**33.6** The evidence available to the Inquiry indicates that, as in other areas, individual haemophilia clinicians formed and followed their own views of the appropriate approach to telling their patients about therapy, and the risks associated with it. It is thus not possible to distil one single approach that might be described as common among them.

#### *Practice in Edinburgh and south east Scotland*

#### **The evidence of patients in Edinburgh and south east Scotland**

**33.7** The witnesses who gave evidence about the effects of their own or their relative's infection with HIV and Hepatitis C included four patients or relatives of patients who were treated in Edinburgh.<sup>5</sup> Three of them gave evidence about the provision of information to them or their relatives. As detailed in Chapter 5, *An Examination of the Effects of Infection with HIV on the Patients and their Families, including Treatment*, the witness given the pseudonym 'Mark' recalled the risk of infection with AIDS being discussed at his clinic appointments, usually at the end of the appointment, from 1983–84.<sup>6</sup>

**33.8** The witness 'Elaine' said that, had her husband, 'Brian', known about the risk of HIV/AIDS from his treatment, he would not have taken Factor VIII treatment. She believed that Brian would have reverted to the old treatment (with cryoprecipitate) instead.<sup>7</sup> As detailed in paragraph 5.213 of Chapter 5, Elaine first heard of a person with haemophilia contracting HIV when she read a newspaper article while on holiday in Canada in the summer of 1984. When she discussed the article with Brian on her return home, he completely dismissed it and said that it wouldn't affect him because he was receiving blood products manufactured in Scotland from Scottish blood. It is, unfortunately, clear on the evidence that, unknown to all, Elaine's husband was already infected with HIV when she returned from Canada with the article. However, it would appear from her evidence that her husband had been aware of the risk of infection from commercial concentrates but had been advised that there was no risk, or much less risk, from SNBTS concentrate.

---

<sup>4</sup> See Chapter 5, *An Examination of the Effects of Infection with HIV on the Patients and their Families, Including Treatment*, and Chapter 6, *An Examination of the Effects of Infection with Hepatitis C on the Patients and their Families, Including Treatment*

<sup>5</sup> See Chapters 5 and 6. Frances, Elaine, Mark and Laura were the witnesses referred to.

<sup>6</sup> Mark – Day 32, page 114

<sup>7</sup> Elaine – Day 31, pages 131–132



**33.9** The witness given the pseudonym ‘Frances’ was unable to say if her father, ‘James’, was specifically warned about the risks associated with his treatment for haemophilia. James took an active interest in his treatment and liked to be kept fully informed, however,<sup>8</sup> and it seems likely that he would have asked and would have received the explanations typically received by those of Professor Christopher Ludlam’s patients who asked about HIV.

### The evidence of Professor Ludlam

**33.10** Professor Christopher Ludlam said that in 1982 very little was known about AIDS in haemophilia patients. By the end of that year a total of seven patients in the USA had been reported to have AIDS out of a population of 20,000 people with haemophilia.<sup>9</sup> He did not discuss AIDS with his patients during 1982 unless they specifically asked him about it and he did not recall there being much concern about AIDS at that time.<sup>10</sup> He said that if he had discussed AIDS in 1982 he would not have had a great deal to say to patients: all he could have said was that there was a possibility that AIDS might be transmitted by blood products.<sup>11</sup>

**33.11** He thought that by the spring of 1983 he had become convinced that AIDS was a syndrome specifically related to a transmissible agent like a virus.<sup>12</sup> There was a meeting of the haemophilia and blood transfusion working group at St Andrew’s House on 22 March 1983,<sup>13</sup> which both he and Professor Charles Forbes attended. It is clear from the minutes of the meeting that there was concern at that time that AIDS might appear in the UK.

**33.12** As the position was understood by Professor Ludlam at that time, the virus was likely to be transmitted through blood products but he did not think that his patients were at risk. It appeared to be a US phenomenon and most of the Edinburgh patients were receiving NHS concentrate manufactured from plasma collected in Scotland, where there was then no evidence of AIDS. The likelihood of the virus being in the Scottish donor pool was small.<sup>14</sup> In early 1983 he therefore did not discuss with his patients the possibility of AIDS infection, or whether they wished to continue with concentrate therapy.<sup>15</sup>

**33.13** Professor Ludlam said that he would not have initiated a discussion about switching from concentrate therapy to cryoprecipitate with patients, although if a patient had asked him he would have discussed it with them. He would have told them that switching from concentrate to cryoprecipitate would not abolish the risk of AIDS but might (or might not) reduce it. He would not have encouraged patients to switch to cryoprecipitate if they were being given home treatment with concentrate.<sup>16</sup>

**33.14** He told the Inquiry that he was not aware of any haemophilia centres in the UK where clinicians initiated discussion of a switch to cryoprecipitate with patients, although he knew of one or two haemophilia centres at which patients had asked about the use of cryoprecipitate.<sup>17</sup>

---

<sup>8</sup> See paragraph 5.125 of Chapter 5

<sup>9</sup> Professor Ludlam – Day 35, page 20

<sup>10</sup> Note of a meeting between Professor Ludlam and the Penrose Inquiry legal team [PEN.012.0774] at 0775

<sup>11</sup> Professor Ludlam – Day 35, page 18

<sup>12</sup> Ibid page 21

<sup>13</sup> Minutes of the meeting of the Haemophilia and Blood Transfusion Working Group, 22 March 1983 [SNB.001.5183]

<sup>14</sup> Note of a meeting between Professor Ludlam and the Penrose Inquiry legal team [PEN.012.0774] at 0774–75

<sup>15</sup> Professor Ludlam – Day 35, page 82

<sup>16</sup> Ibid page 26

<sup>17</sup> Ibid page 22

**33.15** Professor Ludlam was unable to recall specifically whether or not he discussed this question with any particular patient on an individual basis at that time. He thought it was possible that he did, since the issue had been raised in an interview with Dr Peter Kernoff (Director of the Haemophilia Centre at the Royal Free Hospital in London) entitled 'AIDS and haemophilia', reported in one of the Haemophilia Society Bulletins in 1983.<sup>18</sup> During that interview Dr Kernoff had been asked: 'should we stop using concentrates?' His response was:

[Y]ou have to realise that there's no treatment in medicine which doesn't have risks. In deciding to use a treatment, the risks have to be balanced against the benefits. I'm sure that you would agree with me that treatment with concentrates has massive benefits; and there's no doubt in my mind that the benefits far outweigh the possible risks. For people receiving regular treatment with concentrates, I see no reason to make any change from current practice. For particular patients, and at particular Centres, there may be reasons for preferring cryoprecipitate, but these reasons have little to do with AIDS.<sup>19</sup>

**33.16** Professor Ludlam said that if any of his patients had asked him about reducing the amount of concentrate (as distinct from changing to another form of therapy) he would have explained that his investigations into patients' immune systems (discussed below) had shown that there was nothing to suggest that using less concentrate resulted in a lower level of immune abnormalities.<sup>20</sup> By 1983–84, after the AIDS epidemic had been publicised, if a patient had said that they did not want Factor VIII he would have offered them cryoprecipitate. He would have told them, however, that he could not guarantee that cryoprecipitate was free of a putative AIDS agent and that if they wanted cryoprecipitate they would have to attend the hospital for treatment. He could not recall any conversation of that kind taking place.<sup>21</sup>

**33.17** Professor Ludlam said that he made extensive enquiries during 1983 amongst colleagues who might have seen patients with AIDS and people who might collect statistics on AIDS but that he could not find anyone who had any experience of having an individual they thought might have AIDS or who had a 'pre-AIDS' condition or 'AIDS-related complex' disease. At that time there was much less intercontinental air travel and movement of people and the population in Scotland was much more static than in North America or even England. Scotland had a very stable population of people with haemophilia but also he thought the general population was stable. For those reasons he thought the risks were small and that is what he said he told the patients if he spoke about the risk.<sup>22</sup>

### *Practice in Glasgow and south west Scotland: Glasgow Royal Infirmary*

#### **The evidence of patients at the GRI**

**33.18** The witness 'David', who gave evidence about the effects of his infection with HIV and HCV, was treated at the GRI. As detailed in Chapter 5, *An Examination of the Effects of Infection with HIV on the Patients and their Families, including Treatment*, at paragraph 5.171, he stated that he was not warned of risks of infection associated with

---

<sup>18</sup> Ibid pages 20–21

<sup>19</sup> 'AIDS and Haemophilia – An interview with Dr Peter Kernoff', *The Bulletin*, 1983 No. 1, [PEN.016.0595] at 0606

<sup>20</sup> See Chapter 21, *Haemophilia Therapy – Use of Blood Products*

<sup>21</sup> Professor Ludlam – Day 39, pages 20–21

<sup>22</sup> Professor Ludlam – Day 35, pages 22–23

his haemophilia treatment, apart from 1984 when he recalled being warned about the risk of Hepatitis A infection.

### The evidence of Professor Forbes

**33.19** Professor Forbes told the Inquiry that very early on in the progress of the HIV/AIDS story he became aware that it was a blood-borne disease probably transmitted by Factor VIII, perhaps more readily by concentrates than by cryoprecipitate.<sup>23</sup> He was unable to recall an actual date for this realisation.<sup>24</sup> He said that, because there was an element of choice of therapeutic products available, he would always discuss with his patients what he was going to do in terms of treatment. He thought that the doctors in the Haemophilia Centre at the Glasgow Royal Infirmary (GRI) would always give patients what was considered the best advice which, at that time, was that cryoprecipitate should be used.<sup>25</sup> As detailed in Chapter 21, *Haemophilia Therapy – Use of Blood Products*, at paragraph 21.316 Professor Forbes frankly admitted that his recollection was not completely reliable. During his evidence, given the passage of time and despite his best intentions, Professor Forbes was often unable to recall specific matters and he spoke of his memory being ‘defective’ in certain respects.<sup>26</sup> The Inquiry established that use of cryoprecipitate at the GRI was a small proportion of concentrate use, whether of SNBTS origin only or of mixed SNBTS and commercial origin.<sup>27</sup>

**33.20** Professor Forbes said that by 1983 most people thought that AIDS would appear in the UK in due course and that he was already starting to look differently at his patients to see if they had any of the symptoms that might be an early warning of AIDS.<sup>28</sup> Although he could not now remember it, Professor Forbes attended the meeting at St Andrew’s House already referred to at paragraph 33.11. He thought that by March 1983 he knew enough to be concerned about AIDS but not enough, even from his knowledge of the US experience, to be clear about what precisely was happening. He described it as still ‘coming up on the horizon’ at that point.<sup>29</sup>

**33.21** Professor Forbes said that patients were very aware of AIDS because it was widely talked about in the media, ‘with some hysteria’, and there was ‘a lot of anxiety’ amongst the patients.<sup>30</sup> He said, however, that ‘the bottom line’ was that the patients needed to be treated; if they did not have treatment there was a real risk that they might die from bleeding. Up until the 1970s and into the 1980s, that was the usual problem. Not treating patients in order to protect them against the supposed danger of AIDS was not an option; they had to be treated and Professor Forbes felt that he had to choose what he considered to be the safest product from all points of view.<sup>31</sup>

**33.22** He said that he told patients about the risk of AIDS and advised them to continue with treatment.<sup>32</sup> He said that the ‘sensible ones’ agreed that they had to have treatment and were usually, but not always, given cryoprecipitate.<sup>33</sup>

<sup>23</sup> Professor Forbes’ statement on information given to patients [PEN.012.0411] at 0412

<sup>24</sup> Professor Forbes – Day 33, page 97

<sup>25</sup> Ibid page 104. The UKHCDO records of the use of blood products at the Glasgow Royal Infirmary between 1982 and 1985 indicate a relatively low use of cryoprecipitate, at about 15% of the total Factor VIII material used in each year.

<sup>26</sup> Professor Forbes – Day 33, page 159

<sup>27</sup> See Chapter 21, *Haemophilia Therapy – Use of Blood Products*, at paragraph 21.313

<sup>28</sup> Professor Forbes – Day 17, pages 103–104

<sup>29</sup> Professor Forbes – Day 33, pages 100–101

<sup>30</sup> Ibid pages 102–103

<sup>31</sup> Ibid pages 101–102

<sup>32</sup> Ibid page 102

<sup>33</sup> Professor Forbes’ statement on information given to patients [PEN.012.0411] at 0412; Day 33, page 103

**33.23** Professor Forbes said that it was with some excitement that he heard that heat treatment of concentrates was a possibility in 1984. There was, however, a lot of concern about how effective this was and indeed one of the early heat-treated concentrates had transmitted virus, after which set-back it took some time to return to a degree of confidence in the heat treatment process.<sup>34</sup> As indicated in Chapter 21, use of commercial concentrate at the GRI was low in 1982, high in 1983 and very low in 1984. There was significant use in 1985 and that continued thereafter. By 1985 heat treatment of commercial Factor VIII was well established.

**33.24** It appears from his evidence that, at least initially, Professor Forbes did not discuss the possibility of using US heat-treated Factor VIII with his patients. When asked about this he said that he thought there was not enough evidence to say that the commercial heat-treated concentrates were totally safe. He also said that he was a little anxious that the heat treatment which was being proposed might in fact also destroy Factor VIII activity (the effectiveness of the concentrate to contribute to coagulation) and would make the treatment useless. That was certainly his personal view. It was only when clear evidence from studies came from the USA that he started to believe that effective heat treatment was a possibility.<sup>35</sup>

### The evidence of Professor Lowe

**33.25** Professor Gordon Lowe had relatively limited contact with haemophilia patients from 1983 to 1985 when he was on secondment to the NHS Medical Unit at the Glasgow Royal Infirmary.<sup>36</sup> He nevertheless kept an interest in haemophilia and continued to see haemophilia patients when he had the time, perhaps for a few hours a week, although he said that he saw few haemophilia patients at that time apart from treating occasional bleeds.<sup>37</sup> He said that there was increasing concern about AIDS in 1983 and 1984 and some patients did voice concerns about their treatment, but he could not recall any specific patients asking him about AIDS at that time.<sup>38</sup> He also could not recall whether he routinely raised the issue of AIDS with patients he saw.<sup>39</sup>

**33.26** Professor Lowe said that, in addition to telling the patients what he knew about the condition, he would have given them any educational material that was available and referred them to Professor Forbes or, prior to April 1983, Dr Colin Prentice (as the Director and Consultant) if they wanted more information.<sup>40</sup> He said that patients were always encouraged to ask if they had any questions about their treatment.<sup>41</sup>

**33.27** From May 1983 to December 1984 the Haemophilia Society produced a series of Bulletins and other publications on AIDS and haemophilia, including 'Haemofact' fact sheets, which provided information to patients.<sup>42</sup> Professor Lowe recalled that Professor Forbes arranged for these to be made available in the waiting room at the Haemophilia Centre and given to patients. The documents were distributed to patients, partners and families attending the Haemophilia Centre. They provided an update on the developing

---

<sup>34</sup> Professor Forbes' statement on information given to patients [PEN.012.0411] at 0412

<sup>35</sup> Professor Forbes – Day 33, page 105. Note that the use of US Factor VIII rose from 5500 units in 1984 to 381,075 units in 1985.

<sup>36</sup> Professor Lowe's statement on information given to patients concerning HIV [PEN.016.1250]

<sup>37</sup> Professor Lowe – Day 39, pages 157–159

<sup>38</sup> Professor Lowe – Day 40, page 7

<sup>39</sup> Ibid pages 6–7

<sup>40</sup> Ibid pages 5–6

<sup>41</sup> Ibid page 7

<sup>42</sup> See, for example, *Haemofact – A.I.D.S.* Release No. 2, 22 September 1983 [DHF.001.4767]

information on AIDS; gave the consistent message that, while patients should balance the risks for themselves, Haemophilia Centre Directors continued to recommend factor concentrate therapy, because the advantages of treatment far outweighed any possible risk; they stressed that patients should discuss their personal position with their Haemophilia Centre Director.<sup>43</sup>

**33.28** Professor Lowe accepted that the best way for a doctor to give information to a patient about treatment and prognosis was for the doctor to give the information directly to the patient; that had always been his belief. He agreed that it would not be acceptable for a doctor to rely on a patient getting that information from another source such as the Haemophilia Society.<sup>44</sup> However, his assessment of the likely course of events in such a discussion remained hypothetical, since he did not recall any patient ever saying that they wanted to stop treatment. Nor did he recall any patient actually stopping their treatment.<sup>45</sup>

**33.29** He thought that during review clinics there would have been a discussion about the treatment that the patient was receiving at that time and that the patients would have been asked if they had any questions about their treatment, about hepatitis and, from 1983 onwards, about AIDS.<sup>46</sup>

**33.30** Professor Lowe told the Inquiry that if a patient had raised the issue of AIDS with him in 1983 he would have told them what he then knew about the condition: that some haemophilia patients in the United States had developed the condition; that it was possibly transmitted by blood products; that knowledge about the condition was emerging and there was a lot of research going on to try and find out what the explanation for it was. He said that, from memory, the main question that patients asked at that time was whether there had been any cases in Scotland or Britain. There had not been any reported until 1984.<sup>47</sup>

**33.31** Although there were a number of GRI protocols in place from the 1970s for the treatment of patients, Professor Lowe was unable to recall any specific protocol requiring junior doctors to initiate discussion with patients about the risk of AIDS.<sup>48</sup> It seems unlikely that any such written protocol existed. He was adamant that a major decision about a patient's treatment – for example, not taking treatment at all, reducing it or changing to a different type of treatment like cryoprecipitate – should be discussed with a Consultant and said that that remained the position right up until he became a Consultant in October 1985.<sup>49</sup> It continued even after then because Professor Forbes was the Director of the Haemophilia Centre and, as such, attended all the Haemophilia Directors' meetings and was intimately involved in all the research that was being undertaken. Professor Lowe said that, while he did his best to keep up with developments, he did not have the same level of expertise as Professor Forbes.<sup>50</sup>

**33.32** Having said that, he thought that most patients were very happy to talk through the risks and the benefits of treatment with him or any of the other junior doctors and take it from there.<sup>51</sup>

---

<sup>43</sup> Addendum to Professor Lowe's evidence [PEN.018.0559]

<sup>44</sup> Professor Lowe – Day 80, page 43

<sup>45</sup> Professor Lowe – Day 40, page 18

<sup>46</sup> Professor Lowe – Day 39, page 166

<sup>47</sup> Professor Lowe – Day 40, page 13

<sup>48</sup> Ibid page 8

<sup>49</sup> Ibid pages 14–16

<sup>50</sup> Ibid page 15

<sup>51</sup> Ibid page 22

### *Practice in Glasgow and south west Scotland: Yorkhill*

#### The evidence regarding patients at Yorkhill

**33.33** The witness given the pseudonym 'Christine', who gave evidence about her son's infection with HIV, stated that she and her husband were not warned about the risk of infection with HIV or HCV. Her son was treated at Yorkhill until 1991 when his treatment was transferred to the GRI.

#### The evidence of clinicians: Professor Hann

**33.34** Professor Ian Hann's interests before moving to the Royal Hospital for Sick Children (Yorkhill) in 1983 had been in infections in patients with immune deficiencies and leukaemia and cancers associated with immune deficiencies.<sup>52</sup> Those interests had alerted him to the emerging AIDS epidemic in the United States in 1982 and clearly influenced his clinical response as information about AIDS emerged over time.

**33.35** As the new Haemophilia Director, Professor Hann inherited both stocks of therapeutic materials and a new constituency of patients to meet and become familiar with. He used up the limited existing stocks of commercial products at Yorkhill; thereafter, his treatment options were cryoprecipitate or SNBTS Factor VIII concentrate. This is reflected in the UKHCDO data on the use of clotting factors at Yorkhill over the period 1983 to 1985, as set out in Chapter 21, *Haemophilia Therapy – Use of Blood Products*, at paragraph 21.296 and Figure 21.9.

**33.36** Professor Hann said that, in response to AIDS, he and his colleagues made great efforts to speak to every single patient and offer them the possibility of stopping concentrate therapy and returning to cryoprecipitate treatment. Many patients attended the Centre regularly and he instituted a clinic and a parent support group where these issues were discussed. The Haemophilia Society was also putting out information at that time. He said that it was a matter of regret to him if some of the patients 'fell through the net' and had not been offered this change to their treatment.<sup>53</sup> Very young (and newly diagnosed) patients were usually managed as hospital-based patients.<sup>54</sup> They would be offered cryoprecipitate treatment in the first instance if it was logistically possible to give it to them (that is, if their veins were adequate and they did not have any reactions). Professor Hann said that cryoprecipitate treatment may even have been recommended as the first option for these patients in the difficult interim period.<sup>55</sup> That 'difficult interim period' lasted from May 1983 until late 1984 by which time the HTLV-III virus had been isolated and some of the patients were found upon testing to have antibody to the virus.<sup>56</sup>

**33.37** When he joined Yorkhill, most of the patients were already established on home therapy. He thought that it would have been extremely difficult, and unlikely to succeed, for home therapy to have been maintained with cryoprecipitate.<sup>57</sup> Cryoprecipitate treatment was not suitable for all patients, such as those with 'difficult veins' or those who experienced extreme allergic reactions. Professor Hann recalled that adverse reactions to cryoprecipitate, including life-threatening episodes of anaphylaxis, had been one of the

---

<sup>52</sup> See Chapter 9, *Knowledge of the Geographical Spread and Prevalence of HIV/AIDS 1*, paragraph 9.40

<sup>53</sup> Professor Hann – Day 31, page 27

<sup>54</sup> *Ibid* page 26

<sup>55</sup> Professor Hann – Day 21, pages 68–69

<sup>56</sup> Professor Hann – Day 31, pages 16–17

<sup>57</sup> Professor Hann's response to further questions from the Inquiry dated 13 April 2011 [PEN.012.0270] at 0271

reasons early attempts at establishing home treatment programmes with cryoprecipitate had been unsuccessful during the 1970s, before the introduction of factor concentrates. A return to cryoprecipitate treatment would have meant returning to hospital-based treatment and the lives of patients and their families would have changed dramatically as a result. Professor Hann recalled that the Haemophilia Society made similar observations around this time. For these reasons, most patients and families in the UK did not revert to cryoprecipitate treatment.<sup>58</sup>

**33.38** However, established patients at Yorkhill were given the option to switch to cryoprecipitate in 1983–84.<sup>59</sup> He thought that he and his colleagues would have discussed all possible therapies (including DDAVP) depending on the individual severity of the problem.<sup>60</sup> When asked whether he would have offered a child who was already receiving Factor VIII concentrate in late 1983 the possibility of ceasing concentrate therapy and returning to cryoprecipitate he said that he believed that was what they had in fact done at Yorkhill.<sup>61</sup> He said that he was almost certain that in late 1983 he did change some patients over to cryoprecipitate and that other patients, newly diagnosed or young children, remained on cryoprecipitate treatment for longer than would have been the case previously.<sup>62</sup> His recollection was that there were certainly patients in 1984 who returned to cryoprecipitate treatment for a period of time.<sup>63</sup> That is consistent with the record. UKHCDO data on product use show that use of cryoprecipitate at Yorkhill rose from 7050 units in 1982 to around 30,000 units a year from 1983 to 1985 inclusive.

**33.39** However, Professor Hann stressed that it was not a matter of automatically switching every child over to cryoprecipitate. Although there were suggestions in late 1983 – from Dr Peter Jones (Newcastle Haemophilia Centre) and the UKHCDO – that children should be treated with cryoprecipitate, the decision had to be tailored to each individual patient.<sup>64</sup>

**33.40** Professor Hann said that in early 1983 it was not clear what was causing AIDS and there was a great deal of doubt over whether it was going to become a real problem in haemophilia.<sup>65</sup> He thought that by that stage there had been reports of about eight or nine haemophilia patients who had developed AIDS in the USA; the first cases in the UK did not occur until later in 1983.<sup>66</sup> There were many meetings with other haemophilia directors during the year and his recollection was that it was not plainly obvious until the second half of 1983 that AIDS was an issue of blood product transmission in haemophilia care.<sup>67</sup> He said that it ‘sort of hit’ them later in the year that AIDS was going to be a ‘major issue’<sup>68</sup> and that it became clearer still later in 1983 or early 1984, when the first cases of AIDS were reported from Europe.<sup>69</sup>

<sup>58</sup> Professor Hann – Day 31, pages 26–27

<sup>59</sup> Professor Hann – Day 21, page 68

<sup>60</sup> Ibid page 69

<sup>61</sup> Ibid page 25

<sup>62</sup> Ibid page 27

<sup>63</sup> Professor Hann – Day 21, page 68

<sup>64</sup> Professor Hann – Day 31, page 27

<sup>65</sup> Professor Hann – Day 21, pages 32 and 64

<sup>66</sup> Professor Hann – Day 31, page 15

<sup>67</sup> Professor Hann – Day 21, page 67; Day 31, page 15

<sup>68</sup> Professor Hann – Day 21, page 67

<sup>69</sup> Ibid page 32. In fact, the first cases were reported from Europe earlier than this: see Chapter 9, *Knowledge of the Geographical Spread and Prevalence of HIV/AIDS 1*, paragraph 9.26.

**33.41** Professor Hann's approach to the provision of information was also illustrated in relation to new patients. He said that for those patients who were newly diagnosed with haemophilia he had a full discussion with their parents about the disorder and its treatment.<sup>70</sup> The main emphasis in discussion was on bleeds and how to avoid them. In addition, he would have explained what factor deficiency was, how it came about and the genetic aspect of the condition. Parents would have been told how to access the hospital social worker. There would also be a discussion about treatment, which included what it was, when it was required and what the potential side-effects were. He emphasised that the information would not be imparted in one interview; rather, the provision of information was seen as an ongoing process.<sup>71</sup> As well as the initial counselling of newly diagnosed patients, Professor Hann said that he had many discussions with patients following the initial descriptions of HIV transmission risks.<sup>72</sup> He could not recall exactly when these discussions would have taken place but thought that AIDS became a real issue during 1983.<sup>73</sup>

**33.42** He said that he would have explained what he knew at the time.<sup>74</sup> In 1983 he would have said that there had been a few cases of AIDS in haemophilia patients but that it appeared to be a 'rare risk'. He noted that even into 1984, after the prevalence of AIDS in Europe had been reported, experts like Peter Jones were quoting a transmission risk of one in 1200. He said that he hoped and believed that he and his colleagues were not just reassuring the parents but, rather, they were telling them that it was a possibility but that they did not know very much about it or what caused it.<sup>75</sup>

#### The evidence of clinicians: Dr Pettigrew

**33.43** Dr Anna Pettigrew started working at Yorkhill as a part-time Clinical Assistant in May 1980. She thought that she first became aware of the possibility that AIDS was caused by an agent transmitted by blood and blood products in 1983 but could not recall what triggered her awareness at that time.<sup>76</sup> Her recollection was that during 1983 there was a more reliable supply of SNBTS Factor VIII and the doctors at Yorkhill tried to encourage parents to use SNBTS concentrate rather than commercial concentrate.<sup>77</sup>

**33.44** As she recollected matters, the option of stopping factor concentrate altogether and moving back to cryoprecipitate was never raised with parents because of the impracticality of such a change. Dr Pettigrew said that a number of patients were established on home therapy treatment with Factor VIII concentrate before she started working at Yorkhill Hospital and before the risk of AIDS being transmitted through blood and blood products had been confirmed.<sup>78</sup> It would have been very difficult to institute home treatment with cryoprecipitate, although if parents asked about it then she would have discussed it with them.<sup>79</sup>

<sup>70</sup> Professor Hann's response to further questions from the Inquiry dated 13 April 2011 [PEN.012.0270]

<sup>71</sup> Professor Hann – Day 21, pages 65–66

<sup>72</sup> Professor Hann's response to further questions from the Inquiry dated 13 April 2011 [PEN.012.0270] at 0271

<sup>73</sup> Professor Hann – Day 21, page 67

<sup>74</sup> Professor Hann's response to further questions from the Inquiry dated 13 April 2011 [PEN.012.0270] at 0271

<sup>75</sup> Professor Hann – Day 21, pages 67–68

<sup>76</sup> Dr Pettigrew's statement on the use of blood product concentrates [PEN.015.0486]; Dr Pettigrew – Day 20, page 33

<sup>77</sup> Dr Pettigrew – Day 20, page 48. Use of SNBTS F.VIII in 1982 was 516,300 i.u. and of commercial concentrates 485,880 units. By 1984 SNBTS F.VIII use had risen to 1,035,396 units, with no commercial material purchased. The change was not a simple function of availability.

<sup>78</sup> Dr Pettigrew's statement on information to patients concerning HIV [PEN.012.0277]

<sup>79</sup> Dr Pettigrew – Day 20, pages 48–49



**33.45** She did not think that discussions about AIDS would necessarily have been recorded in the patient's medical notes because often parents called into the day bed area and she would not have had the child's notes with her. She said that she would only have had the child's notes if the child attended for medical advice or treatment.<sup>80</sup>

**33.46** When asked whether she would routinely discuss the risk of AIDS with parents even if they did not raise it themselves, she said that the majority of parents did voice concerns because they were a well-informed group and most of them were in contact with the Haemophilia Society and were therefore aware of the risk.<sup>81</sup>

**33.47** If parents voiced concerns, she told them that there was a possibility that AIDS was caused by an agent transmitted by blood but that there was no definite proof at that time. There was still a lot of debate, even among the experts, as to whether or not there was definitely an infectious agent and the advice at that time was that they should continue with therapy. She said that she would have been following the advice of her seniors at that time.<sup>82</sup> She could not recall any specific policy regarding discussing the risk of AIDS with parents.<sup>83</sup>

**33.48** She could not recall giving initial counselling to parents of newly diagnosed haemophilia patients, although she did sometimes attend such appointments. The Consultant would normally have a full discussion with parents at this time, with the main aim of these initial meetings being to ensure that the parents understood the risk of bleeding episodes. Her recollection of the meetings that she attended was that Professor Hann would recommend concentrate therapy unless the parents specifically stated that they did not want it, in which case their wishes would have been respected. She did not think that any parents did so.<sup>84</sup>

### The evidence of clinicians: Sister Christine Murphy

**33.49** Sister Christine Murphy provided evidence in a written statement. She began working in the Haemophilia Department as a part-time staff nurse in September 1983.<sup>85</sup> She told the Inquiry that when she started working at Yorkhill there was no talk about HIV although Hepatitis B was spoken about and the children were being tested for that. She said that she presumed the parents had been warned about the risks of Hepatitis B. She thought it was 1984 or into 1985 when HIV was discussed, when it appeared in the press.<sup>86</sup>

**33.50** She said that Scottish Factor VIII was used when she worked at Yorkhill. Although there was 'a bit of panic to start with about the blood products', it was explained to the parents what would happen to their child if they did not use the blood products.<sup>87</sup> She could not recall the exact words that were used but the parents were advised of the consequences of leaving bleeds untreated. They would be informed that joints could suffer irreparable damage and that any internal injuries or head injuries could be life-threatening, depending on their severity. They were also told that untreated bleeds would most likely cause problems later in life, although most parents already knew this.<sup>88</sup>

---

<sup>80</sup> Ibid page 49

<sup>81</sup> Ibid pages 45–46

<sup>82</sup> Ibid page 45

<sup>83</sup> Ibid page 46

<sup>84</sup> Ibid pages 49–50

<sup>85</sup> Sister Murphy's statement [PEN.018.1149] at 1149

<sup>86</sup> Ibid [PEN.018.1149] at 1151–52

<sup>87</sup> Ibid [PEN.018.1149] at 1153

<sup>88</sup> Ibid

**33.51** She recalled that at one point one of the parents had their child put back onto cryoprecipitate rather than Factor VIII as at that point in time the parent felt that cryoprecipitate was safer. The child had severe haemophilia so had to have some treatment for bleeds. Eventually the child was returned to Factor VIII, on the commencement of heat treatment of blood products.<sup>89</sup>

### *The wider context*

#### **AIDS and the Haemophilia Society**

**33.52** The Haemophilia Society performed two important functions in this context: it collected intelligence and data relating to what was happening to its members and it obtained and published the views and advice of medical experts. The Society was not responsible for the validity of the expert medical advice published in newsletters and fact sheets and it has to be emphasised that in narrating the evidence that follows, the Society is properly to be seen as a reporter of others' views and advice. However, what the Society put into the public domain inevitably bore the stamp of its authority among its members and helped set the context for their understanding of their condition and their expectations of the clinicians advising and treating them.

**33.53** For present purposes, it is sufficient to note events from May 1983. The first article published by the Society which provided information on AIDS, by Dr Anthony J Pinching, a noted pioneering AIDS clinician from London, appeared in *Haemophilia Society Bulletin* 2, 1983.<sup>90</sup> In the same issue, comments by Professor Bloom in a talk given to the Annual General Meeting of the Haemophilia Society in April 1983 were quoted. In respect of AIDS, he said:

I cannot end without a comment on one new problem which may turn out to be the greatest myth or the most significant reality of all.<sup>91</sup>

**33.54** Professor Bloom was then Honorary Director of the Cardiff Haemophilia Centre and Chairman of the UK Haemophilia Centre Doctors Organisation. His remarks provide a clear illustration of the extent of the uncertainty about the significance of AIDS within the medical community and, consequently, for the Society's members.

**33.55** Professor Bloom underlined his opinion in a letter he wrote in response to what had been seen as unduly alarmist reports on AIDS in the media. The letter, which was published by the Society on 4 May, contained the comment that:

[I]t is important to consider the facts concerning AIDS and haemophilia. The cause of AIDS is quite unknown and it has not been proven to result from transmission of a specific infective agent in blood products .... [W]hilst it would be wrong to be complacent it would equally be counter-productive to alter our treatment programmes radically. We should avoid precipitate action and give those experts who are responsible a chance continually to assess the situation.<sup>92</sup>

---

<sup>89</sup> Ibid

<sup>90</sup> *The Bulletin*, 1983 No. 2, The Haemophilia Society [PEN.016.0607] at 0617

<sup>91</sup> Ibid [PEN.016.0607] at 0608

<sup>92</sup> Professor Bloom's letter, issued by the Haemophilia Society, 4 May 1983 [DHF.001.4474]

**33.56** Leaving aside the media comments that had prompted the Society to approach Professor Bloom,<sup>93</sup> Mr David Watters, General Secretary of the Society between 1986 and 1994 (and Coordinator for five years before that), explained that the Society's letter was intended to reassure members that there were no known cases of AIDS in the UK haemophilia population. He was confident that the letter had been circulated in draft to members of the Society's medical advisory panel. No one expressed dissent from what was said in the letter.<sup>94</sup>

**33.57** Dr Frank Boulton, a former Deputy Director of the SEBTS who had a long and distinguished career in haematology in both Scotland and England, proposed a theory to explain the Haemophilia Society's preference for continued use of existing therapy, which included commercial products. He said:

[A]t that time, the early 1980s, I think it would be fair to say that the Haemophilia Society was very reluctant to accept the validity – they wanted the risk of nasty things from their blood products to be really proved before they would agree to reducing the availability of material for their patients.

So there was a drive from the haemophiliacs themselves, including the Haemophilia Society, to maintain the amounts of therapeutic material available.

So there was, in other words, a feeling that the risk was probably acceptable.<sup>95</sup>

**33.58** An excerpt from the transcript of his evidence was read out to Mr Watters who commented that what Dr Boulton said sounded reasonable.<sup>96</sup> He added:

I think that what he says is not too different from the attitude taken by both the Haemophilia Society and by the medical advisory panel of the Haemophilia Society. That is that people with haemophilia and the Society and the treaters were in a very difficult situation and they could either decide not to treat patients or to continue treating patients because there was no magic solution, and as such they took the judgment in the light of knowledge in those days – not in the light of knowledge in 2012 but in the light of knowledge available at that time – that it would be best to continue to treat with imported plasma products.<sup>97</sup>

**33.59** A similar view was taken by haemophilia clinicians. The Haemophilia Reference Centre Directors met on 13 May 1983 to discuss AIDS.<sup>98</sup> By that stage, as they understood it, there was one suspected case of a haemophilia patient suffering from AIDS in the UK. The importance of immediate reporting of any suspected cases was stressed so that the clinical course of the patient could be followed and a definitive diagnosis of AIDS attached if the patient developed intractable disease, at that time the sole criterion for a positive diagnosis in the UK (applying the definition of AIDS adopted by the US Centers for Disease Control). General treatment policy was discussed and it was agreed that there was, at that point, insufficient evidence to warrant restriction of the use of imported concentrates in patients other than children and mildly affected haemophilia patients, in view of the immense benefits of therapy.

---

<sup>93</sup> See Chapter 10, *Knowledge of the Geographical Spread and Prevalence of HIV/AIDS 1*, at paragraphs 9.83 to 9.88

<sup>94</sup> Mr Watters – Day 87, pages 64–72

<sup>95</sup> Dr Boulton – Day 24, page 39

<sup>96</sup> Mr Watters – Day 87, page 105

<sup>97</sup> Mr Watters – Day 87, page 109

<sup>98</sup> Minutes of Special Meeting of Haemophilia Reference Centre Directors, 13 May 1983 [DHF.001.4384]

**33.60** The Haemophilia Society's medical panel and the Reference Centre Directors collectively represented the views of senior, and eminent, UK haemophilia clinicians. Other experts may have taken different views, as noted below, but a balanced assessment of the position was given by Professor Andrew Lever. He emphasised that around mid-1983 there were competing hypotheses as to the cause of acquired immunodeficiency in patients, some of which had powerful advocates. He thought that the balance of evidence at that stage was in favour of an infectious agent.<sup>99</sup> He continued:

However, as one knows, the amount of distress and concern and worry, sometimes unnecessarily, that you can induce in people by raising the fear of an infectious agent in something like a blood product would be undesirable unless it was absolutely the case, or as near certain as you could be that that was the case.

I think people would not necessarily have been very understanding had this turned out to be a false alarm and individuals had either bled or died by withdrawal of the clotting factors and then it having been found that there was not the threat which had been assumed.<sup>100</sup>

### The evidence of Dr Winter

**33.61** Some haemophilia clinicians took the same view of the cause of AIDS as Professor Lever. Dr Mark Winter discussed his experience in England. He was appointed Consultant Haematologist at the Canterbury and Thanet Health Authority in 1983, and thereafter managed haemophilia patients throughout his career. In 1984 he was designated HIV physician for the area and was responsible for all patients who had AIDS. For the rest of his career he specialised in AIDS. He was also the medical officer appointed by the Department of Health (DoH) to serve on the MacFarlane Trust and the Eileen Trust.<sup>101</sup>

**33.62** With this background, Dr Winter was in a position to speak from first-hand experience about developments in the response to AIDS during the reference period. His contact with haemophilia patients had begun before 1983 while he was a Senior Registrar at Guy's Hospital, London where he discussed with his patients the risk of contracting the new virus. He would explain that there were worrying data which suggested that a new virus might be transmitted by concentrates but that, on balance, the advice was to continue with treatment because the risk of giving up treatment was greater.<sup>102</sup>

**33.63** Due to policy decisions in England and Wales, Dr Winter did not have ready access to NHS concentrates in his Kent centre, and largely had to rely upon licensed commercial concentrates of US origin.<sup>103</sup> By 1984 he and his colleague, Professor Savidge (St Thomas' hospital) had concluded that NHS Factor VIII concentrates not only transmitted NANB Hepatitis but also probably contained the new virus.<sup>104</sup> In May 1984 heat-treated concentrate from the USA became available on a named patient basis and he managed to obtain a small supply of the product.<sup>105</sup> The heat treatment was intended to destroy viruses including

---

<sup>99</sup> Professor Lever noted that by this stage HTLV-I had been implicated in human disease, targeting lymphocytes; that AIDS was associated with dysfunction of the lymphocytes; and that there were similarities in epidemiology, among factors suggesting an infectious aetiology.

<sup>100</sup> Professor Lever – Day 26, page 92

<sup>101</sup> Dr Winter – Day 15, pages 42–45

<sup>102</sup> Dr Winter – Day 16, pages 150–151

<sup>103</sup> See Chapter 21, *Haemophilia Therapy – Use of Blood Products*, paragraphs 2.262–63

<sup>104</sup> Dr Winter's submission to the Archer Inquiry [PEN.015.0283] at 0286

<sup>105</sup> Dr Winter – Day 16, page 107

NANB Hepatitis and HIV. That same month, he approached a small number of patients with mild haemophilia who required major surgery, or who had suffered acute trauma, and had received little or no Factor VIII concentrate in the past. He offered them a choice between the currently available licensed, unheated NHS concentrate, prepared from voluntary donations, or the new, unlicensed, heat-treated Alpha Therapeutics concentrate prepared from paid donations.<sup>106</sup> He advised his patients to take the new American product in preference to the licensed, unheated US product and the unheated NHS concentrate.<sup>107</sup>

**33.64** He described it as an especially critical and difficult time because patients were being asked to switch from concentrate of UK origin to concentrate of US origin which they had always distrusted. He told the Inquiry that considerable time had to be spent with each patient and their family to explain the basis of this recommendation.<sup>108</sup> He thought that he would have spent about half an hour with each patient.<sup>109</sup>

**33.65** During these meetings he conveyed the following information to the patients:

- There was increasing evidence that AIDS could be transmitted through the use of Factor VIII concentrate which was a matter of growing concern.
- There was a new type of Factor VIII concentrate which was heat-treated and therefore in theory might inactivate the (very recently discovered) virus that caused AIDS. There was however no proof of this at that stage.
- There was strong evidence that patients were likely to get hepatitis from unheated NHS Factor VIII concentrate if they did not already have it and that it might also contain the new virus that was causing AIDS.
- The new heat-treated commercial Factor VIII was designed to inactivate hepatitis viruses.
- The new heat-treated commercial Factor VIII came from US blood donors and was not licensed in the UK.<sup>110</sup>

**33.66** Many of the patients he approached instinctively resisted his advice, relying on their long-held belief that UK concentrates were safer than US concentrates. In the event, all agreed to the use of the heat-treated product.<sup>111</sup> By July 1984 he was able to get sufficient supplies of the heat-treated Factor VIII and the heat-treated Factor IX, to switch all of his haemophilia patients to whichever product they required. From 1 July 1984 the St Thomas' centre and Dr Winter's centre in Kent used, exclusively, heat-treated concentrate.<sup>112</sup>

**33.67** On the evidence available to the Inquiry, the practice described by Dr Winter was followed in a few centres only. The majority of treating doctors in the UK in 1984 continued using unheated NHS Factor VIII rather than switching to imported, heat-treated commercial Factor VIII. Dr Winter said that to the best of his knowledge, only the centres in Sheffield, University College Hospital, St Thomas' and Canterbury made the decision to switch to heat-treated commercial Factor VIII in May 1984. The decision was criticised at this time at meetings of the UKHCDO by other Directors who thought that viral transmission of the HIV/AIDS virus through the use of concentrate derived from voluntary UK donors was unlikely.<sup>113</sup>

---

<sup>106</sup> Dr Winter's submission to the Archer Inquiry [PEN.015.0283] at 0286

<sup>107</sup> Dr Winter's statement [PEN.015.0292] at 0299

<sup>108</sup> Dr Winter's statement [PEN.015.0292] at 0299

<sup>109</sup> Dr Winter – Day 16, page 154

<sup>110</sup> Ibid pages 152–153

<sup>111</sup> Ibid pages 152–154

<sup>112</sup> Ibid page 106

<sup>113</sup> Dr Winter's statement [PEN.015.0292] at 0299

**33.68** In his evidence Dr Winter noted<sup>114</sup> that what he did was contrary to what Professor Bloom had said a year earlier in the letter of 24 June 1983<sup>115</sup> about heat-treated commercial product.

#### Developing UKHCDO advice: 1984

**33.69** The UKHCDO response to imported heat-treated Factor VIII had, meantime, moved forward. On 29 March 1984, Professor Bloom sent a memorandum to all UK Haemophilia Centre Directors advising on the appropriate response to proposals by commercial companies to trial new heat-treated products.<sup>116</sup> The memorandum listed different types of Factor VIII concentrate available for trial at that time, with another about to become available:

- (1) Heated products from Armour, Cutter, Travenol and Alpha Therapeutics. The three former are 'dry heat' preparations and the latter (Alpha Therapeutics) is a wet heat product.
- (2) NHS factor VIII prepared from a specially selected donor panel which is monitored for abnormal LFT's, hepatitis etc.
- (3) Heated NHS factor VIII; one brand is manufactured at the PFC in Edinburgh and will be shortly available. The second, manufactured at Elstree, should be available later this year.
- (4) A heated preparation manufactured by Behringwerke ....<sup>117</sup>

**33.70** The memorandum noted that clinical trials had already been completed on one product, the 'Hemofil HT' Factor VIII concentrate which was prepared using a dry heat method. The results indicated that there was still a 63% attack rate of NANB Hepatitis on first exposure in patients who had not received Factor VIII concentrate previously. The memorandum also noted that all products except those derived from NHS Factor VIII were made from plasma imported from the USA and therefore carried a putative risk of transmission of AIDS. The memorandum did not comment on the approach to be adopted in dealing with patients who might be appropriate subjects for clinical trials. That was left to individual practitioners.

**33.71** Professor Ludlam was not willing to participate in the trials<sup>118</sup> as he thought that there was nothing to be lost and the possibility of a lot to be gained by not using the heat-treated product.<sup>119</sup> Professor Ludlam told the Inquiry that he did not discuss the possibility of using heat-treated commercial Factor VIII (as part of a clinical trial or on a named patient basis) with his patients because he did not think it was in their best interests. He considered that not only would the trials have exposed them to concentrate that was likely to contain hepatitis, but also the product was derived from a donor population that appeared to have HTLV-III and at that stage there was no evidence that heat treatment would inactivate it.<sup>120</sup> Effectively, therefore, Professor Ludlam took the opposite view to Dr Winter at this time. The Inquiry recognises the logic of each position in its context.

---

<sup>114</sup> Dr Winter – Day 16, page 109

<sup>115</sup> Professor Bloom's letter of 24 June 1983 [SGH.002.2175]

<sup>116</sup> Professor Bloom's memorandum to Haemophilia Centre Directors dated 29 March 1984 [DHF.002.8963] at 8964

<sup>117</sup> Ibid [DHF.002.8963] at 8963

<sup>118</sup> Letter from Professor Ludlam to Miss Spooner, UKHCDO, dated 10 April 1984. [SNF.001.3211]

<sup>119</sup> Professor Ludlam – Day 39, page 8

<sup>120</sup> Ibid pages 8–10

## Haemophilia Society publications 1984–85

**33.72** Haemophilia Society publications continued to provide information and advice on treatment, backed by eminent practitioners. In Bulletin 1, 1984, K E Milne wrote:

We have no evidence as yet to whether AIDS may be acquired more readily from commercial Factor VIII than from the NHS product but, of course, if AIDS becomes established in the UK then NHS blood and plasma supplies are just as likely to transmit AIDS as commercial materials. All things considered, haemophiliacs have no reason to be worried about using commercial concentrates.<sup>121</sup>

**33.73** Having regard to the date of publication, and Dr Winter's evidence about supply, this was probably written shortly before the first heat-treated products began to be available. The comment was sustainable only on the assumption that there was no choice whether to have therapy and that the sole question was which form to use. That was a universally held assumption amongst clinicians at the time.

**33.74** It was reflected in the views of haemophilia staff and of the mothers of haemophilia patients when they were expressed in Bulletin 1 of 1985:

All blood products cannot be guaranteed free of the viruses associated with hepatitis and other disorders such as AIDS. However, the minimal risks associated with this treatment are in our opinion outweighed by the advantages of using these products which ensure our children do not grow up crippled.<sup>122</sup>

## Product inserts

**33.75** In the course of the Oral Hearings there was discussion of the function of the leaflets containing information on risks of concentrates, which leaflets were prepared by the SNBTS and issued with products manufactured by the PFC, Liberton.<sup>123</sup> The information was brief and, if it had been directed to patients, was less than comprehensive. A series of questions specific to HIV/AIDS were drafted by Messrs Thompsons for answer by Dr Robert (Bob) Perry relating generally to the period 1982–85. In this part of the discussion, it is appropriate to deal with the period to 1984.

**33.76** Dr Perry explained that the formal product documentation issued by the SNBTS was prescribed by regulatory standards and pharmacopoeia monographs in force at the time. He referred to the British Pharmacopoeia Monograph on dried Factor VIII fraction.<sup>124</sup> The leaflets were included in the packages issued to patients, especially those on home treatment. However, at the material time, manufacturers were not permitted or expected to engage in direct contact with patients.<sup>125</sup> Until 1984 the regulatory requirement was for Technical Information Labels only and the SNBTS leaflets were directed at health care professionals and were primarily intended for prescribing doctors.<sup>126</sup> Until 1984 (and indeed later), the leaflets were not an appropriate vehicle for providing information to

---

<sup>121</sup> *The Bulletin*, 1984 No. 1, The Haemophilia Society [PEN.016.0623] at 0624

<sup>122</sup> *The Bulletin*, 1985 No. 2, The Haemophilia Society [PEN.016.0631] at 0636

<sup>123</sup> *Hepatitis Risk Warnings*, SNBTS [PEN.012.0286]

<sup>124</sup> Dr Perry's statement in response to questions on SNBTS package inserts [PEN.018.0543] at 0547

<sup>125</sup> *Ibid* [PEN.018.0543] at 0544; Dr Perry – Day 38, pages 95–96. The position changed in 1994 when Patient Information Leaflets became a legal requirement.

<sup>126</sup> Dr Perry's statement in response to questions on SNBTS package inserts [PEN.018.0543] at 0544

patients and were not prepared for that purpose.<sup>127</sup> In 1994 it became a legal requirement to provide product information leaflets specifically for patients. The SNBTS then issued appropriate patient information with PFC products.<sup>128</sup>

**33.77** While this necessarily limited Dr Perry's attempts to answer the specific questions drafted by Messrs Thompsons, the questions were important to the patient core participants and it is appropriate to set out his evidence. The questions specific to HIV/AIDS related to:

- Discussions between staff about the possibility of including reference to the risk of HIV transmission on package inserts included with factor concentrates between 1982 and 1985.
- Why and by whom it was decided that there should be no reference to the risk of HIV transmission in PFC factor concentrate package inserts between 1982 and 1985.
- From whom the PFC staff took advice about the risks of transmission of HIV via PFC concentrates between 1982 and 1985.
- The advice given to the PFC over that time period about the risk of HIV transmission from PFC factor concentrates.
- Whether there was awareness within the PFC of the fact that US products had such warnings on their inserts from around October 1983.
- To what extent such awareness impacted upon the attitudes of PFC staff to include such a warning on their factor concentrate inserts.

**33.78** The virus, originally LAV/HTLV-III and renamed HIV in 1986, was not generally understood to be the causal agent of AIDS until Dr Gallo announced in the spring of 1984 that he had discovered the virus.<sup>129</sup> Consequently, the relevant period begins, at the earliest in the spring of 1984. Dr Perry's attempt to answer the first question in terms was not productive. He could not recall if he discussed the possibility of including HIV warnings in PFC product inserts with Mr Watt, the PFC Director in 1982 and 1983, and he did not know if Mr Watt had discussed that possibility with any others at the SNBTS.<sup>130</sup> Dr Perry led a review of packaging systems for PFC Factor VIII and IX in 1982–83 but product warnings remained unchanged.<sup>131</sup>

**33.79** In answer to the second question, Dr Perry said that he had been advised by Dr Peter Foster that the inclusion of such an HIV warning had been rejected at a meeting in 1983. The SNBTS has found no record of this.<sup>132</sup> Dr Perry pointed out that PFC products were produced for use by a small group of haemophilia doctors who were well informed about the situation concerning AIDS. He expressed the view that the amendment by the SNBTS of its product leaflet to include an unquantifiable risk warning would have done little to enhance doctors' knowledge or their communications and discussions with patients, especially as the topic of AIDS was being widely discussed by haemophilia doctors.<sup>133</sup> The Inquiry subsequently took statements from Dr Foster and Professor John Cash on this point.

---

<sup>127</sup> Inevitably some witnesses read the leaflets as if they were addressed to patients. However, criticism of their terms on that basis was misconceived.

<sup>128</sup> Dr Perry's statement in response to questions on SNBTS package inserts [PEN.018.0543] at 0544

<sup>129</sup> As discussed in Chapter 9 *Knowledge of the Geographical Spread and Prevalence of HIV/AIDS 1*, Montagnier's discovery of LAV in 1983 was not widely recognised at the time.

<sup>130</sup> Dr Perry's statement in response to questions on SNBTS package inserts [PEN.018.0543] at 0544

<sup>131</sup> *Ibid* [PEN.018.0543] at 0545

<sup>132</sup> *Ibid*

<sup>133</sup> *Ibid* [PEN.018.0543] at 0546



**33.80** In his statement, Dr Foster said that he remembered attending a meeting on 14 November 1983<sup>134</sup> when Professor Cash proposed that a product warning about AIDS should be added to the leaflets issued with PFC concentrates. However the haemophilia doctors were generally against that proposal because such a warning would cause ‘unnecessary anxiety to patients’. He also stated that the Haemophilia Directors believed that there was little or no risk of AIDS being transmitted by PFC products.<sup>135</sup> In his statement<sup>136</sup> Professor Cash agreed in general terms with the recollections of Dr Perry and Dr Foster but recalled that his proposal had, in fact, referred to hepatitis warnings rather than to AIDS. He thought that after one of his trips to Australia he proposed that a hepatitis risk warning should be included. The proposal did not enjoy much support and a legal opinion was sought by Jim Donald (CSA General Manager). No risk warning was included.

**33.81** Dr Perry explained that the PFC did revise its product leaflets in April 1985 when FVIII NY (Factor VIII heat-treated at 68°C for 24 hours) was introduced. The revised leaflet and package label stated: ‘the freeze dried product has been heat treated but cannot be assumed to be non infective’. He explained that the term ‘non-infective’ was intended to encompass all potential blood-borne infections, including HIV/AIDS. In addition, when the new heat-treated Factor IX product, DEFIX, was issued in October 1985 it stated:

In addition, product, plasma pools and individual donations are tested for the presence of antibody to HTLVIII. The product has been heat treated at 80°C for 72 hours in the freeze dried state. This treatment is expected to inactivate viruses associated with the Acquired Immune Deficiency Syndrome.<sup>137</sup>

**33.82** Dr Perry explained that he had been unable to find any evidence of a process whereby individuals had discussed the merits of the introduction of AIDS warnings. Prior to 1985, product information supplied by the PFC/SNBTS reflected the background of knowledge and guidance available between 1982 and 1984. He stressed that, prior to 1984, there was no consensus on a causal relationship between AIDS and treatment with coagulation factor concentrates. The inclusion of such warnings in product literature required some measure of evidence that a genuine risk existed. The inclusion of warnings could cause anxiety to patients who may have read the leaflets and might have caused them to reject life-saving treatment.<sup>138</sup>

**33.83** In answer to the fourth point, Dr Perry explained that there were various discussions and meetings involving the SNBTS and government health departments and other regulatory bodies but he did not recall that this produced any guidance or advice. The PFC maintained an awareness of international developments through its network of professional and scientific contacts and regular discussions with haemophilia directors and SNBTS experts such as Dr Boulton and Professor Cash.<sup>139</sup>

**33.84** Dr Perry mentioned that an application for a licence for the PFC product FVIIIINNY made in 1983 to the Committee on the Safety of Medicines included a product insert leaflet which made no mention of HIV or AIDS. The application was approved. He considered that this indicated that the Committee did not expect leaflets issued with

<sup>134</sup> Minutes of the meeting of the Haemophilia and Blood Transfusion Working Group on 14 November 1983 [SNB.001.5188]

<sup>135</sup> Dr Foster's response to Dr Perry's statement [PEN.018.1147]

<sup>136</sup> Professor Cash's response to Dr Perry's statement [PEN.018.1145]

<sup>137</sup> Dr Perry's statement in response to questions on SNBTS package inserts [PEN.018.0543] at 0545

<sup>138</sup> Ibid [PEN.018.0543] at 0546

<sup>139</sup> Ibid [PEN.018.0543] at 0547

plasma products derived from UK donors to carry warnings about AIDS. He stated that 'The PFC received no subsequent request or advice from the Licensing Authority ... to include AIDS warnings'.<sup>140</sup>

**33.85** Dr Perry did not recall the PFC receiving any specific advice or guidance concerning the risk of transmission of HIV/AIDS by its products. Even with the benefit of hindsight, he thought it was difficult to identify what advice could have been given to the PFC which could have been translated into warning statements.<sup>141</sup>

**33.86** In relation to North America, Dr Perry's attention was drawn to a passage from page 399 of the Report of the Commission of Inquiry on the blood systems in Canada (the Krever Commission) which mentioned that US fractionators included warnings about the risk of AIDS to the information in the product inserts.<sup>142</sup>

**33.87** Dr Perry commented that the quotation related to concentrates prepared from plasma collected in the USA. Page 400 of the Krever report noted that, although Cutter Laboratories did include warnings with its products prepared from US plasma, it did not provide such warnings in 1984–85 with products derived from plasma collected in Canada. Dr Perry suggested that the fact that the same company was adopting different positions in relation to the origin of the plasma indicated that the risk of AIDS was still considered to be primarily associated at that time with plasma collected in the USA from paid donors.<sup>143</sup>

**33.88** He explained that, although product literature from commercial companies was periodically received at the PFC, he was unable to recollect the extent to which these documents would have been examined at the time, either by him or other senior PFC colleagues. He would have been aware that products carried warnings of product infectivity but he could not recall if he was aware of specific AIDS or HTLV-III warnings.<sup>144</sup>

**33.89** He said he had been unable to find evidence for the precise time when mandatory AIDS warnings were universally required. His understanding was that different manufacturers adopted them at different times. He explained that when it became clear, in October 1984, that there was a risk from SNBTS products, 'we quickly issued heated NY product (68°/2hr) and subsequently modified the leaflet for inclusion with the later FVIII product (NY 68°/24hr)'.<sup>145</sup>

**33.90** In answer to the final question, Dr Perry responded that he could not recall any discussions amongst PFC staff, or with Professor Cash or Dr Boulton, concerning the introduction of AIDS warnings in PFC product inserts. He believed that the general view held by the PFC, the SNBTS and the Haemophilia Directors was that the epidemiology of AIDS in the US, and particularly amongst US paid donors, was quite different from that in the UK.<sup>146</sup>

**33.91** Dr Perry provided evidence on information leaflets enclosed in packages of PFC products from 1978. The exploration of these questions has not provided the Inquiry with relevant information on the topic of communications with patients and their families in

---

<sup>140</sup> Ibid [PEN.018.0543] at 0548

<sup>141</sup> Ibid [PEN.018.0543] at 0548

<sup>142</sup> Krever Commission (1997) *Final Report: Commission of Inquiry on the blood system in Canada* Available: [http://epe.lac-bac.gc.ca/100/200/301/hcan-scan/commission\\_blood\\_final\\_rep-e/](http://epe.lac-bac.gc.ca/100/200/301/hcan-scan/commission_blood_final_rep-e/) Last accessed 8 October 2014.

<sup>143</sup> Dr Perry's statement in response to questions on SNBTS package inserts [PEN.018.0543] at 0548–49

<sup>144</sup> Ibid [PEN.018.0543] at 0549

<sup>145</sup> Ibid [PEN.018.0543] at 0549–50

<sup>146</sup> Ibid [PEN.018.0543] at 0550

relation to HIV/AIDS save in one respect. It is clear from the evidence of Dr Foster, Professor Cash and Dr Perry that, notwithstanding that there was no legal requirement, SNBTS officers discussed modification of the information documents to include warnings related to AIDS (and additional warnings related to hepatitis). Discussions in 1983 were clearly influenced by the views of haemophilia clinicians. Their views primarily reflected their own understanding of risk and their practice in relation to the provision of information, and have been dealt with in the course of this chapter. The concerns expressed were substantially those identified by Professor Lever in paragraph 33.60.

**33.92** So far as the questions posed relate to the provision of information to patients about risks of transmission of HIV, the contents of the SNBTS product inserts do not raise, or provide a focus for, new issues relating to clinical practice in the period to 1984.

### **The testing of patients' blood samples**

**33.93** Two specific issues of some importance arise in relation to the testing of haemophilia patients' blood samples in the period to 1984. The first of these relates to studies carried out in Glasgow and Edinburgh of changes in the immune functions of patients receiving concentrate therapy. Questions arise whether the studies were directly associated with patient management (in which case they might at some stages in developing ethical theory have been considered to be 'therapeutic' research) or were research studies more broadly defined that required ethical consent from an appropriate regulatory research body, and in either case whether patient consent to the use of their blood was required. The second issue relates to testing carried out on stored samples of patients' blood or serum in the late autumn of 1984 following the development of the first assays for anti-HTLV-III. The question arises whether patient consent was required for these tests. There are then consequential questions that extend over some years following the receipt of the results of the tests that relate to the communication of test results to patients and the information and advice that was appropriate in the light of individual patients' results. To set the context for the discussion, it is necessary first to discuss practice relating to the routine testing of patients' blood over the period to 1984.

#### ***Routine blood tests to 1984: practice in Scotland***

**33.94** Throughout the material period, routine testing of coagulation disorder patients' blood for identifiable infections and for biometric indications of the progression of their primary condition and of possible infections was common in Scotland, as elsewhere, as an aspect of patients' general management. Use of stored samples of haemophilia patients' blood for comparison, or to enable a full assessment of a patient's condition to be made and reviewed, was routine.

**33.95** Testing procedures were not static throughout the period, however. Routine testing inevitably changed as knowledge of the natural history of infectious diseases and of the risks of transmission of infection increased. Similarly, the technology available to assess risks and to respond to the implications for patients improved throughout this period. It is important to bear this background in mind as doctors were confronted by what were clearly, with the benefit of hindsight, new risks of transmission of viral infection and by the technology developed to identify and respond to those risks. In an ever-changing environment of therapy and patient management, what is truly new, requiring a step change in practice, may not necessarily appear so at first sight. In this, as in other areas, the scope for variation in clinical practice makes it necessary to look at practices in individual centres separately.

## Edinburgh and south east Scotland

**33.96** Professor Ludlam said that the Edinburgh Haemophilia Centre had a long tradition, starting in the 1960s and 1970s, of systematically studying the bleeding patterns of patients with haemophilia. It was among the first centres to assess hepatitis infection and the risks of virus transmission with the initial studies on Hepatitis B virus (HBV) infection.<sup>147</sup> Blood was taken for testing when patients attended at review clinics for scheduled sessions, for out-patient treatment of acute bleeds, or when patients had been admitted to hospital. While not necessarily carried out on every attendance, taking blood samples for testing was a routine procedure associated with what became the long-term systematic assessment of the viral safety of treatment. Testing of samples to monitor patients' conditions was carried out in a laboratory in the Department of Haematology.<sup>148</sup>

**33.97** The frequency of a patient's attendances depended on their clinical situation. For example, in the early 1980s, when cryoprecipitate was generally used in treating patients at the hospital, those with severe haemophilia might attend the treatment room two or three times a week where they would be seen, reviewed and treated. If they had not been reviewed for a while or if there was something unusual about their clinical state, blood samples would be taken for review or to investigate why they were unwell.<sup>149</sup> Other patients, such as those on home treatment, might only be seen for review every three or four months provided there were no problems. Part of their regular review would involve taking blood samples for routine monitoring.<sup>150</sup>

**33.98** Professor Ludlam explained the routine for taking blood. About a tablespoon of blood (15 millilitres) was taken.<sup>151</sup> Although not a great quantity of blood, the procedure was nonetheless significant: the patient understood the process although perhaps not the precise range of tests then carried out. Professor Ludlam said that a sample would be taken for a full blood count, assessment of blood chemistry (for example, urea and electrolytes and liver function tests), assessment for the presence of inhibitors (resistance to Factor VIII treatment) and assessment for viral infection.<sup>152</sup> He said:

It was important to make sure that the patient's haemoglobin and white [cell] count and platelets were in the normal range .... [O]ne of the complications, particularly of the early Factor VIII concentrates, was they contained antibodies to red cells and so you could get destruction of the red cells and hence anaemia.

The other reason for checking the haemoglobin was that sometimes patients had silent bleeding into their gastrointestinal tract. That was not uncommon. So this was a way of being alerted to that possibility.<sup>153</sup>

---

<sup>147</sup> Professor Ludlam's note on long term safety monitoring for transfusion-transmitted infections [PEN.012.0351]. These practices probably began under Professor Ludlam's predecessor, Dr Davies; see Professor Ludlam's note on the development of the Edinburgh Haemophilia and Thrombosis Centre [PEN.012.0386] at 0395

<sup>148</sup> Professor Ludlam's note on long term safety monitoring for transfusion-transmitted infections [PEN.012.0351] at 0351–52; Note of a meeting between Professor Ludlam and the Penrose Inquiry legal team [PEN.012.0774] at 0777; Professor Ludlam's note on the development of the Edinburgh Haemophilia and Thrombosis Centre [PEN.012.0386] at 0388

<sup>149</sup> Professor Ludlam – Day 35, page 7; Note of a meeting between Professor Ludlam and the Penrose Inquiry legal team [PEN.012.0774] at 0777

<sup>150</sup> Professor Ludlam – Day 35, pages 7–8

<sup>151</sup> Note of a meeting between Professor Ludlam and the Penrose Inquiry legal team [PEN.012.0774] at 0777–78

<sup>152</sup> Professor Ludlam's note on long term safety monitoring for transfusion-transmitted infections [PEN.012.0351]

<sup>153</sup> Professor Ludlam – Day 35, pages 5–6

**33.99** At the laboratory a full blood count of the different types of cells in the patient's blood was carried out. This was a useful test for providing an overview of a patient's general state of health.<sup>154</sup> Testing monitored the patient's total white cell count and the number of different white cells (polymorphs, eosinophils, monocytes and lymphocytes) in the samples. These measurements were routinely made and recorded without reference to the patient for consent.

**33.100** Professor Ludlam said that in the 1980s he did not obtain explicit consent from his patients for each individual test.<sup>155</sup> At that time he relied on implied consent. When a patient came for their routine visit they were used to having blood taken for tests that were deemed to be necessary for monitoring their health.<sup>156</sup> It is very likely that the same practice was followed in many clinics, and for many diseases, throughout the UK at that time. He stated that his practice in this regard had changed (as indeed it had for medical practitioners generally):

I did not go through each individual investigation, like I think I would now. Times have changed and I would [now] very clearly go through [and] list the tests in the case notes and make a note that the patient agreed to these investigations.<sup>157</sup>

#### **Practice in Glasgow and south west Scotland: the Glasgow Royal Infirmary**

**33.101** Practice at the GRI was similar to that in Edinburgh: monitoring blood tests were undertaken as part of routine attendance at the clinic. Blood samples for monitoring were also taken from patients attending for treatment of acute bleeds and from patients who had been admitted to hospital.

**33.102** Professor Forbes said that from about 1987 patients were asked for specific consent before testing but that often before that time they were not. In his experience, seeking consent to carry out tests came in gradually.<sup>158</sup>

**33.103** When asked what obtaining specific consent involved he said:

I think the important thing is that you are telling patients what is going to happen and why it's to happen and to ask their consent for it to happen. This was very much a change in the ethos of medicine. Until then the implication was that if you went to a doctor with a problem, he would do his best to find the cause of it, without asking your consent for blood samples or whatever, and that was how things were at that time.

I'm not saying that's the right thing because I think that now clearly it is not the right thing, and I think that before one does very much to people, there has to be implied consent and if you are doing anything invasive, like blood samples or endoscopy, you actually have to tell them exactly what you are doing, what it will find for them and what you can do about it and that is implied [sic – specific] consent and often [it] is now written down and that is certainly safer.<sup>159</sup>

---

<sup>154</sup> Professor Ludlam's note on long term safety monitoring for transfusion-transmitted infections [PEN.012.0351]

<sup>155</sup> Note of a meeting between Professor Ludlam and the Penrose Inquiry legal team [PEN.012.0774] at 0779

<sup>156</sup> Professor Ludlam – Day 35, page 60

<sup>157</sup> Ibid page 60

<sup>158</sup> Professor Forbes' statement on information given to patients [PEN.012.0411] at 0413

<sup>159</sup> Professor Forbes – Day 33, pages 123–124

**33.104** At the material time for present purposes, up to 1984, there was clearly no practice of obtaining patient consent to any specific tests carried out on the blood taken from patients on a routine basis in the centres in Edinburgh and the GRI.

*Immunological studies: Edinburgh and south east Scotland*

**33.105** Professor Ludlam said that, by the spring of 1983:

[I]t was becoming clearer that there was [sic] some strange things happening to the immune system of people with haemophilia. A number of reports in the medical press of immune abnormalities in patients with haemophilia who were otherwise feeling well. It was – the interpretation that you could put upon those that was puzzling us. I would say that similar abnormalities were shown in gay men who were otherwise feeling well. And the question is in fact: were all these ... individuals in the United States already infected with a latent, if you like, AIDS virus?<sup>160</sup>

**33.106** The background is set out in Chapter 9, *Knowledge of the Geographical Spread and Prevalence of HIV/AIDS 1*, and Chapter 11, *HIV/AIDS Aetiology*. Until 1983 there had been very few reports of AIDS in haemophilia patients. Most reports of AIDS related to homosexual men and drug users. In patients with clinical AIDS, immune tests revealed a severe deficiency of T-helper (CD4) and an increase in T-suppressor (CD8) lymphocytes, together with disturbance in the normal ratio of CD4:CD8 cells. Many homosexual men who had no symptoms suggestive of AIDS were also found to have similar immune abnormalities although in milder form.<sup>161</sup> A letter highlighting immune abnormalities in haemophilia patients in the USA was published in *The Lancet* on 30 April 1983.<sup>162</sup>

**33.107** These findings led to studies being undertaken in the USA to assess the immune status of apparently well, asymptomatic haemophilia patients. The initial studies demonstrated that many asymptomatic haemophilia patients had immune abnormalities similar to those found in asymptomatic homosexuals. The cause of the immune abnormalities was unclear and it was uncertain whether they were progressive. As with homosexual men, there were, at the outset, a number of possible explanations apart from an 'AIDS virus' for the abnormal immune test results found in haemophilia patients. In his statement, Professor Ludlam explained that the cause of the immune changes might have been related to the widespread prevalence of an 'AIDS virus' or due to some side effect of Factor VIII treatment or it might even have been a previously unreported feature of the condition of haemophilia.<sup>163</sup> For him, the finding in 1982–83 of immune abnormalities in asymptomatic haemophilia patients in the USA was 'perplexing and worrying'.<sup>164</sup>

**33.108** With the possibility that some US haemophilia patients had apparent immune dysfunction which might have been related to their treatment, might have been progressive and might lead to an AIDS state, Professor Ludlam sought the help of a colleague, Dr C. M. Steel, at the Medical Research Council Unit at the Western General Hospital in Edinburgh, to investigate the possibilities. They decided to monitor the immunological status of some

---

<sup>160</sup> Professor Ludlam – Day 35, page 21

<sup>161</sup> Professor Ludlam's note on long term safety monitoring for transfusion-transmitted infections [PEN.012.0351] at 0352

<sup>162</sup> Gordon, 'Factor VIII products and disordered immune regulation', *The Lancet*, April 30 1983 [LIT.001.0911]

<sup>163</sup> Professor Ludlam's note on long term safety monitoring for transfusion-transmitted infections [PEN.012.0351] at 0352

<sup>164</sup> Professor Ludlam – Day 35, pages 33–34

of Professor Ludlam's patients. This was called the 'AIDS study' and these words were written on forms used for requesting blood to indicate that the sample should be sent to Dr Steel for further analysis.<sup>165</sup>

### The 'AIDS study'

**33.109** Professor Ludlam approached Dr Steel around January or February 1983. He thought it took a few weeks to negotiate what they wanted to do and that the first blood samples were probably sent to Dr Steel's laboratory around March 1983.<sup>166</sup> The earliest available evidence known to the Inquiry of blood being taken for the 'AIDS study' is a haematology form so annotated and dated 14 March 1983.<sup>167</sup>

**33.110** In his laboratory, Dr Steel established a facility using specific antibodies to measure by microscopy the proportion of CD4 and CD8 lymphocytes in patients' blood. When patients attended the haemophilia clinic for review or for treatment, blood taken for routine investigations would be sent to the Haematology Laboratory in the Royal Infirmary of Edinburgh (RIE) as normal. There the full blood count would be assessed in the usual way by the haematologists except that instead of counting 100 white cells under the microscope to quantify the different types of white cells, as was usual, 200 cells were counted to obtain a more accurate estimate of the number of lymphocytes. Lymphocytes only constitute a relatively small proportion, approximately 15–25%, of the total number of white cells. Counting a larger number of total white cells made it more likely that a 'precise estimate' of the number of the lymphocytes was obtained before proceeding to divide the number of cells further into CD4 and CD8 lymphocytes.<sup>168</sup>

**33.111** No extra blood was taken for the lymphocyte studies. The same sample was processed and analysed by the RIE Haematology Laboratory and by the Western General Hospital, Edinburgh.<sup>169</sup> Once the Haematology Laboratory had counted the 200 cells, the same blood samples were then couriered to Dr Steel's laboratory, where the proportions of CD4 and CD8 lymphocytes were assessed. By this means it was possible to measure the proportion of each type of lymphocyte in the blood, as well as their absolute number.<sup>170</sup>

**33.112** Professor Ludlam said that he did not specifically select particular individuals for study. The patients studied were attending the clinic for review or for treatment of an acute bleed and needed to have blood taken for their routine monitoring. He said that all the patients would have been seen by either himself or one of his Registrars. It had been agreed between Professor Ludlam and his Registrars that if blood was being taken from patients it would be assessed for lymphocytes. That would have arisen out of discussion, probably initiated by Professor Ludlam.<sup>171</sup>

---

<sup>165</sup> Professor Ludlam's note on long term safety monitoring for transfusion-transmitted infections [PEN.012.0351] at 0352–53

<sup>166</sup> Professor Ludlam – Day 35, page 39

<sup>167</sup> RIE Haematology Report [WIT.001.1491]

<sup>168</sup> Note of a meeting between Professor Ludlam and the Penrose Inquiry legal team [PEN.012.0774] at 0777–78; Professor Ludlam – Day 35, page 43; Professor Ludlam's note on long term safety monitoring for transfusion-transmitted infections [PEN.012.0351] at 0352.

<sup>169</sup> Professor Ludlam – Day 35, page 44

<sup>170</sup> Ibid pages 36–37; Professor Ludlam's note on long term safety monitoring for transfusion-transmitted infections [PEN.012.0351] at 0352–53; Note of a meeting between Professor Ludlam and the Penrose Inquiry legal team [PEN.012.0774] at 0777–78

<sup>171</sup> Professor Ludlam – Day 39, page 30; Note of a meeting between Professor Ludlam and the Penrose Inquiry legal team [PEN.012.0774] at 0779

**33.113** There may well have been patients who attended the clinic but did not have blood taken for the 'AIDS study'. Samples were taken from patients with severe and moderate haemophilia because they were the patients who had received large quantities of factor concentrates. Professor Ludlam said that if a patient with mild haemophilia attended the clinic they might not have sent a sample of their blood to Dr Steel because the patient might not have had any blood product treatment at all in their life. Even amongst patients with severe and moderate haemophilia, Professor Ludlam said that he might not have needed to take blood from them for other routine reasons and, in that case, he would not have taken blood just to do these tests. It also probably depended to some extent on the time of day a patient was seen. Because the samples had to be ferried across from the RIE to the Western General and processed the same day, if a patient came in late in the afternoon the technicians may not have put that sample through for the lymphocyte assessment due to time constraints.<sup>172</sup>

**33.114** Professor Ludlam estimated that 50–70% of his patients had samples taken from them for the purposes of the 'AIDS study' over the 'next little while'.<sup>173</sup> Data published in the follow-up article in *The Lancet* on 30 June 1984 were derived from samples from a smaller cohort, 47 individuals, around 25–30% of his patients.<sup>174</sup>

#### Characterisation of the 'AIDS study'

**33.115** Professor Ludlam told the Inquiry that he did not obtain ethical approval for the 'AIDS study' because he considered it to be an extension of routine monitoring of his patients and not medical research. He considered that the lymphocyte studies became part of the general monitoring of patients for potential adverse effects of therapy in 1983: if the CD4 and CD8 cells could have been distinguished visually in the routine haematology laboratory procedures, there would have been no need to send them to Dr Steel.<sup>175</sup> He said:

We viewed this endeavour as part of our obligation to monitor people with haemophilia .... [I]t was my responsibility to monitor patients for side effects of therapy ....

And as immune abnormalities had been demonstrated in apparently well haemophiliacs in the United States, it seemed appropriate that I should assess our patients here in Edinburgh, to see whether they had any immune abnormalities. This was something completely new and important as part of the monitoring process.<sup>176</sup>

**33.116** This led to discussion of the proper characterisation of the study, in light of accepted ethical rules at the time. Professor Ludlam distinguished the 'AIDS study' described above from a later extension of his study of the immune functions of his patients in 1984 – the 'skin test' series of investigations. It is important to compare and contrast his approach to the two studies in considering the position he adopted.

---

<sup>172</sup> Professor Ludlam – Day 39, pages 28–30

<sup>173</sup> Professor Ludlam – Day 35, Pages 58–59

<sup>174</sup> Carr et al, 'Abnormalities of circulating lymphocyte subsets in haemophiliacs in an AIDS-free population', *The Lancet*, 30 June 1984 [LIT.001.0425]

<sup>175</sup> Professor Ludlam – Day 39, pages 32–33

<sup>176</sup> Professor Ludlam – Day 35, pages 44–45



## Skin tests

**33.117** The skin tests were carried out after the lymphocyte studies and provided another immune function measurement. Professor Ludlam said that he wanted to look at the patients in a 'rather more holistic way' and that the skin tests assessed many more aspects of the functioning of the immune system than counting the CD4 and CD8 cells.<sup>177</sup>

**33.118** Professor Ludlam sought and obtained ethical approval for the new test by writing to the RIE Ethics Committee and explaining what he wanted to do. In particular, he sought approval to ask patients with haemophilia and about 15 or 20 controls if he could use a commercially available 'Merieux multitest' device on their forearm to measure their immune system to try and better define the apparent immune deficiency that had been shown up by the CD4 and CD8 counts.<sup>178</sup> Professor Ludlam's letter dated 3 May 1984 seeking approval is not available but the skin tests were approved by the Ethics Committee by letter dated 24 May 1984.<sup>179</sup> The letter, from Dr de Bono, is entitled, 'Skin tests in patients with congenital bleeding disorders'. It states that Dr de Bono considered that it would be 'perfectly in order to proceed with the tests outlined in your letter'.

**33.119** The 'multitest' device was a much more holistic way of testing the immune system than measuring the CD4 and CD8 counts. Professor Ludlam thought that 20 or 30 patients were tested in this way. Although some of the patients may have been asked to attend the clinic for this purpose, he thought that it was likely to have been more opportunistic: he probably asked patients who were attending the clinic for review, for treatment or to collect home treatment if they would mind volunteering.<sup>180</sup>

**33.120** Professor Ludlam told the Inquiry that patient consent was obtained before the skin tests were done.<sup>181</sup> He did not think that the patients' consent was recorded in their notes, however, and there was no record of any written consent for blood tests obtained at that time.<sup>182</sup> He said that he obtained verbal consent which is what he had been asked to do by the ethics committee.<sup>183</sup>

**33.121** Professor Ludlam said that he explained to patients what the skin tests involved. It was slightly invasive and it inconvenienced the participants because they had to come back to the clinic two days later.<sup>184</sup> He said that he would have told patients that he was testing their skin because the reactions that he could measure reflected the way in which the immune system was working. He was certain that he would have told the patients that this was part of a study into the lowering of the immune system of haemophilia patients in Edinburgh.<sup>185</sup>

**33.122** When asked what the difference between carrying out the skin tests and carrying out the investigation of CD4/CD8 counts was from a consent point of view, Professor Ludlam said:

---

<sup>177</sup> Professor Ludlam – Day 39, pages 35–36

<sup>178</sup> Ibid page 38; Note of a meeting between Professor Ludlam and the Penrose Inquiry legal team [PEN.012.0774] at 0779–80

<sup>179</sup> Dr de Bono's Letter [LOT.001.4972]; Day 39, pages 37–38

<sup>180</sup> Professor Ludlam – Day 35, pages 66–67; see also Note of a meeting between Professor Ludlam and the Penrose Inquiry legal team [PEN.012.0774] at 0779

<sup>181</sup> Professor Ludlam – Day 35, page 67

<sup>182</sup> Note of a meeting between Professor Ludlam and the Penrose Inquiry legal team [PEN.012.0774] at 0780

<sup>183</sup> Professor Ludlam – Day 39, page 37

<sup>184</sup> Professor Ludlam – Day 35, pages 67–68

<sup>185</sup> Professor Ludlam – Day 39, pages 36–37

[T]he skin tests, involved something being done to the patient. It was invasive ... and it wasn't quite as clear what we might gain out of this. So it was a much more speculative investigation compared with the CD4/CD8 counts.<sup>186</sup>

**33.123** Whether or not the line drawn between steps taken in 'monitoring patients' on the one hand and research on the other was correctly drawn, or was indeed fully rationalised at the time, is not clear. What is clear is that when his studies of the immune functions of his patients crossed what he perceived to be the line between routine management and research he sought ethical approval for what he proposed to do.

**33.124** Some witnesses who were part of the AIDS study only found out that they were part of it when they recovered their medical records at a later date. From their perspective, a study was carried out on their blood samples and details of the study subsequently published in *The Lancet* without their consent or knowledge. Professor Ludlam said that he believed that he had implied consent to 'monitor' his patients by testing their blood for immunological abnormalities as part of general monitoring. Patients were used to blood tests being taken for various purposes. He did not require fresh blood samples for the study.<sup>187</sup>

**33.125** He told the Inquiry that he was sure that he would have explained to those people who were part of the immune studies, commenced in 1983, that there was a very new condition called AIDS about which very little was known and that there was a possibility that it might be spread by blood products. He thought that he would have tempered that by saying that the risk to patients in Edinburgh was minimal as they had received only Factor VIII prepared from plasma collected from donors in Scotland and at that time there were no cases of AIDS in Scotland.<sup>188</sup>

**33.126** It would have been understandable if his position in evidence had been that the study was no more than a preliminary investigation, that he did not set out systematically to inform patients about the study, that some may have got information about the study by asking questions or casually from observing documents but that he could not express any view as to the proportion of those in the study who knew about it. Unfortunately, the evidence became rather confused as Professor Ludlam sought to explain how patients would or might have become aware that the study was being carried out. The problem began with notations on the haematology request forms.

### Haematology request forms

**33.127** Professor Ludlam explained that there was a routine haematology request form in use at the RIE. The form started off beside the patient and went with the patient's blood sample to the laboratory. Normally the form did not go to Dr Steel but was returned to the haemophilia centre once routine haematology had been completed.<sup>189</sup> The haematology forms accompanying samples destined for Dr Steel had the words 'AIDS study' written on them.<sup>190</sup> That informed the haematology laboratory of the need to count 200 cells and send the sample on to Dr Steel. Professor Ludlam was referred to one of the forms and he explained how the form was filled out and what the various data recorded on it represented.<sup>191</sup>

---

<sup>186</sup> Professor Ludlam – Day 35, page 68

<sup>187</sup> Note of a meeting between Professor Ludlam and the Penrose Inquiry legal team [PEN.012.0774] at 0779

<sup>188</sup> Professor Ludlam – Day 35, page 22

<sup>189</sup> Ibid page 43

<sup>190</sup> Extract from medical records [WIT.004.0800]

<sup>191</sup> Professor Ludlam – Day 35, page 42

**33.128** The labelling of the samples as ‘AIDS study’, intended as a form of shorthand to identify them for processing in Dr Steel’s laboratory, was, as Professor Ludlam put it, ‘unfortunate’.<sup>192</sup> This was later to give rise to suspicion on the part of some patients that he was carrying out experiments on his patients. In the view of this Inquiry, that suspicion is entirely without foundation. In oral evidence, Professor Ludlam said:

We weren’t studying AIDS, we were assessing CD4 and CD8 lymphocytes, but we were doing that because of the reports of immune abnormalities in people with haemophilia from the United States, who were well but had abnormal lymphocyte counts ....

And a few patients with haemophilia in the US developed AIDS .... The overall topic, the umbrella topic was ... AIDS ....

Subsequently it emerged much later on, when one or two patients asked for... copies of their case notes and they saw these report forms in the case notes, they wondered whether, I think, we had undertaken some sort of AIDS – some sort of different AIDS study, whether we had given people AIDS, whether we had given patients concentrates, clotting factor concentrate, that we knew was infected with an AIDS virus. One story that came to me was that we had put HTLV-III into bottles of clotting factor concentrate, heat-treated them and then given it to the patients to see whether the heat treatment was effective.<sup>193</sup>

**33.129** The emergence of these suspicions appears to be an important link in the chain of events which has led to this Inquiry. This is a matter to which the Inquiry will return.

**33.130** These anecdotes emerged after the event and cast doubt on the extent to which patients knew of the study at the time it was carried out. However, as the evidence emerged, it became clear that the form was the first possible intimation to patients that they were involved in the ‘AIDS study’. Professor Ludlam explained:

[T]o make sure that they were correctly carried out in the laboratory, I labelled the blood forms “AIDS Study”. These would be forms that would be handed to patients to get their blood taken and, you know, patients could read it. So I must have explained something about AIDS because I wouldn’t write “AIDS Study” on a form, which I then either handed to the patient or was sitting in front of the patient while they were having their blood taken, without some explanation.<sup>194</sup>

**33.131** When patients attended the review clinic at the Medical Out-patient Department there would be an opportunity to discuss what investigations were being carried out as the doctor was talking to the patient. Professor Ludlam thought that the doctors would have explained to their patients why the immune studies were being done at the point of completing the form. He thought that they would have said that there had been reports from North America of a few haemophilia patients developing AIDS and they were keen to do some tests to assess the immune function of patients at the Edinburgh Haemophilia Centre, who they did not think had been affected by whatever the AIDS agent was.<sup>195</sup> Professor Ludlam told the Inquiry that the staff at the Haemophilia Centre were keen for

---

<sup>192</sup> Note of a meeting between Professor Ludlam and the Penrose Inquiry legal team [PEN.012.0774] at 0778

<sup>193</sup> Professor Ludlam – Day 35, Pages 49–50

<sup>194</sup> Ibid page 19

<sup>195</sup> Professor Ludlam – Day 36, page 7

patients to know about the immune function studies and that doctors had 'no inhibitions' about writing 'AIDS study' on the request forms which were then given to patients.<sup>196</sup>

**33.132** The patient would take the form (possibly along with one or two other routine monitoring forms) into another room and give it to a nurse who would take the blood sample. Professor Ludlam noted that until that time it had generally been deemed to be a doctor's responsibility to take blood and that the RIE haemophilia clinic was one of the first in which nurses were able to take blood.<sup>197</sup> Sometimes the patient would have to sit in a queue with other patients and wait for the nurse with the form in their hands.<sup>198</sup> After drawing the sample, the nurse would put the tube containing the blood sample into a polythene bag along with the request form and put it out for a porter to collect and take to the laboratory.<sup>199</sup> Professor Ludlam thought that at that time the polythene bags had two compartments to them, with the blood sample put into one compartment and the request form put into the other before the bag was then sealed. Professor Ludlam was certain that the request form was not wrapped around the sample in case the sample leaked and the tube and form were covered in blood.<sup>200</sup> Professor Ludlam stated that patients will generally examine forms if they are given to them: 'if you give them forms, they read them'.<sup>201</sup>

**33.133** He said that his Registrars and the nurses in the centre worked as a team and had agreed the approach described. He therefore thought that it was very likely that the nurse taking the blood would have told the patient about the study, although he did not think that he would have formally instructed them to do so. He accepted that it was an 'informal', although not 'casual', arrangement.<sup>202</sup>

**33.134** Samples were also taken from in-patients, such as those admitted for the treatment of an acute bleeding episode. In such cases, on occasion the forms would have been completed the previous day because the ward doctor would have a lot of patients to go round and take blood from: it was quicker if the forms were all made out in advance.<sup>203</sup> The form would be taken to the patient's bedside and the sample taken and put in the polythene bag and sent off to the laboratory in the manner described above. The completed request form would often be put down next to the patient who would be able to read the request form while the blood was being taken.<sup>204</sup>

**33.135** If a patient had not been seen for a while or if there was something unusual about their clinical state, blood samples would be taken to investigate their condition. All samples would be taken when the patient was treated: the centre staff did not take blood for investigation and then puncture patients again later for treatment.<sup>205</sup>

**33.136** Professor Ludlam could not recall any written protocol for taking blood samples within the Haemophilia Centre or the hospital generally. He thought 'custom and practice' dictated procedures.<sup>206</sup>

---

<sup>196</sup> Professor Ludlam – Day 35, page 54

<sup>197</sup> Professor Ludlam – Day 36, page 6

<sup>198</sup> Ibid page 3

<sup>199</sup> Professor Ludlam – Day 35, page 51

<sup>200</sup> Professor Ludlam – Day 36, page 2

<sup>201</sup> Professor Ludlam – Day 35, page 58

<sup>202</sup> Ibid Pages 55–56

<sup>203</sup> Professor Ludlam – Day 36, pages 3–4

<sup>204</sup> Professor Ludlam – Day 35, page 51

<sup>205</sup> Ibid page 7

<sup>206</sup> Professor Ludlam – Day 36, page 5

**33.137** Professor Ludlam referred to a letter from Dr John Tucker, Consultant Haematologist at the Borders General Hospital, dated 11 January 2006, which explained the process of taking blood from patients. The letter states:

When patients were inpatients the medical staff completed the request forms and obtained verbal consent which included explaining the need for the samples. They would then draw the sample. This was my practice and I would expect that my colleagues behaved in the same way. Certainly no additional samples would be taken if the patient were to express any reservation or objection. In 1984 we were monitoring immune function of haemophilia patients and used the shorthand notation of 'AIDS study' when taking surveillance specimens. Again patients were aware of this practice when taking immune surveillance samples.<sup>207</sup>

**33.138** In her statement, Sister Billie Reynolds, who worked in the Edinburgh Haemophilia Centre from 1988, said that blood was usually taken first and then the label for the sample would be completed. She also said that she would be asked for samples by Professor Ludlam's Registrar. She would be told simply to tell the patient that the sample was 'for research'. Some patients would consent readily, while others would ask what the research was. If she did not know, she would refer the patient to the doctor who had requested the sample.<sup>208</sup>

**33.139** As the narrative of this evidence indicates, it would have been altogether simpler to have told patients directly and explicitly that studies in the USA had suggested that concentrate therapy might be associated with changes in patients' immune systems, that it was important to find out whether similar changes were happening in patients treated with SNBTS products and, if they were, to consider how best to deal with the situation. Professor Ludlam suggested that, up to a point, an approach along these lines had been taken.

**33.140** Professor Ludlam said that he was not trying to keep the immune tests secret. He said that patients knew that he had an interest in monitoring the safety of clotting factor concentrates. He thought that the patients were aware that the immune function tests were being carried out.<sup>209</sup> When asked whether the patients knew whether they were involved in the 'AIDS study' at the time, however, Professor Ludlam said that he was not sure if they all knew:

I can't assure you that every patient understood exactly what was done but we were making it clear that we were doing this.<sup>210</sup>

**33.141** He said that it was possible that not all patients were told about the 'AIDS study' but he considered that at least some were told, although he was unable to estimate how many patients that might have been.<sup>211</sup>

---

<sup>207</sup> Dr Tucker's letter to Professor Ludlam dated 11 January 2006 [PEN.018.1567]

<sup>208</sup> Sister Reynolds' affidavit [PEN.018.0810] at 0820-21

<sup>209</sup> Professor Ludlam – Day 35, page 57

<sup>210</sup> Ibid page 55

<sup>211</sup> Ibid page 57

**33.142** However, he also said that he was not surprised that some patients did not understand that they were being involved in an AIDS study:

I think it's not always possible to convey ... information ... to people. They may have forgotten they had been told. We may not have told them. This was part of the monitoring of patients that was my responsibility ... if we had asked them exactly what was happening to the full blood counts that we had been doing for years they might be a bit vague and the same for the chemistry tests, and this was just another test that was important – it was something ... new, but it was my responsibility to do this and to see what the results were.<sup>212</sup>

### Findings of the immune function studies

**33.143** Professor Ludlam said that it was observed from the initial studies in 1983, to great surprise, that the pattern of lymphocyte abnormalities in Edinburgh patients was similar to those observed in the USA; yet none of the individuals had any symptoms or signs suggestive of AIDS. As the majority of patients had only received blood components or products prepared from Scottish blood donors, and there were at that time no AIDS cases in Scotland, it seemed rather unlikely to Professor Ludlam that the lymphocyte changes were due to a possible ubiquitous AIDS virus. The cause of the immune changes in the Edinburgh patients was unknown but there were a number of possible explanations related to the underlying condition of haemophilia and its treatment. It was thought to be imperative to monitor the patients because, if the immune changes were becoming progressively more abnormal, there might be a risk of their developing opportunistic infections (such as *Pneumocystiscarinii* pneumonia or Kaposi's sarcoma) which were characteristic of AIDS.<sup>213</sup>

**33.144** Patients were only advised of the results of the lymphocyte studies if they asked.<sup>214</sup> Professor Ludlam accepted that, since at least some of the patients were not aware that they were being studied, those patients could not have asked for their results.<sup>215</sup> He said that he did not take any steps to advise patients of the results because he did not know how to interpret them. He was, he explained, 'perplexed' by the findings of the study and was not sure what their clinical significance was. The clinicians had expected them to be normal. They were themselves uncertain as to what the results might mean and it did not seem helpful to go back and pass on the information to the patients.<sup>216</sup>

**33.145** Professor Ludlam said that he was also a little hesitant because the technology that they were using was not what would be used today:

It doesn't have the high degree of sophistication for counting numbers of cells ... we counted cells manually. It's a very imprecise way, particularly when there are small numbers of lymphocytes.

So the results didn't seem to have the same degree of precision as I would have liked and I think these were not standard laboratory tests for which there were well defined normal ranges ....

This was not, and couldn't be at that stage, well quality controlled.<sup>217</sup>

---

<sup>212</sup> Ibid page 56

<sup>213</sup> Professor Ludlam's note on long term safety monitoring for transfusion-transmitted infections [PEN.012.0351] at 0353

<sup>214</sup> Note of a meeting between Professor Ludlam and the Penrose Inquiry legal team [PEN.012.0774] at 0780

<sup>215</sup> Professor Ludlam – Day 35, page 81

<sup>216</sup> Ibid 78; Note of a meeting between Professor Ludlam and the Penrose Inquiry legal team [PEN.012.0774] at 0780

<sup>217</sup> Professor Ludlam – Day 39, pages 14–15

**33.146** The results of the lymphocyte tests carried out were initially recorded on paper records.<sup>218</sup> Professor Ludlam explained:

It was much later in fact, when we were moving hospitals, that we were tidying up and came across a box of these and one of my staff said, 'Well, what do we do with these?' I was told all the information was in the computer so should we not just throw them out? And I thought, 'Well, it's part of the clinical record, we should put it back in [the] case notes ....' so they were added very much later, about 2003.<sup>219</sup>

**33.147** He explained that they were not part of individual patients' case notes from the beginning because they had the information on computer along with a lot of other information. The forms had to be kept while they were waiting for the results to come back from the Western General and they did not all come back at the same time so they accumulated in a box. Professor Ludlam explained that when AIDS 'became more of an anxiety' there emerged a desire not to put such information in patients' case notes.<sup>220</sup>

**33.148** Three aspects of this evidence cause particular difficulty in classifying the immune studies as 'monitoring' of patients' immune systems. Firstly, the request forms referred to the exercise as a 'study'. The exercise was limited in scope, and did not involve structured follow-up or sequential studies of the patients. Secondly, the suggestion that comparison with contemporary technology made Professor Ludlam 'hesitant' about the investigation is irrelevant to the perception at the time: later technological developments could not have been anticipated in any but the most general of terms. Publication on the assumption that later technology might undermine the conclusions of the study is an unlikely occurrence. Thirdly, and perhaps most significantly, omitting the forms and results from patients' case notes inevitably meant that the information was not available to clinicians and others consulting the notes unless they had been involved in the study and knew of the existence of an independent record. Thus far, the evidence tends to support the notion that the 'AIDS study' was research.

#### Publications in *The Lancet*, May 1983 and June 1984

**33.149** Professor Ludlam told the Inquiry that, as he had data showing abnormalities in his patients with haemophilia, who had been treated with blood products collected in a non-AIDS country but which were similar to those highlighted in US patients in the letter in *The Lancet* on 30 April 1983,<sup>221</sup> it seemed important to submit the data for publication. He considered that the report would offer alternative explanations, other than widespread infection by a putative virus causing AIDS, for the immune abnormalities observed in US haemophilia patients.<sup>222</sup>

**33.150** A preliminary report of Professor Ludlam's findings was published in *The Lancet* on 28 May 1983.<sup>223</sup> The study related to samples from 23 patients with severe haemophilia and von Willebrand's disease who had only received SNBTS Factor VIII, Factor IX or cryoprecipitate in the past five years. All were clinically well.

---

<sup>218</sup> Note of a meeting between Professor Ludlam and the Penrose Inquiry legal team [PEN.012.0774] at 0776

<sup>219</sup> Professor Ludlam – Day 35, page 40

<sup>220</sup> Ibid pages 40–41; Note of a meeting between Professor Ludlam and the Penrose Inquiry legal team [PEN.012.0774] at 0776

<sup>221</sup> Gordon, 'Factor VIII products and disordered immune function', *The Lancet*, 30 April 1983 [LIT.001.0911]

<sup>222</sup> Professor Ludlam's note on long term safety monitoring for transfusion-transmitted infections [PEN.012.0351] at 0353

<sup>223</sup> Ludlam et al, 'Disordered immune regulation in haemophiliacs not exposed to commercial Factor VIII', *The Lancet*, 28 May 1983 [LIT.001.0416]

**33.151** This preliminary report was followed up by a more detailed description of the observations in a further article in *The Lancet* on 30 June 1984.<sup>224</sup> By this stage samples from 47 patients (including the 23 patients sampled previously) had been taken.<sup>225</sup>

**33.152** It is clear from the reports of these studies that as late as June 1984, Professor Ludlam had formed, and continued to hold, the view that something other than a putative AIDS virus, associated with possible 'antigen overload', was causing immune abnormalities in some at least of his patients, similar to but less severe than those associated with AIDS. He did not discuss the antigen overload theory with his patients because it was not clear what should be done if that was the cause of the apparent immune dysfunction.<sup>226</sup>

**33.153** Later, by analysing stored samples retrospectively, it was shown that at the time the samples had been analysed the patients were all negative for anti-HTLV-III. The changes in distribution of lymphocyte cells that were observed and reported in the published article were not associated with viral infection. However, retrospective examination also showed that, by the time the paper was published on 30 June 1984, some of the patients included in the study had become infected with HTLV-III in the interval.<sup>227</sup>

**33.154** Professor Ludlam said that reporting the results of his monitoring of the patients was not limited to the 1983–84 publications describing lymphocyte abnormalities:

[T]his stretched on into ... the [Edinburgh] cohort.<sup>228</sup> It was new information that came out of examining the immune systems of these patients. So it was new information. In that sense it was research but I would call it "new information" – if I had not published it, it would have been monitoring. I don't see that it necessarily becomes research because I have published it. In a sense it's what we might call these days an "audit".<sup>229</sup>

**33.155** This answer added to the difficulty of accepting that the study was properly characterised as 'monitoring' of the patients. New information is, perhaps invariably, what one hopes to derive from research. Until it is published, it remains unpublished research. It is difficult to understand how a decision to withhold new information from publication of itself transforms it into monitoring of patients. It is less difficult to envisage a situation in which new information derived from research becomes relevant to monitoring as part of the follow-up of the patient: it might be hoped that would be normal. That would not, however, change the character of the exercise from which the new information was derived.

### *Immunological studies: the Glasgow Royal Infirmary*

**33.156** Immunological studies were also carried out in Glasgow. In contrast to practice in Edinburgh, Glasgow patients were exposed to a mixture of blood products, including imported concentrates. In this respect the context for the study was different.

---

<sup>224</sup> Carr et al, 'Abnormalities of circulating lymphocyte subsets in haemophiliacs in an AIDS-free population', *The Lancet*, 30 June 1984 [LIT.001.0425]

<sup>225</sup> Professor Ludlam – Day 35, page 75

<sup>226</sup> Professor Ludlam – Day 35, pages 82–83

<sup>227</sup> *Ibid* page 77

<sup>228</sup> For discussion of the 'Edinburgh cohort' see Chapter 10, *Knowledge of the Geographical Spread and Prevalence of HIV/AIDS 2*, from paragraph 10.16

<sup>229</sup> Professor Ludlam – Day 35, pages 63–64



**33.157** Like Professor Ludlam, Professor Forbes said that early in 1983 a variety of investigations had shown evidence that haemophilia patients who had received multiple transfusions of Factor VIII and Factor IX concentrates had immunological abnormalities. Professor Forbes and his colleagues therefore undertook to look at their own patients to see if any abnormalities were occurring in them as a result of concentrate infusion.<sup>230</sup> The minute of the meeting of the haemophilia and blood transfusion working group at St Andrew's House on 22 March 1983 already mentioned, indicates that Dr Forbes (as he then was) was conducting a study of the immunological status of haemophilia patients at that time.<sup>231</sup>

**33.158** He and his colleagues were able to show that there was indeed suppression of immunological function in their patients. Again in common with Professor Ludlam, it was not clear to Professor Forbes at the time that the suppression was necessarily due to the transfusion of blood products over a period of time. Although that was certainly felt to be a possibility there was some doubt. He explained that there might have been something else happening at the time to cause immune suppression, apart from a ubiquitous AIDS-causing virus, that they did not know about. He and his colleagues were cautious about drawing their conclusions.<sup>232</sup>

**33.159** In Glasgow, blood samples were taken specifically for the immunological study. The patients all knew about the study because they volunteered to give blood and all of the tests were carried out on fresh blood samples, although the patients were not informed in great detail of the implications of the study. It was not clear to Professor Forbes himself what the implications might be.<sup>233</sup> He said that patients were asked if they would mind giving a sample of blood, that they were going to look at some immunological tests and required fresh blood samples to look at their cells and see if there was anything happening that they should know about. Professor Forbes said that it was probably mostly himself who asked the patients for samples, although Dr Madhok and Professor Lowe may also have asked.<sup>234</sup>

**33.160** Dr Froebel, who had participated in the running of the study, could not remember the exact date it had commenced, although she thought it was in 1982 when she moved into the new Department of Medicine research laboratory at the GRI.<sup>235</sup> She was a post-doctoral research fellow at the time, working on the cellular immunology of rheumatoid arthritis. Soon after the move, Professor Forbes approached her about a new syndrome of immune deficiency that appeared to be affecting, among others, patients with haemophilia in California. She responded by saying that apart from one assay (the 'natural killer assay') which she thought that she would be able to develop, she was already able to apply all of the other tests that were used on the Californian patients. She suggested testing samples from 10 patients to see if there were any similarities. In the end she carried out numerical immunological tests, for proportions of lymphocyte sub-populations, and functional tests, looking at T cells and natural killer cells, for their response to mitogens and their natural killer activity, on samples from 19 patients.<sup>236</sup>

---

<sup>230</sup> Professor Forbes' statement on immunological testing in Glasgow [PEN.012.1328]

<sup>231</sup> Minutes of the meeting of the Haemophilia and Blood Transfusion Working Group, 22 March 1983 [SNB.001.5183] at 5185

<sup>232</sup> Professor Forbes – Day 33, pages 109–110

<sup>233</sup> Professor Forbes' statement on immunological testing in Glasgow [PEN.012.1328]; Day 33, pages 109–110

<sup>234</sup> Day 33, pages 109–111

<sup>235</sup> Dr Froebel's statement on immunological testing in Glasgow [PEN.012.1628]

<sup>236</sup> Dr Froebel's statement on immunological testing in Glasgow [PEN.012.1628]. Dr Froebel's statement refers to testing 17 patients, whereas the published paper discussed below refers to 19 patients, 17 with Haemophilia A and two with Haemophilia B.

**33.161** After the study was completed the results and implications of the results were not communicated to the patients. Professor Forbes said that he was not sure if he knew that there were implications or, if there were, what they meant:

I don't think we understood what was really happening. We were able to show that using these particular tests, no matter how primitive they were, there was something happening and it seemed to be associated with the amount of material given to them.

Whether it was a direct effect of some component of the blood products given, we weren't clear. So this was very much a preliminary paper, suggesting that there were immunological abnormalities. What they meant, I don't think at that time we knew, and I'm not sure that we even know at this time.<sup>237</sup>

### Publication

**33.162** An article by Dr Froebel and others entitled, 'Immunological abnormalities in haemophilia: are they caused by American Factor VIII concentrate?' was published in the *BMJ* on 15 October 1983.<sup>238</sup> The article reported the study of cellular immunity in the group of 19 haemophilia patients at the GRI referred to above. These 19 patients were all treated at the Haemophilia Centre at the GRI and all had received different treatments over the preceding years.

**33.163** Table 1 of Dr Froebel's paper showed a significant difference between the patients and the controls. She had presented it a meeting of the Scottish Medical Society, she thought, in the spring of 1983 and it was published soon after as an extended abstract in the *Scottish Medical Journal (SMJ)*. She thought the *SMJ* paper was the first report in the UK of what was later understood to be HIV/AIDS.<sup>239</sup>

### Consent to publication

**33.164** Professor Ludlam told the Inquiry that patient consent to publish was not obtained for his papers. He did not think that it would be necessary because the results were anonymised.<sup>240</sup> It never occurred to him to get the patients' consent because that was not usual practice when patients were not identifiable from the information published and there was no information in the two publications that would allow the identification of any individual patient: it was group data. He thought that it would have been unusual at that time to go back to the patients and say 'these are the results, we would like your permission to publish them'. If he was going to publish a case report on an individual who might be identifiable then he would have discussed his intentions with the patient, explained why it was interesting and asked for permission. He thought that he would have done that for a (specific) 'case report' at the time, although it was not then an ethical requirement.<sup>241</sup>

**33.165** As already noted, Professor Forbes did not go back to his patients with the results of the Glasgow study.

---

<sup>237</sup> Professor Forbes – Day 33, page 111

<sup>238</sup> Froebel et al, 'Immunological abnormalities in haemophilia: are they caused by American factor VIII concentrate?', *British Medical Journal*, 1983; 287 [LIT.001.0215]

<sup>239</sup> Dr Froebel's statement on immunological testing in Glasgow [PEN.012.1628] at 1629

<sup>240</sup> Note of a meeting between Professor Ludlam and the Penrose Inquiry legal team [PEN.012.0774] at 0781; Professor Ludlam – Day 35, page 79

<sup>241</sup> Professor Ludlam – Day 35, pages 79–81

***Skin test: the Glasgow Royal Infirmary***

**33.166** It appears that the Glasgow skin test exercise was carried out later. It was referred to in a letter to patients circulated on 8 January 1985 as a test Professor Forbes and Professor Lowe *wanted* to carry out, indicating that it still lay in the future at that time.<sup>242</sup> Whether ethical consent was sought is not known but patients were at least informed of the wish to test.

**Testing for anti-HTLV-III*****The UK context***

**33.167** Between 1982, when treating doctors first became aware of AIDS in the USA, and 1984, when the first tests became available, there was a lot of uncertainty about all aspects of the condition. By the end of 1983 most haemophilia clinicians would have accepted the view that the condition was caused by a blood-borne infectious agent which was transmissible by blood products. Commercially produced factor concentrates were thought by many to be more likely to transmit infections than concentrates made from local (UK) blood. However, the medical consequences of infection were unclear. The 'antigen overload' theory, that immune deficiencies in recipients of factor concentrates occurred without an infective agent of transmission, persisted (and was ultimately shown to be valid, at least to some extent in some cases).

**33.168** The number of diagnosed cases of AIDS among persons with haemophilia was relatively low in 1983: possibly only two in the UK. The CDC definition of 'AIDS' had been adopted for reporting purposes. The CDC criteria stressed the importance of the diagnosis of opportunistic infection. A definitive diagnosis would be attached if the patient developed intractable disease.<sup>243</sup> By November 1984, 21 cases of AIDS or AIDS-related illness (none in Scotland) had been reported to Dr John Craske of the Public Health Laboratory Service (PHLS).

**33.169** Emphasis on this diagnostic test necessarily underestimated the prevalence of HIV infection in the haemophilia population, given the potentially long period before evidence of opportunistic infection might appear in individual patients. The focus changed in 1984 when testing for antibodies to HTLV-III had become a reality.

**33.170** By July 1984, Professor Richard Tedder at the Department of Virology at the Middlesex Hospital, along with Professor Robin Weiss of the Chester Beatty Laboratories and a group of colleagues, had developed an early competitive radioimmunoassay test for the detection of antibodies to the putative virus causing AIDS. The test was still under development at that time and was considered to be a 'research assay', but it was used to carry out an extensive programme of research.<sup>244</sup> The result was the article by Cheingsong-Popov and others already mentioned which was published in *The Lancet* on 1 September 1984. Two thousand people in the UK had been tested for antibody to HTLV-III.<sup>245</sup>

**33.171** Blood samples had been made available by healthcare professionals in a number of clinical areas: GUM physicians, haematologists looking after haemophilia patients and people providing care to intravenous drug users. Following this publication, clinicians

---

<sup>242</sup> Letter from Dr Lowe and Dr Forbes to GRI haemophilia patients dated 8 January 1985 [LOT.003.4244] at 4245

<sup>243</sup> See Chapter 9, *Knowledge of the Geographical Spread and Prevalence of HIV/AIDS 1*, at paragraph 9.102

<sup>244</sup> See Chapter 10, *Knowledge of the Geographical Spread and Prevalence of HIV/AIDS 2*, from paragraph 10.3

<sup>245</sup> Cheingsong-Popov et al, 'Prevalence of antibody to human T-Lymphotropic virus Type III in AIDS and AIDS-risk patients in Britain', *The Lancet*, 1 September 1984 [LIT.001.0417]

caring for each of these risk groups contacted Professor Tedder asking him to test their patients, to delineate the size of the problem in their respective patient groups.<sup>246</sup> Samples were submitted for examination from around the UK. Professor Tedder told the Inquiry that the period following the publication of the data in the September paper 'was an incredibly difficult and busy time'.<sup>247</sup>

**33.172** Professor Tedder had the only laboratory in the UK which could carry out HTLV-III antibody tests at that time without access to US technology and know-how. By the end of 1984, Dr Philip Mortimer at the PHLS was also carrying out the tests developed by Professor Tedder.

**33.173** On 10 December 1984, the UKHCDO held a meeting to discuss recent developments in HTLV-III testing, although it is clear that, as in Glasgow and Edinburgh, some regional Haemophilia Centre Directors had information about the availability of tests before this meeting. The minutes show that it was known that Professor Tedder had a test available but that any expanded test programme would require large quantities of virus culture, which would depend on engaging third parties. Only the PHLS and Wellcome were interested in industrial scale production. After long discussion, it was agreed that each clinician would decide whether individual patients found to be antibody-positive should be informed but that, in general, information should be provided if asked for. Professor Tedder advised that information about the risks of sexual transmission should be provided.<sup>248</sup>

**33.174** On 14 December 1984, Professor Arthur Bloom (Chairman of the UKHCDO) sent a document entitled 'AIDS Advisory Document' to all Haemophilia Centre Directors, intended to express the position adopted at the meeting four days earlier.<sup>249</sup> The document recommended that haemophilia patients should be tested for HTLV-III antibody and that antibody-positive patients should be informed, reassured and counselled regarding transmission of infection, including the possible use of barrier contraception. It noted that tests for HTLV-III antibody were available for haemophilia patients via Professor Tedder and Dr Mortimer. The intent of the letter of 14 December, read in the light of the discussion, appears to have been that information, reassurance and advice should relate to transmission of infection. The discretion of the individual clinician, discussed at the meeting, was not dealt with in the document.

**33.175** Until mid-December 1984, there had been no 'universal' HTLV-III antibody testing of haemophilia patients in the UK. There had been no discussion among haemophilia directors. Nor was there any general agreement to test for HTLV-III antibody prior to this date. It appears that whether or not patients were tested prior to 14 December 1984 depended on whether the particular haemophilia director knew that Professor Tedder had a test available and had been in contact with his laboratory to arrange testing on an individual basis, or had contact with Dr Robert Gallo or Professor Luc Montagnier that provided for testing in their laboratories.<sup>250</sup> The larger haemophilia centres were actively concerned about the whole situation and had started to contact Professor Tedder to see if he could test their patients.

---

<sup>246</sup> Professor Tedder – Day 49, pages 78–79

<sup>247</sup> *Ibid* page 79

<sup>248</sup> Note of meeting of Haemophilia Reference Centre Directors, 10 December 1984 [SNF.001.3850]

<sup>249</sup> UKHCDO AIDS Advisory Document dated 14 December 1984 [SGF.001.2388]

<sup>250</sup> The Institut Pasteur also produced a test for the isolate discovered by them. The Inquiry does not have evidence of its actual use in the United Kingdom.

**33.176** The patients at Dr Winter's centre (at Kent and Canterbury Hospital) were informed in late 1984 that a test had become available and that their blood was being sent to Professor Tedder for testing. Dr Winter noted that a number of other haemophilia centres saw the availability of the new test as merely an extension of their pre-existing screening programme and did not perceive any need to inform patients.<sup>251</sup>

**33.177** Dr Winter's clinic did not have stored samples and it was necessary for him to make appointments to take a fresh blood sample from his patients. He explained:

If you had to call for the patient to have blood taken, as I did, that was different because the patient would come in and say, "Why have you called for me?" So if you like, in other centres because they had had to summon the patients, inevitably they would be saying, "I know you were only here a month ago for your review but we have asked you to come back because we have now got access to this new blood test and this is what it's all about".<sup>252</sup>

**33.178** Dr Winter's evidence highlighted the differences between centres which sent stored blood samples and centres (like his own and the GRI) which had to take fresh blood samples from patients. He explained that centres with stored blood samples would have probably 'just gone off to the deep freeze and thawed them and sent them because they would have thought this is just yet another virus test'. It would not have occurred to them to tell the patients because (1) it wasn't their practice to tell patients about blood tests; and (2) they were not having to bleed the patients so they were not actually seeing the patients.<sup>253</sup>

**33.179** Dr Winter said that in 1984 there was no pre-test counselling. This concept emerged one or two years later as a result of the HIV epidemic and as the impact that a positive test had on a patient's life generally, including the possibility of not obtaining life insurance and mortgages, became clear.<sup>254</sup> He explained that it became apparent a few months after the AIDS test became available that, if a patient had this test performed, even if the result was negative, an insurance company or mortgage adviser might subsequently want to decline a proposal or increase the premium on the basis, presumably, of 'we think you might have been something of a risky individual to have wanted that test done in the first place'.<sup>255</sup> He said:

Never before in medical practice had there been a blood test where just by having it changed your prospects for things like insurance and mortgages. Whatever the result was. So for the first time in medicine, I think, it became necessary to talk to patients who had come in and say – these are all patients – remember, I'm an HIV physician. A patient would come in and say, "I split up with my boyfriend 6 months ago and I'm in a new relationship and I would like to have this test done". To reassure them you would say to them, "Before you do that, there are things we need to discuss. If you have this test done, even if it is negative, you might find it more difficult to get life insurance. If you have this test done, even if it is negative, you might find it more difficult to get a mortgage." So you talked the patients through really what the consequence

---

<sup>251</sup> Dr Winter – Day 16, pages 154–155

<sup>252</sup> Ibid pages 156–157

<sup>253</sup> Ibid, page 156

<sup>254</sup> Dr Winter's submission to the Archer Inquiry [PEN.015.0283] at 0287

<sup>255</sup> Dr Winter – Day 16, pages 157–158

was of a negative result and what the consequence was of a positive result. And that was a completely new concept, now standard; and that was what pre-test counselling became.<sup>256</sup>

**33.180** Dr Winter said this completely new concept evolved from mid-1985 onwards. He explained that pre-test counselling subsequently became standard practice. He emphasised that at that time (late 1984) there was no stigma about having a blood test done and there had never been any impetus for doctors to tell patients that they were carrying out certain blood tests. The fact of simply having a test had never previously affected the patient.<sup>257</sup>

### *Testing for HTLV-III: Edinburgh*

**33.181** Professor Ludlam knew Professor Tedder and, when he found out that an HTLV-III antibody test had been developed, he telephoned and asked Professor Tedder if he would test samples from some of the haemophilia patients at the Edinburgh Haemophilia Centre.<sup>258</sup> Professor Ludlam said that, at the time that he made contact, Professor Tedder was inundated with requests from various sources and had only a limited amount of reagent to carry out the tests. Following some discussion, agreement was reached to test 10 samples from Edinburgh.<sup>259</sup>

**33.182** Professor Ludlam's recollection was that he had contacted Professor Tedder in October 1984,<sup>260</sup> while Professor Tedder thought that he had tested the samples for Professor Ludlam sometime around August 1984. Unfortunately there are no paper records of this testing as Professor Tedder's laboratory was dismantled a few years ago and all papers from the early period of HIV were destroyed.<sup>261</sup>

**33.183** Whatever the precise date, the work carried out in Edinburgh in 1982–84 in pursuit of Professor Ludlam's immunological studies lost much of its significance, at least for the time being, when the first HTLV-III antibody test results became available. The belief among Scottish practitioners that the Scottish blood donor population was free from infection and that Scottish blood products prepared from Scottish plasma were therefore likely to be safe was undermined.

### **Selection of initial samples**

**33.184** The first group of samples sent to Professor Tedder were recent blood samples taken from storage in the deep freeze in the RIE Haematology Department. Blood samples routinely taken for virological testing were stored in the virology department and a parallel store was kept in the haematology department so that clotting assays could be carried out as part of the routine monitoring of haemophilia. Professor Ludlam thought that, at that time, the 'indefinite' storage of all blood samples was 'a very appropriate thing to do ... [and] seen as extremely good virological practice' and noted that this was done in many other centres throughout the UK.<sup>262</sup> No fresh blood samples were taken to send to Professor Tedder for testing for HTLV-III.<sup>263</sup>

---

<sup>256</sup> Ibid page 158

<sup>257</sup> Ibid pages 157–158; Dr Winter's submission to the Archer Inquiry [PEN.015.0283] at 0287

<sup>258</sup> Professor Ludlam – Day 35, page 91; Day 39, page 73

<sup>259</sup> Professor Ludlam – Day 39, page 73; Professor Ludlam's note on long term safety monitoring for transfusion-transmitted infections [PEN.012.0351] at 0354. Professor Tedder told the Inquiry that he recalled testing 'something like 10 to 15 samples' – see response from Professor Tedder to questions on anti-HTLVIII testing dated 11 May 2011 [PEN.012.0856].

<sup>260</sup> Professor Ludlam's note on long term safety monitoring for transfusion-transmitted infections [PEN.012.0351] at 0354

<sup>261</sup> Response from Professor Tedder to questions on anti-HTLVIII testing dated 11 May 2011 [PEN.012.0856]

<sup>262</sup> Note of a meeting between Professor Ludlam and the Penrose Inquiry legal team [PEN.012.0774] at 0783

<sup>263</sup> Professor Ludlam – Day 39, page 72; Note of a meeting between Professor Ludlam and the Penrose Inquiry legal team [PEN.012.0774] at 0782–83

**33.185** Consent was not obtained from patients prior to their blood samples being sent to Professor Tedder. Professor Ludlam thought it unlikely that at the time that the samples were taken patients would have been told that they might be used for anti-HTLV-III testing:

I don't think they would have been told because we had no idea when the testing would become available, that a viral aetiology would be forthcoming. And these were samples that were laid down ... periodically when patients attended.<sup>264</sup>

**33.186** Professor Ludlam said that he may have instructed one of his laboratory staff to look out 10 recent samples from the deep freeze in haematology, probably from patients with severe or moderate haemophilia who were frequent users of concentrate.<sup>265</sup> He could not recall whether he chose the names of the patients whose samples were sent to Professor Tedder himself or if he simply gave the instruction that 10 samples from patients with severe haemophilia were to be sent and left it to the laboratory staff to go through a list of patients and choose the samples.<sup>266</sup>

**33.187** On the first day of his evidence on this topic, Professor Ludlam told the Inquiry that he thought that he had specifically sent Professor Tedder 10 samples from patients who had only received SNBTS product.<sup>267</sup> Upon reflection, however, he acknowledged that his initial recollection was probably wrong. He later said that he thought that the 10 samples were probably from a mixture of patients who had received only SNBTS concentrates and patients who had also received commercial concentrates.<sup>268</sup>

**33.188** Professor Ludlam did not think that the immune function results from the earlier study informed his selection of the samples. He pointed out that, in retrospect, at that stage the CD4 and CD8 counts of those who were found to be anti-HTLV-III positive were the same as those who were anti-HTLV-III negative, and had not started to decline. He said that he was 'pretty certain' that the selection was made on the basis of concentrate history and not on participation in the prior immune tests. He said that there were no clinical signs of AIDS at that stage in any of the patients.<sup>269</sup>

#### Test results received 26 October 1984

**33.189** Professor Ludlam said that he received the test results from Professor Tedder in late October 1984.<sup>270</sup> He said that he remembered the conversation vividly and that Professor Tedder had telephoned him at home around 8pm.<sup>271</sup> Professor Ludlam then telephoned Dr McClelland at home, within five to 10 minutes of getting the results, to inform him of the fact that the SNBTS blood supply appeared to be infected.<sup>272</sup>

**33.190** Dr McClelland recorded the initial disclosure in a memorandum dated 20 November 1984 which he sent to Dr Perry and Professor Cash. The memorandum stated that Professor Ludlam had telephoned him at home on the evening of Friday 26 October 1984.<sup>273</sup>

---

<sup>264</sup> Professor Ludlam – Day 35, page 92

<sup>265</sup> Professor Ludlam – Day 35, pages 91–92; Note of a meeting between Professor Ludlam and the Penrose Inquiry legal team [PEN.012.0774] at 0783

<sup>266</sup> Professor Ludlam – Day 39, page 66

<sup>267</sup> Professor Ludlam – Day 35, page 99

<sup>268</sup> Professor Ludlam – Day 36, page 57

<sup>269</sup> Professor Ludlam – Day 39, page 81

<sup>270</sup> Professor Ludlam – Day 35, page 98

<sup>271</sup> Ibid page 95

<sup>272</sup> Professor Ludlam – Day 36, pages 54–55; Note of a meeting between Professor Ludlam and the Penrose Inquiry legal team [PEN.012.0774] at 0784–86

<sup>273</sup> Memorandum from Dr McClelland to Drs Perry and Cash, 'Events Leading up to the Recall of Factor VIII Batch 023110090', dated 20 November 1984 [SNB.006.5996]

**33.191** Professor Ludlam's initial recollection was of being told that three patients had tested positive for HTLV-III antibody.<sup>274</sup> He was subsequently shown a copy of Dr McClelland's memorandum, which he did not recall having seen previously.<sup>275</sup> Paragraph one of the memorandum states:

On the evening of Friday 26/10/84 Dr Christopher Ludlam telephoned me at home to let me [Dr McClelland] know that six haemophiliac patients of his had developed antibody to HTLV3. He thought that three of these sero conversions could be attributable to the use of PFC products.<sup>276</sup>

**33.192** Professor Ludlam accepted that Dr McClelland's memorandum (which was written within a month of the phone call) was more likely to be accurate than his memory and that it was likely that six patients (not three) had been found to be HTLV-III antibody positive by 26 October 1984.<sup>277</sup> Professor Ludlam offered an explanation for his initial recollection:

The figure of three sticks in my mind because these were people who had all received SNBTS-only material and there may have been another three who had had commercial material and who were positive. And I would have made the quick assumption that maybe they got it from the commercial material. This would be before we had looked at the transfusion records. So that is a possible explanation. It was a long time ago – I just remember the – there were three that got one batch. That's what impressed me ....

And it may be that there were three others who had got commercial and because – as I say, I assumed that that they, in the first instance, without inspecting the transfusion records – assumed that they might have got it from the commercial [products].<sup>278</sup>

**33.193** The telephone call from Professor Ludlam to Dr McClelland on 26 October 1984 was the first indication to the transfusion service that the SNBTS blood supply had been infected. By 1 November 1984 a specific batch of Factor VIII concentrate, batch 023110090, was deemed the most likely source of infection and was recalled. Subsequent investigation of the source of infection is described in Chapter 10, *Knowledge of the Geographical Spread and Prevalence of HIV/AIDS 2*.

#### Further testing by Professor Tedder

**33.194** To investigate the situation further, Professor Tedder agreed to test additional samples from other patients<sup>279</sup> and Professor Ludlam arranged for further samples to be sent within a few days of receiving the initial results.<sup>280</sup> He could not recall how he selected which further samples were to be sent, although he thought that he might have selected samples from other patients who had received batch 023110090.<sup>281</sup> The results of the further tests were received on Friday 2 November 1984, when Professor Tedder reported

---

<sup>274</sup> Professor Ludlam – Day 35, page 98

<sup>275</sup> Professor Ludlam – Day 36, page 8

<sup>276</sup> Memorandum from Dr McClelland to Drs Perry and Cash, 'Events Leading up to the Recall of Factor VIII Batch 023110090', dated 20 November 1984 [SNB.006.5996]

<sup>277</sup> Professor Ludlam – Day 36, pages 12–13

<sup>278</sup> *Ibid* pages 10–11

<sup>279</sup> Professor Ludlam's note on long term safety monitoring for transfusion transmitted infections [PEN.012.0351] at 0354

<sup>280</sup> Professor Ludlam – Day 35, page 103

<sup>281</sup> Professor Ludlam – Day 39, page 75



that a total of 16 patients in Edinburgh were apparently anti-HTLV-III positive.<sup>282</sup> Fifteen of these patients appeared to have been infected by a single batch. The number of patients infected by the implicated batch was later thought to be 18. These patients became known as the Edinburgh Cohort and are discussed further in Chapter 10, *Knowledge of the Geographical Spread and Prevalence of HIV/AIDS 2*.

**33.195** Professor Ludlam said that, in total, samples from between 50 and 70 patients were tested by Professor Tedder.<sup>283</sup> He thought it unlikely that they were all tested in one batch given that Professor Tedder had limited supplies of reagents and was receiving a lot of requests. He thought that they would have been tested 'over a month or two or three' but admitted that this was a guess.<sup>284</sup>

**33.196** All of the samples that were sent to Professor Tedder were labelled with the names of the patients from whom they had been taken.<sup>285</sup> Professor Ludlam said that this was the usual way of sending samples to the laboratory for testing because they were worried about transcription errors:

If identifying details about a patient, either their name or a number or an initial or a date [are used] – every time it is written there is a finite chance there will be a mistake .... [If] you have got a row of tubes in a rack and someone is writing numbers, for example, on them. It is very easy indeed to get numbers a bit confused, not to remember to up to the next number when you number the next tube. So if you write a name, it is rather more specific and is probably less likely to result in error.<sup>286</sup>

**33.197** The effect of Professor Ludlam's evidence was that the question whether testing should be anonymised did not raise ethical issues in late 1984 and that it did not do so in this context until the 1990s, partly in response to the HIV situation. He said that when the HTLV-III antibody tests became available it felt as if at last clinicians had some control of the situation and that it would be useful to know whether individual patients were negative or positive for anti-HTLV-III. Therefore the samples were sent as named samples.<sup>287</sup>

**33.198** When asked whether he had anticipated the problem which would be caused by obtaining positive test results for patients who had been tested without their consent, Professor Ludlam said:

I think it fair to say that we hadn't, or we certainly hadn't anticipated all the consequences of testing and why informed consent became so important. This was at a time when AIDS was – increasing numbers of people were developing AIDS and we were desperate to have a reliable marker and that's why it was useful to have them on a named basis. I entirely agree that, come 1985 ... the whole picture of testing changed and it became desirable to talk to patients in advance of testing.<sup>288</sup>

<sup>282</sup> Memorandum from Dr McClelland to Drs Perry and Cash, 'Events Leading up to the Recall of Factor VIII Batch 023110090', dated 20 November 1984 [SNB.006.5996]

<sup>283</sup> Note of a meeting between Professor Ludlam and the Penrose Inquiry legal team [PEN.012.0774] at 0782

<sup>284</sup> Professor Ludlam – Day 35, pages 90–91

<sup>285</sup> Ibid page 102

<sup>286</sup> Ibid pages 102–103; see also Note of a meeting between Professor Ludlam and the Penrose Inquiry legal team [PEN.012.0774] at 0786

<sup>287</sup> Professor Ludlam – Day 39, pages 66–67

<sup>288</sup> Ibid page 68

### *Testing for HTLV-III: the Glasgow Royal Infirmary*

**33.199** The history of the testing for HTLV-III antibody in Glasgow is confused. There is evidence that by the end of 1984 some patients from the GRI and Yorkhill Hospital had been tested for HTLV-III antibody. It is not clear who carried out the tests for Yorkhill hospital.<sup>289</sup> While the RIE sent samples to Professor Tedder at the Middlesex Hospital for testing, as described above, the GRI sent samples to Dr Gallo in the USA. How that came about, and whether there was a connection with Dr Gallo that facilitated the test, remains unclear.

**33.200** As he expressly admitted, Professor Forbes had difficulty recalling many of the events that had occurred nearly three decades ago. He informed the Inquiry that the initial testing of patients for the Glasgow Haemophilia Centre was carried out by Dr Mads Melbye at his laboratory in Denmark.<sup>290</sup> After he had given evidence, however, Dr Karin Froebel provided a written statement to the Inquiry indicating that the initial testing had in fact been performed by Dr Gallo in the USA.<sup>291</sup> The relevant paragraph for these purposes is:

Things were moving very quickly in the field. In the spring of 1984, two reports, from Montagnier in France, and Gallo in the US, claimed to have isolated a virus from patients with AIDS. Both were working on an antibody (ELISA) assay, a blood test that would show exposure to the virus. We were interested to know as soon as possible whether the Glasgow haemophiliac patients had antibody to the virus. In Glasgow there was a freezer-full of stored serum samples from an earlier study, which Dr Forbes suggested could be used. I wrote to both Montagnier and Gallo and had a reply from Dr Gallo directing me to send the samples to his research scientist. The samples (77) were located, I think by Dr Madhok, packed in dry ice, and Dr Forbes and I took them to Glasgow airport to be air-freighted to the laboratory in the US. At this point, I still thought the results would be negative; that we were dealing with something different in Scotland and I can still recall the shock when the news came back that 12 of our 77 samples, i.e. 16%, tested positive. Very soon after that, Mads Melbye appeared, and suggested writing a joint paper, pooling our results with his 22 Danish samples, and this resulted in the Lancet paper in December 1984.

At this point I recall Dr Forbes saying that he would speak to all the haemophiliac patients and tell them that they were at risk of infection, and should take the necessary safe sex precautions, ie use condoms. The test carried out in the US had not yet been approved by the regulatory body; therefore we could not say for sure that the 12 were definitely infected or that the 65 were definitely not. I also recall Dr Forbes telling me soon after, that he had spoken to all the patients. I had no direct contact with patients at any time.<sup>292</sup>

**33.201** Subsequently, in a letter to the Inquiry dated 27 June 2011, Professor Forbes advised that he was happy to defer to Dr Froebel's recollection of events on this matter and that what she described was a logical explanation of events although he did not actually remember sending samples to Dr Gallo.<sup>293</sup> As noted by Dr Froebel, the stored

---

<sup>289</sup> Professor Hann's response to further questions from the Inquiry dated 13 April 2011 [PEN.012.0270] at 0271–72; Professor Hann – Day 21, pages 69–70; Dr Pettigrew's statement on the use of blood product concentrates [PEN.015.0486]

<sup>290</sup> Professor Forbes' statement on information given to patients [PEN.012.0411] at 0412

<sup>291</sup> Dr Froebel's statement on immunological testing in Glasgow [PEN.012.1628] at 1629

<sup>292</sup> Ibid [PEN.012.1628] at 1629

<sup>293</sup> Immunological testing in Glasgow – Professor Forbes' comments on Dr Froebel's statement [PEN.012.1677] at 1678

samples were 'from an earlier study'. It is not possible to determine which study that was. The only near contemporaneous study about which the Inquiry has evidence is the immune abnormality study referred to at paragraph 33.159 above.

**33.202** Professor Forbes could not recall when he started collecting the samples. In the article mentioned by Dr Froebel, it is noted in the section on the materials and methods employed that blood was taken from patients enrolled in the Regional Haemophilia Reference Centre, Glasgow, between December 1983 and July 1984.<sup>294</sup> Professor Forbes agreed that the samples that were sent for HTLV-III antibody testing were taken from patients between those dates. There were other samples from the same patients going back to 1979 and they were later able to use the samples to determine dates of seroconversion.

**33.203** When asked if the patients were told that their blood was being tested at this time, Professor Forbes said:

I think that the answer would be probably not at that time. It's difficult to remember but this was very much a moving situation and the whole question of consent at that time was very woolly. Certainly later on it tightened up immensely and has changed even more since then. So I don't think that we would be asking for consent for storing samples but they might be told that they were being stored. So I'm very unclear as to when all these things happened.<sup>295</sup>

**33.204** Questioned further, Professor Forbes said that he was 'quite sure' that patients were not asked for their consent to be tested. He said:

I don't think that at that time there was any concern about consent because we assumed that people would want to know about what was happening and what the implications of this new test would be. So I don't think that we asked for consent.<sup>296</sup>

**33.205** It is difficult to reconcile the careful practice of obtaining specific consent to take blood for the limited purpose of a preliminary investigation of immune abnormalities with the retention of the samples, without obtaining consent, for the potentially more serious exercise of testing for HTLV-III infection when a test became available. On the basis of Professor Forbes' evidence, however, and the December article, the procedure adopted in preparation for the test did not involve obtaining patient consent. If the timetable for collection was as described above, the dispatch of samples to Dr Gallo's laboratory could have happened in or soon after July 1984. Professor Lowe was unable to assist as he was on secondment at the material time. He told the Inquiry that he was not involved in collecting samples from patients or sending them to the laboratory for HTLV-III testing.<sup>297</sup> His first exposure to the study which was published in *The Lancet* in December 1984 was when he read the draft paper.<sup>298</sup>

---

<sup>294</sup> Melbye et al, 'HTLV-III seropositivity in European haemophiliacs exposed to Factor VIII concentrate imported from the USA', *The Lancet*, 22/29 December 1984 [LIT.001.1702]

<sup>295</sup> Professor Forbes – Day 33, page 122

<sup>296</sup> Ibid page 122–123

<sup>297</sup> Professor Lowe – Day 40, page 26

<sup>298</sup> Ibid page 24

**33.206** The next witness who might have assisted in providing a date for Dr Gallo's investigation was Dr Patricia Wilkie, a researcher working at the GRI. In 1982 she was engaged in a study of the social and psychological implications of adult polycystic kidney disease and the implications for counselling.<sup>299</sup> She initially told the Inquiry that she thought that she had begun working with Professor Forbes around March or April 1983, although she could not be sure of the date.<sup>300</sup> She had found boxes of cuttings from newspapers and academic journals about HIV dating from 1983 onwards, which, she thought, showed that she was thinking about HIV at that stage, but accepted that she might have begun working for Professor Forbes in early 1984.<sup>301</sup>

**33.207** Dr Wilkie said that Dr Forbes contacted her and asked her to help with counselling haemophilia patients about AIDS.<sup>302</sup> She said that he had wanted her to work with him for some time but that she had been reluctant to do so because she was much more interested in diseases that were transmitted in an autosomal dominant way, rather than haemophilia which had been well-researched.<sup>303</sup> However, she said that there was an emerging realisation at this time that it was possible that a new virus, then called HTLV-III, might be transmitted through blood and blood products.<sup>304</sup> HTLV-III was the designation of the isolate published by Dr Gallo in April 1984. If Dr Wilkie's recollection that HTLV-III was a material factor influencing her engagement with Professor Forbes is reliable, that must have happened in or after April 1984 and no earlier.

**33.208** Her recollection was that Professor Forbes told her that he had recently returned from a haemophilia conference in the USA where it had been reported that HTLV-III had been found in the blood of some patients with haemophilia.<sup>305</sup> She recalled that he told her that he had brought back some testing kits from the USA which were not yet licensed but which could test for the presence of HTLV-III in the blood. She said that Professor Forbes had told her that he had anonymously tested the blood samples of a couple of patients with haemophilia and discovered that both samples were HIV-positive.<sup>306</sup> She added in oral evidence:

This is what he told me, and that he had realised that this should not go any further and that's why he phoned me ....

I was already a member of a research ethics committee in Edinburgh and I had a very great interest in ethics and how things should be done and consenting people and transparency, things that are still not quite with us.<sup>307</sup>

**33.209** Dr Wilkie said that the reason that Professor Forbes had contacted her was because he was agitated about the test results. He wanted her to use her skills to help his patients: to establish what people with haemophilia knew about HTLV-III, whether they knew about the existence of the virus and whether the patient thought that they may be affected. He also wanted her to find out if the patients would like to be tested for the virus if a test was available.<sup>308</sup>

---

<sup>299</sup> Dr Wilkie's statement [PEN.016.1297]: Day 32, page 9

<sup>300</sup> From a payslip Dr Wilkie found it seems she began in August 1982: Day 32, pages 8–9

<sup>301</sup> Dr Wilkie – Day 32, pages 17–18

<sup>302</sup> Dr Wilkie's statement [PEN.016.1297]

<sup>303</sup> Day 32, Pages 15–16

<sup>304</sup> Dr Wilkie's statement [PEN.016.1297]

<sup>305</sup> Ibid [PEN.016.1297] at 1298

<sup>306</sup> Ibid

<sup>307</sup> Dr Wilkie – Day 32, pages 18–19

<sup>308</sup> Dr Wilkie's statement [PEN.016.1297] at 1298

**33.210** Professor Forbes told the Inquiry that he did not think Dr Wilkie's recollection about testing with a US testing kit was correct. He said that he certainly did not bring anything back from the United States in his hand but he was sure that they had some connection in which tests were provided to them.<sup>309</sup> Asked if it could be the Melbye tests that he and Dr Wilkie discussed he thought that that was possible although he had no recollection of the discussion.<sup>310</sup> When he gave this evidence, he was unaware of Dr Froebel's evidence and had not then deferred to her version of events. Professor Forbes also explained that he would not personally be able to do a test like that.<sup>311</sup> He said that the initial samples were all labelled as he felt it was important to know who tested positive as action would require to be taken on the basis of the results.<sup>312</sup>

**33.211** Professor Lowe could not recall the precise month that Dr Wilkie came to the haemophilia unit but thought that she was coming regularly and speaking to the patients by the beginning of 1985. He said that she came to all the clinics and was always around and tried to see all patients who had been treated with blood products and were therefore at risk of having a positive result. She was very dedicated and made herself fully available to all patients, partners and relatives. He said that she spent a lot of time, particularly in 1985, discussing the implications of HIV test results.<sup>313</sup>

**33.212** Dr Wilkie explained that she was involved in two interconnected projects. The initial project was funded by the Scottish Home and Health Department (SHHD) and administered by Ivana Markova at Stirling University,<sup>314</sup> to establish what patients knew about the genetics of haemophilia, what treatments the patients thought were available and what patients and their families knew about infections associated with haemophilia treatment and what could be done about them.<sup>315</sup> Dr Wilkie told the Inquiry that she, Professor Forbes and Ivana Markova drafted the research proposal<sup>316</sup> although Dr Wilkie does not appear to be named on the documentation. She said that, when the project started, patients had not been tested (apart from those subjected to the initial tests) nor had they been informed of the availability of tests, to the best of her knowledge, and it was not until a little later on in the project that a decision was made by Drs Forbes and Lowe that the patients should be told that tests were available and that they should be tested.<sup>317</sup> After the Oral Hearings the Inquiry received more information from Dr Wilkie in a letter dated 7 August 2012. In it she said that she did not start interviewing patients until late summer 1985 and when she did start interviewing, none of the patients had been told their test results. In addition, she was not told of their results until she had completed the interviews.<sup>318</sup> It seems likely that Dr Wilkie started work on the HIV project in early 1985.

**33.213** Gradually, Dr Wilkie's role as a counsellor took over from her role as a researcher. She met patients both individually and with their partners or families. She would discuss the implications of being tested for HTLV-III and there being a positive result as well as the

---

<sup>309</sup> Professor Forbes – Day 33, page 125

<sup>310</sup> Ibid pages 126–127

<sup>311</sup> Ibid page 126

<sup>312</sup> Ibid page 161

<sup>313</sup> Professor Lowe – Day 40, page 58

<sup>314</sup> Dr Wilkie – Day 32, page 23

<sup>315</sup> Dr Wilkie's statement [PEN.016.1297] at 1298

<sup>316</sup> Dr Wilkie – Day 32, page 24

<sup>317</sup> Ibid page 22

<sup>318</sup> Letter from Dr Wilkie to the Inquiry Team dated 7 August 2012 [PEN.019.1473]

implications of not taking the test. This was done as part of the research interview, prior to testing being carried out.<sup>319</sup>

**33.214** When asked to expand on how an interview would proceed, Dr Wilkie said:

There was a schedule, which I sent in actually, and one would ask them first of all how haemophilia had affected them in their life, what were their fears ....

....

One would discuss the implications if they were tested, the implications for their partner, or partners ....<sup>320</sup>

Dr Wilkie went on to say:

[O]nce I collected this information I fed this back to Dr Forbes – that these patients had been seen, this is what they knew and then there was a discussion about testing, that this patient was happy to be tested, that patient wasn't .... There were one or two who didn't want immediately to be tested.<sup>321</sup>

**33.215** Asking whether patients wanted to have a test, and counselling them about the implications of being tested, whatever the result, was a vital part of Dr Wilkie's work. If a patient told her that they did not want to be tested she would inform Professor Forbes and that information would go into the patient's notes so that their wishes were known.<sup>322</sup>

### *Practice in Glasgow and south west Scotland: Yorkhill*

**33.216** The position at Yorkhill is unclear. Neither Professor Hann, Head of Department of Haematology 1983–87, nor Dr Pettigrew, a part-time Clinical Assistant in Haematology 1980–89, could recall who organised blood testing there. It was not possible for the Inquiry to ascertain how this testing took place.

## **Communication of the results of HTLV-III testing**

### *The evidence of patients*

**33.217** The majority of witnesses who gave statements to the Inquiry did not know that they had been tested and did not consent to being tested for HIV before they were diagnosed with the virus. The patient or relative witnesses who gave evidence about the effects of their own or their relative's infection with HIV told the Inquiry of the circumstances surrounding their own or their relative's diagnosis with HIV. 'Christine' found out that her son 'John' had HIV when she attended a routine clinic appointment at Yorkhill Hospital in about 1984 or 1985.<sup>323</sup> 'Amy' was told by her son's GP in about 1986 that her son 'Luke' had acquired HIV from a blood transfusion.<sup>324</sup> Frances' father 'James' was told by Professor Ludlam that he had HIV on 21 December 1984.<sup>325</sup> Elaine's husband 'Brian' arranged an appointment in December 1986 with the Haematology Department of the RIE so that he, his wife and his son could be tested for the virus. He found out that

---

<sup>319</sup> Dr Wilkie – Day 32, pages 30–31

<sup>320</sup> Ibid pages 31–32

<sup>321</sup> Ibid page 34

<sup>322</sup> Ibid page 35

<sup>323</sup> See Chapter 5, *An Examination of the Effects of Infection with HIV on the Patients and their Families, Including Treatment*, at paragraph 5.13

<sup>324</sup> Ibid at paragraph 5.56

<sup>325</sup> Ibid at paragraph 5.127

he had the virus when he returned to the department for the results of these tests that same month.<sup>326</sup> 'David' was told by Professor Lowe at the Glasgow Royal Infirmary at a specifically arranged appointment on 2 December 1985 that he had acquired HIV.<sup>327</sup> His diagnosis with HIV is discussed in more detail in paragraph 33.325. 'Mark' did not find out that he had acquired HIV until January 1991 when Professor Ludlam told him at a clinic appointment.<sup>328</sup> The circumstances surrounding the communication of Mark's test results to him are discussed at paragraphs 33.304 to 33.307. 'Stephen', who was treated for haemophilia at a regional hospital, was told he had acquired HIV by the consultant treating him there in February 1986.

### Meeting in November 1984

**33.218** On 29 November 1984, a meeting was convened of Scottish Haemophilia Directors, SNBTS representatives and SHHD personnel to discuss the implications of the test results thus far obtained.<sup>329</sup> It was expected that there would be a UK-wide meeting on 10 December. Professor Ludlam intimated the finding of anti-HTLV positive results in 16 patients treated exclusively with SNBTS Factor VIII concentrate. Professor Forbes described the findings in the Glasgow patients and said that a comparative study of infection in Glasgow and Denmark would soon be published in *The Lancet*. Professor (then Dr) Brenda Gibson reported that five out of 10 patients already tested at Yorkhill were HTLV-III antibody positive. The minute noted:

Views were exchanged on the very difficult ethical problems which had arisen. These included whether patients and patients' relatives should be informed and perhaps subjected to needless worry; whether publicity additional to that already provided should be given, and how directors should respond to direct enquiries or requests for advice. The chairman [Dr Bell] advised members that ministers had been informed and that SIO had been briefed. While a press statement would not be issued by the Department at present any enquiries would be answered. It was agreed that every effort should be made for patients to have the situation explained to them before the impending publicity.<sup>330</sup>

**33.219** The problem existed in haemophilia centres throughout the UK. On 10 December 1984, as anticipated at the 29 November meeting, there was a meeting of Haemophilia Reference Centre Directors at the BPL, Elstree.<sup>331</sup> At that stage, testing had not been carried out in every centre. The notes of the meeting record that the chairman, Professor Bloom, said, in summarising the discussion, that testing should be instituted as soon as possible. It was also noted that:

A long discussion took place on whether persons found to be +ve were to be informed. Several differing views were expressed. It was agreed that each clinician would decide for each case depending on the facts of the case but in general to provide information if asked for.<sup>332</sup>

---

<sup>326</sup> Ibid at paragraph 5.215

<sup>327</sup> Ibid at paragraph 5.174

<sup>328</sup> Ibid from paragraph 5.253

<sup>329</sup> Minutes of meeting of Haemophilia Directors and SNBTS representatives held on 29 November 1984 [SNF.001.0255]

<sup>330</sup> Ibid [SNF.001.0255] at 0256

<sup>331</sup> Note of meeting of Haemophilia Reference Centre Directors, 10 December 1984 [SNF.001.3850]

<sup>332</sup> Ibid [SNF.001.3850] at 3853

After further discussion:

It was agreed that haemophiliacs should all be given the same advice with selective advice being given based on the results of HTLV III testing.<sup>333</sup>

**33.220** In his summary, Professor Bloom repeated the view that information on test results should not be given automatically but only if asked for.<sup>334</sup> It is significant that, at this stage, the Reference Centre Directors did not acknowledge an overriding ethical obligation to inform patients: it was left to the discretion of the individual director.

### ***Meeting of 19 December 1984***

#### **Background**

**33.221** By this time, no steps had been taken in Edinburgh or Glasgow to inform patients who had been tested of their results. On Tuesday 11 December 1984, the day after the meeting, Professor Ludlam received a telephone call from a reporter at *The Yorkshire Post*.<sup>335</sup> The reporter appeared to have all the details about what was then known of the seroconversions in Edinburgh. It is not clear how the reporter obtained these details but it appears that they may have been leaked following the meeting of Haemophilia Reference Centre Directors on 10 December.<sup>336</sup> The reporter wanted to speak to Professor Ludlam about the story and indicated that he intended to publish it. Professor Ludlam agreed to meet with the reporter the following day.<sup>337</sup>

**33.222** On the evening of Tuesday 11 December 1984, Professor Ludlam telephoned Dr Bell at the SHHD. The call was reported in a note by Dr Bell written the next day:

I had phone calls last night from Dr McClelland, Dr Ludlam and Dr Cash (in that order) letting me know that that there is likely to be publicity in the Yorkshire Post, tomorrow, relating to the Edinburgh haemophiliacs with HTLV-III antibodies attributable to contamination of a Scottish batch of factor VIII. It has to be presumed that this has been leaked by one of the English haemophilia directors involved in last Monday's meeting of the UK Haemophilia Reference Centre Directors.

One of Lothian [Health Board's] Press Officers has been in touch with SIO. You may wish to discuss what should be the Department's response to this development. I understand that Dr Cash has also spoken to you direct.<sup>338</sup>

**33.223** On Wednesday 12 December 1984, the reporter travelled to Edinburgh and met Professor Ludlam. Professor Ludlam told the Inquiry that he begged the reporter not to publish the story as he felt it was no way for the patients to find out. He said that the reporter thought it was a scoop and was very keen to publish and that he had to negotiate fairly hard to delay publication for one week to give him time to organise a meeting for the patients. He promised that the information would not go out to any other newspaper in the meantime.<sup>339</sup>

---

<sup>333</sup> Ibid [SNF.001.3850] at 3854

<sup>334</sup> Ibid [SNF.001.3850] at 3854

<sup>335</sup> Professor Ludlam – Day 35, Page 111

<sup>336</sup> Dr Bell's letter of 12 December 1984 concerning 'Haemophiliacs with Antibodies to HTLV III' [SGH.002.6503]

<sup>337</sup> Professor Ludlam – Day 35, page 111

<sup>338</sup> Dr Bell's letter of 12 December 1984 concerning 'Haemophiliacs with Antibodies to HTLV III' [SGH.002.6503]

<sup>339</sup> Professor Ludlam – Day 35, page 111



**33.224** Having negotiated the extension, Professor Ludlam telephoned Dr Bell again on 12 December 1984 to inform him of the development. Dr Bell appears to have interpreted the information from Professor Ludlam as an indication that ‘the haemophilia consultants’ intended to hold a meeting. The second part of Dr Bell’s note of 12 December 1984 reads:

Since dictating the above Dr Ludlam has informed me that the Yorkshire Post journalist has agreed to postpone his report until Thursday, 20 December. This will enable the Haemophilia Consultants to call a meeting of haemophilia patients to explain the situation. In view of this development I advise that SHHD should not publicise this matter before the patients themselves have been informed professionally.<sup>340</sup>

**33.225** Professor Ludlam explained that a meeting was called because ‘[w]e thought this was the quickest and most open way to start to inform the patients’ about the situation.<sup>341</sup> The purpose of the meeting was ‘to inform patients that HTLV-III tests had been carried out and that some patients were positive for HTLV-III antibody and to tell patients what we knew about AIDS’.<sup>342</sup> He acknowledged that such a meeting was not ideal for communicating the test results: ‘It’s a very public place, a meeting. People might be quite anxious about what was being said, quite concerned, and there is not much privacy in a meeting with lots of other people’.<sup>343</sup> He told the Inquiry that, had *The Yorkshire Post* not taken an interest in the story, the meeting would not have taken place at the end of December 1984. Rather, he would have devised another means by which patients would have been informed. He said a meeting ‘would not be my first choice, given a completely blank sheet and without other constraints’.<sup>344</sup>

**33.226** By the time *The Yorkshire Post* contacted Professor Ludlam, he had been in possession of some patients’ results for almost two months, the first test results having been received at the latest on 26 October 1984. No steps had been taken to inform the patients prior to contact from *The Yorkshire Post*. Professor Ludlam told the Inquiry that was because he was still ‘assessing the situation’.<sup>345</sup> Professor Forbes had results from Dr Gallo at the latest in early October, having regard to the time required to prepare and revise the article published in *The Lancet* in December, but possibly earlier. He too had taken no steps to inform patients, although it appears that he had engaged Dr Wilkie to counsel patients.

### The invitation to attend a meeting

**33.227** On 12 December 1984, a letter was sent to all patients registered at the Edinburgh Haemophilia Centre. The terms of the letter were as follows:

Dear Patient/Parent

There has been much publicity in the press and television about the HTLV III virus and AIDS. Dr Forbes, Director of the Glasgow Haemophilia Centre, and I are holding a meeting to discuss with patients some of the anxieties and issues that have been raised. You, along with a member of your family are cordially

---

<sup>340</sup> Dr Bell’s letter of 12 December 1984 concerning ‘Haemophiliacs with Antibodies to HTLV III’ [SGH.002.6503]

<sup>341</sup> Professor Ludlam – Day 35, page 112

<sup>342</sup> Note of a meeting between Professor Ludlam and the Penrose Inquiry legal team [PEN.012.0774] at 0787

<sup>343</sup> Professor Ludlam – Day 35, page 117

<sup>344</sup> Ibid page 116

<sup>345</sup> Ibid page 115

invited to this meeting which will be held in the Large Surgical Theatre, Royal Infirmary, Edinburgh, on Wednesday, 19<sup>th</sup> December at 7:30pm.

Dr Forbes and I will each speak for a few minutes on AIDS, Haemophilia and Blood Transfusion. We shall then open the meeting for questions and general discussion. If you do not wish, or are unable to attend the meeting, but would like to talk to me, or another member of the Haemophilia team, we should be delighted to see you by appointment with my secretary.<sup>346</sup>

**33.228** Professor Ludlam thought that he had drafted the letter. His understanding was that letters had been sent out from each of the other haemophilia centres – Glasgow Royal Infirmary and Yorkhill in the west of Scotland and Dundee, Aberdeen and Inverness in the east – and that all of the haemophilia patients in Scotland were invited to the meeting. In the case of the east coast Haemophilia Centres, Professor Ludlam thought it likely that he had sent copies to each of the centres, possibly by fax, and asked them to send out something similar. He did not specifically recall doing so but was sure that was the course of action he would have taken.<sup>347</sup>

**33.229** In the case of the GRI, Professor Ludlam told the Inquiry that Professor Forbes would have written to his own patients. Professor Ludlam thought that he would have given Professor Forbes details of the venue and left the rest to him.<sup>348</sup> Professor Ludlam could not say with any certainty that there were any Glasgow patients at the meeting. He told the Inquiry that there were quite a lot of people that he did not recognise at the meeting and he assumed that they had come from Glasgow or somewhere else in Scotland. By a process of elimination he concluded that patients from outwith Edinburgh had attended the meeting.<sup>349</sup>

**33.230** Professor Forbes said in his statement that he thought that the meeting was held to inform a group of patients from Edinburgh about what was happening with the virus and the implications thereof.<sup>350</sup>

**33.231** Professor Hann and Dr Pettigrew from Yorkhill Hospital were asked if they recalled sending invitations to the meeting to the parents of their patients. Professor Hann had no recollection of the meeting being held and did not remember being asked to write to any of the parents of his patients inviting them to the meeting.<sup>351</sup> Dr Pettigrew also had no recollection of the meeting in Edinburgh, although she thought that a meeting had been held at the Glasgow Royal Infirmary to inform haemophilia patients about the situation regarding the transmission of AIDS through blood products.<sup>352</sup>

**33.232** The evidence of events at this crucial period is again confused. Professor Ludlam remembers the meeting as a joint arrangement, involving Professor Forbes and himself among others informing Scottish patients of the outcome of investigations to date. Professor Forbes remembered it as an Edinburgh exercise, in relation to which he was 'neutral'. None of the evidence heard by the Inquiry would have suggested that Professor Ludlam had been alerted to any preparations Professor Forbes already had in hand for dealing with his own infected patients.

---

<sup>346</sup> Letter from Professor Ludlam to patients and parents dated 12 December 1984 [PEN.018.1405]

<sup>347</sup> Professor Ludlam – Day 35, pages 112–113

<sup>348</sup> Ibid page 114; Note of a meeting between Professor Ludlam and the Penrose Inquiry legal team [PEN.012.0774] at 0788

<sup>349</sup> Professor Ludlam – Day 35, page 127

<sup>350</sup> Professor Forbes' statement on information given to patients [PEN.012.0411] at 0414; Day 33, page 143

<sup>351</sup> Professor Hann – Day 31, pages 60–62

<sup>352</sup> Dr Pettigrew – Day 20, pages 68–69

**33.233** The meeting was held in the large surgical lecture theatre at the RIE. It started at 7:30pm and ran for about an hour to an hour and a half.<sup>353</sup> The Inquiry has been unable to establish even an approximate number of patients and relatives who attended the meeting because there is some discrepancy in the evidence. It is clear, however, that fewer people attended than Professor Ludlam had anticipated. Professor Ludlam said:

I thought a lot of people might come. As you know, there are about 400 people with haemophilia in Scotland and if each brought a friend, relative or spouse, that was potentially 800 people ....

I had reserved two large lecture theatres, anticipating that we might get a large number of people and if we had have done so, Dr Forbes would have spoken in one and I would have spoken in the other, and Dr McClelland would have spoken in both ....

But we had a smaller number. So they all fitted into the large surgical lecture theatre in the Royal Infirmary.<sup>354</sup>

**33.234** He said that he, Professor Forbes and Dr McClelland all spoke at the meeting.<sup>355</sup> Mrs Geraldine Brown, a social worker, also attended the meeting in a listening capacity and did not speak.<sup>356</sup> Professor Ludlam thought that there were between 30 and 40 people there.<sup>357</sup> Mrs Brown thought that there were between 50 and 100 people there.<sup>358</sup> Professor Forbes thought that there were around 20 people at the meeting but could not be sure.<sup>359</sup> Dr McClelland could not recall how many people had attended the meeting.<sup>360</sup> The attendees were spread out, with pairs and small groups of people sitting together and some people sitting alone.<sup>361</sup> The group of patients and their families was, in any event, much smaller than Professor Ludlam had anticipated on his approach to it as a Scotland-wide exercise.

#### *Order of speakers at the meeting*

**33.235** On 10 January 2012, the Inquiry obtained a statement from the wife of a haemophilia patient who was given the pseudonym 'Witness A'.<sup>362</sup> She attended the meeting and took handwritten notes which have been provided to the Inquiry.<sup>363</sup> In her statement she explained that she was accustomed to taking notes during meetings as a result of her work. The notes taken by Witness A indicate that Professor Forbes spoke first followed by Professor Ludlam. Dr McClelland is not mentioned in the notes, although it is clear from his own evidence and the contemporaneous newspaper reports that he did speak. The notes run to four pages and it appears that Dr McClelland's contribution is recorded at some point on pages three and/or four. It is not possible to be certain where it begins or ends.

---

<sup>353</sup> Note of a meeting between Professor Ludlam and the Penrose Inquiry legal team [PEN.012.0774] at 0789

<sup>354</sup> Professor Ludlam – Day 35, page 126; Professor Ludlam noted that, had all the patients from Edinburgh and Glasgow attended, there would have been around 250 patients. Note of a meeting between Professor Ludlam and the Penrose Inquiry legal team [PEN.012.0774] at 0788.

<sup>355</sup> Note of a meeting between Professor Ludlam and the Penrose Inquiry legal team [PEN.012.0774] at 0789

<sup>356</sup> Mrs Geraldine Brown – Day 34, pages 11–12

<sup>357</sup> Note of a meeting between Professor Ludlam and the Penrose Inquiry legal team [PEN.012.0774] at 0788

<sup>358</sup> Mrs Geraldine Brown – Day 34, page 15

<sup>359</sup> Professor Forbes' statement on information given to patients [PEN.012.0411] at 0414

<sup>360</sup> Dr McClelland – Day 40, page 105

<sup>361</sup> Professor Ludlam – Day 36, pages 14–15

<sup>362</sup> Statement of Witness A [PEN.018.1367]

<sup>363</sup> Ibid [PEN.018.1367] at 1369. Unfortunately, because these notes were found after Professor Ludlam, Professor Forbes and Dr McClelland had given evidence they did not have an opportunity to comment on them.

### ***What was said at the meeting***

**33.236** The Inquiry was fortunate to receive these contemporaneous notes of the meeting. They represent the most reliable evidence of statements made, although there will be omissions from the witness's record. It may even be that, as the wife of an Edinburgh patient, she did not record statements relating only to Glasgow. The Inquiry cannot know. From Witness A's notes, Professor Forbes appears to have spoken about the number of people infected in the UK and worldwide, the immune function studies ('tested when visiting hospital'), and the helper cell depletions and skin tests carried out by haemophilia centres. He referred to the fact that further investigation of supposed immune deficiency would be carried out on asymptomatic patients.<sup>364</sup>

**33.237** From the notes taken by Witness A, Professor Ludlam appears to have told the meeting that heat treating Factor VIII killed the virus and that the virus could be transmitted by semen, needle stick injuries, blood, or dental treatment.<sup>365</sup>

**33.238** He also made a number of recommendations for patients and their families:

- 1) Make up own & administer own factor VIII

IX

- 2) If not family wear gloves and aprons
- 3) Cinbins [for disposal of needles and other equipment]
- 4) Protective sheaths
- 5) Close members of family don't give blood<sup>366</sup>

**33.239** On the third page of her notes, Witness A has noted that the following was said:

- 1) [he was] prepared to inform if have antibody
- 2) Not having the antibody does not mean you have not been exposed to the virus 3–4 years for implications of antibody to become known<sup>367</sup>

**33.240** The notes continue as follows:

Link HTLV3 & AIDS does not mean  
cause & effect  
State of ignorance – Research going  
very fast  
Cryoprecipitate made from smaller pool  
but not as effective  
Virus easy to kill  
Genetic engineering of factor VIII  
far away yet – not made from  
plasma from Gene therefore No chance of getting any virus  
90% USA antibody

---

<sup>364</sup> Statement of Witness A [PEN.018.1367] at 1369

<sup>365</sup> Ibid

<sup>366</sup> Ibid

<sup>367</sup> Statement of Witness A [PEN.018.1367] at 1369

33% England  
<10% Scotland<sup>368</sup>

From the references to the future of haemophilia therapy and to rates of infection, it appears reasonable to deduce that all of the above represents Professor Ludlam's contribution.

**33.241** On the final page, the following is recorded:

Science Correspondent – Observer & Times  
fact sheet being sent out to all Haemophiliacs  
Batches            1 or several batches  
half developed antibody  
What are your plans for heat treating  
factor IX – technically more difficult  
1/3 less patients get HTLV3 antibody  
BTS procedure – less likely to be with factor IX  
Mild Mod Haem A treat DDAVP  
Live Virus HTLV3 used to test for Antibody  
younger shorter incubation  
older months – years  
Saliva – Very late stages of disease  
Not transmitted readily<sup>369</sup>

From the references to heat treating, it is possible that these remarks were made by Dr McClelland but it is not possible to be sure. The Inquiry also heard evidence from Professors Forbes and Ludlam, and Dr McClelland about their recollection of the meeting.

### Professor Forbes

**33.242** Professor Forbes found it very difficult to recall any details of the meeting. He had 'a major blank' in parts of his recollection.<sup>370</sup>

**33.243** Professor Ludlam admitted that he could not actually recall the detail of what Professor Forbes had said.<sup>371</sup> He thought it likely that Professor Forbes would have told the meeting some of the background to HTLV-III (ie that a probable virus that caused AIDS had been identified) and explained that a new test for HTLV-III antibody had been developed and that samples from patients in both Edinburgh and Glasgow had been tested and found to be antibody positive.<sup>372</sup> Professor Ludlam thought that Professor Forbes would then have talked about the findings in Glasgow and that he would have talked about his findings in Edinburgh.<sup>373</sup>

---

<sup>368</sup> Statement of Witness A [PEN.018.1367] at 1370

<sup>369</sup> Statement of Witness A [PEN.018.1367] at 1370

<sup>370</sup> Professor Forbes – Day 33, page 143

<sup>371</sup> Professor Ludlam – Day 35, page 130

<sup>372</sup> Ibid pages 130–131

<sup>373</sup> Ibid Page 130

**33.244** Professor Ludlam thought that Professor Forbes would have explained what was known about the implications of being antibody positive and what the chance was of developing AIDS. At that time it was thought that the risk of progression to AIDS was in the order of one in 500 or one in 1000. One of the important messages that they were trying to convey at the meeting was that patients' sexual partners could be at risk and that all patients should use condoms during sexual intercourse. Professor Ludlam thought it likely that Professor Forbes had addressed this issue. Professor Ludlam's recollection was that Professor Forbes dealt with the generalities of anti-HTLV-III testing and positivity.<sup>374</sup>

### Professor Ludlam

**33.245** Professor Ludlam thought that he would have spoken for approximately ten minutes. He did not speak from a prepared script or notes.<sup>375</sup> He told the Inquiry that he would have addressed what had been happening in Edinburgh: that blood samples from patients in Edinburgh had been tested for HTLV-III antibody by Professor Tedder and that some samples had tested positive. He thought that he would also have told the meeting that it appeared that a single batch of Factor VIII was responsible for the infections in Edinburgh but that other people might also be antibody positive:

It was a time of great uncertainty and we were very careful also to convey the message that if you were antibody negative, you weren't necessarily free of HTLV-III infection, and so the advice was for everybody to consider they might be infectious, everyone with haemophilia might be infectious, and ... the safety advice applied not only to the possibility of sexual transmission but if there was spillage of blood, it should be cleaned up carefully with gloves on and using dilute bleach to sterilise the surface.<sup>376</sup>

**33.246** Professor Ludlam said:

[T]he very clear message given out was that we hoped that patients would come and see us and ask about their situation. We were keen to discuss it with people individually. That was not just the people who were HIV positive. They didn't know who they were. We were keen to see everybody.<sup>377</sup>

**33.247** He said that he was keen for people to make appointments to see him to discuss whether there was an anti-HTLV-III result for them and whether they would like to know the result. He recalled telling the meeting that he would give patients their results if they wanted to know.<sup>378</sup> He could not recall, but thought it likely that he would have told the meeting how many patients had tested positive for the antibody. He said that he and his colleagues were there to give out any information they had and, as there was a number available, he would have said something like: 'So far it looks like there were 15 or 16 people' who had antibody to the virus and that it had arisen from Scottish product.<sup>379</sup>

---

<sup>374</sup> Ibid pages 131–133

<sup>375</sup> Professor Ludlam – Day 36, page 15

<sup>376</sup> Professor Ludlam – Day 35, pages 133–134

<sup>377</sup> Ibid page 134

<sup>378</sup> Ibid pages 135–135

<sup>379</sup> Professor Ludlam – Day 36, page 22

## Dr McClelland

**33.248** Dr McClelland told the Inquiry that the purpose of his attendance at the meeting was twofold. In the first instance he was there in a very specific capacity as representing the organisation which had manufactured the product believed to have been the source of infection, the SNBTS. There was also a general knowledge element to his presence at the meeting: by the time of the meeting he had been actively involved in work around AIDS and was relatively well informed about AIDS generally and the issues surrounding the interpretation of HTLV-III tests results.<sup>380</sup>

**33.249** Dr McClelland could not recall what he spoke about at the meeting, although he thought it likely that he would have spoken in terms comparable to patient information leaflets about what he understood at the time from his own knowledge of the situation.<sup>381</sup> He referred to an article in *The Edinburgh Evening News* on 21 December 1984<sup>382</sup> and confirmed that the information contained in that article was the sort of information that he would have given in respect of what was understood at the time about the nature of the virus, the nature of the test and the likely prognosis for people who were found to be antibody positive. He thought that he would also have told the meeting about the measures that the SNBTS, as a manufacturer, was taking to try to minimise future risks in terms of donor selection and plans to introduce routine donor testing.

## Question and answer session

**33.250** After Dr McClelland had finished speaking, Professor Ludlam's recollection was that Professor Forbes as the chairman invited questions and Professor Ludlam, Professor Forbes and Dr McClelland answered them depending on what the questions were. The question and answer session went on until all the questions were exhausted – perhaps half an hour or three-quarters of an hour.<sup>383</sup>

**33.251** Dr McClelland also recalled the question and answer session at the end of the meeting:

[T]here were some questions from patients. I think they were probably fairly muted because I think they were probably in a state of shock and having considerable difficulty in orientating themselves. Partly because of the nature of the information, partly because it was a very strange spot. It was a very strange situation altogether. So I think it would have been very difficult for patients to really absorb what was happening at that time.<sup>384</sup>

**33.252** Professor Ludlam and Mrs Brown described a feeling of dismay among the patients. Professor Ludlam told the Inquiry that there was 'surprise and I think some dismay' that individuals who had been treated exclusively with SNBTS product appeared to have been exposed to the virus.<sup>385</sup>

---

<sup>380</sup> Dr McClelland – Day 40, pages 99–100

<sup>381</sup> Ibid pages 101–102

<sup>382</sup> 'Plea to donors in AIDS alert', *The Edinburgh Evening News*, 21 December 1984 [PEN.016.1294]

<sup>383</sup> Professor Ludlam – Day 36, page 27

<sup>384</sup> Dr McClelland – Day 40, page 106

<sup>385</sup> Professor Ludlam – Day 36, page 21; Mrs Brown – Day 34, page 23

### Dr Alison Richardson's evidence

**33.253** Dr Alison Richardson, Clinical Psychologist, began seeing haemophilia patients from 1988 onwards. In her statement to the Inquiry she said:

Most of the patients I subsequently saw, after being referred to me by Dr Ludlam, recall being asked to come to an urgent meeting with Dr Ludlam. I am not exactly sure when this meeting was but I presume it was after these blood test results came back in about 1985. I think Dr Ludlam invited all the patients with haemophilia and not just those who were infected with HIV. Dr Ludlam wanted to warn them about HIV in the blood supply. I think that Dr Ludlam intended to persuade all the people with haemophilia to have a test for HIV. I was not present at that meeting, since this was before I had taken up my post. From what I have heard from the patients I spoke to subsequently, Dr Ludlam told them that some people with haemophilia in Scotland were infected with HIV. Two of my patients said that they were told at the meeting to use condoms when having sexual intercourse with their wives. From what I have heard from these two patients, the general feeling leaving that meeting was 'well, thank goodness, I don't have it, because if I had, he would have told me'. So, they left the meeting thinking that they did not have HIV.<sup>386</sup>

**33.254** In fact, these were two patients who had tested positive. Professor Ludlam was referred to this section of Dr Richardson's statement and was asked whether he would accept that these two patients did not appear to have received the message that they might be positive. He said:

They have not synthesised the information that was available to them, in that they ... would like to believe that they were in the larger group, who were anti HTLV-III negative.<sup>387</sup>

**33.255** Professor Ludlam told the Inquiry that he was clear that the message that he had given at the meeting was: 'you might be positive'.<sup>388</sup> He said that he had emphasised that, if patients wished to know their test results, they were to contact their haemophilia consultant to discuss their individual situations.<sup>389</sup> He said that the other side of that was that the majority of patients were in fact negative. As the majority of people had tested negative, Professor Ludlam believed that this may have influenced how attendees at the meeting assessed their own situation:

So there were a lot of people who were negative and more people actually who were negative than positive. So a patient might have gone away with the message, "Oh, well, I'm likely – because there were more people negative than positive, I'm likely to be one of the lucky ones." It's how one accepts bad news. We always like to think, to begin with, that we are on the winning side, if I can put it that way.<sup>390</sup>

---

<sup>386</sup> Dr Richardson's statement [PEN.016.1284] at 1288

<sup>387</sup> Professor Ludlam – Day 36, page 34

<sup>388</sup> Ibid page 30

<sup>389</sup> Professor Ludlam's note on long term safety monitoring for transfusion-transmitted infections [PEN.012.0351] at 0355

<sup>390</sup> Professor Ludlam – Day 36, page 31



**33.256** It was suggested to Professor Ludlam that the fact that patients were at risk didn't appear to have been effectively communicated to the patients. Professor Ludlam replied:

I would see it differently. They went away appreciating the need to use condoms. So they must have picked up that there was a possibility that they had got HIV or HTLV-III. That was why we were saying, "You have to use condoms" ....

I appreciate that they may not have seen it that way.<sup>391</sup>

**33.257** Professor Ludlam noted that patients were given condoms when collecting their concentrates from the Haemophilia Centre and that additional supplies, in plain paper bags, were placed on a shelf in the waiting room for patients to help themselves to.<sup>392</sup>

#### **Mrs Geraldine Brown's evidence**

**33.258** Mrs Brown told the Inquiry that, on the basis of what she recalled of the meeting, it would have been clear to anyone who attended that there was a group of patients infected in Edinburgh, that they might be a member of that group and that if they wished clarification of that, to know whether they were in the infected group and had tested positive, they had to approach Professor Ludlam and ask.<sup>393</sup>

**33.259** It was suggested to Mrs Brown that there were people at that meeting who did not appreciate that they would only be told their test results if they asked for them. In response to that, Mrs Brown said:

I think giving information to people of this kind, people who are in this situation, it can't just be a one-off thing. I think all sorts of things interfere with the way people process the information that you give them, which is why it was really important to have written information after the meeting, which people could read at their leisure and refer to ....

[I]t is difficult to give people information about such issues. I was ... a disinterested observer in the sense I wasn't personally involved. For me the information was quite clear but I can see that for other people perhaps it wasn't.<sup>394</sup>

**33.260** *The Yorkshire Post* published its article on Thursday 20 December 1984. In relation to the situation in Edinburgh it stated:

Dr Christopher Ludlam, a consultant haematologist and director of the haemophilia centre at Edinburgh Royal Infirmary, admitted yesterday that antibodies to the suspected AIDS virus had been found recently in 16 of his patients who were receiving only the NHS material. He told the *Yorkshire Post*:

'We picked up the HTLV 3 antibodies as part of a research project. We had hoped they would not be there. What this means is that these patients have been exposed to the virus.

We know it was not from an American blood product – because all these patients have been treated only with Scottish Factor 8. They may or may not still have the virus – it is something we cannot tell.

---

<sup>391</sup> Ibid page 34

<sup>392</sup> Professor Ludlam – Day 39, Page 101

<sup>393</sup> Mrs Brown – Day 34, page 75

<sup>394</sup> Ibid pages 75-76

This amounts to evidence that the material in Scotland has been contaminated with HTLV 3 and this must have come from a donor or donors who have the virus.

I can categorically say that to date there have been no cases of AIDS in Scotland attributable to Scottish Factor 8. My patients are all clinically well at the moment.

On present evidence it would appear that although AIDS may be caused by HTLV 3 only a small percentage of people who become infected actually develop the disease'.<sup>395</sup>

**33.261** The article went on to say:

News of the positive testing was broken to haemophiliacs from Edinburgh and Glasgow at a meeting last night. They were told collectively that some of them were carrying AIDS antibodies.

Dr Ludlam said: 'If individual patients want to know where they stand I shall tell them'.

Patients were strongly advised that from now on they should wear contraceptive sheaths during intercourse to protect their partners from danger.

They were also urged to take every precaution when making up their Factor 8 for home injections, and disposing of needles, syringes and plastic gloves.<sup>396</sup>

***Follow-up in Edinburgh***

**33.262** Following the meeting Professor Ludlam wrote to Dr McClelland about the need for precautions, in a letter dated 31 December 1984:

Dear Brian

Thank you for your letter of 12 December concerning our recent discussions about the desirability of close family members of haemophiliacs not donating blood.

As we agreed in our discussion it would be better to disseminate this information in the haemophiliac community by our existing lines of communication, rather than add these potentially high risk donors to your 'formal' list as published by the SNBTS. At the meeting of haemophiliacs on 19 December, at which you were present, this point was made clear. To make sure that the wider haemophiliac community is made aware that they should not be blood donors, we are arranging for a circular to be sent to every patient with moderate and severe haemophilia A and B.

I hope this will prevent any further donations within the Edinburgh and Glasgow areas. We are planning to send the circular to the other three East Coast Haemophilia Centres asking them to distribute it amongst their patients.<sup>397</sup>

---

<sup>395</sup> 'NHS blood carries killer AIDS virus', *The Yorkshire Post*, 20 December 1984 [SGH.002.6491]

<sup>396</sup> *Ibid* [SGH.002.6491] at 6491–92

<sup>397</sup> Professor Ludlam's letter to Dr McClelland dated 31 December 1984 [SNB.006.4686]

**33.263** Professor Ludlam also arranged for an advice sheet for adult patients and their families to be circulated.<sup>398</sup> It was sent to all patients on the Edinburgh Haemophilia Centre Register (around 170 patients) regardless of whether or not they had already been tested.<sup>399</sup> Paragraph 7(d) states: 'All relatives living in the same house with the family should refrain from giving blood. This is a simple precaution only'.<sup>400</sup> Professor Ludlam told the Inquiry that the circular was prepared in conjunction with Professor Forbes and was intended to be sent to all haemophilia patients in Scotland.<sup>401</sup> It is clear from the letter to Dr McClelland of 31 December 1984 that Professor Ludlam intended to send the circular to the other three east coast Haemophilia Centres.

**33.264** In the end, the circular was not sent to patients at the GRI. Rather, Professor Forbes seems to have incorporated parts of it into a letter which he sent to his patients on 8 January 1985, discussed below.<sup>402</sup>

**33.265** It is not clear exactly when the circular was sent out to Edinburgh patients as the document is undated. Professor Ludlam thought that it was probably sent out on 31 January 1985,<sup>403</sup> the same date on which letters were sent to GPs.<sup>404</sup> He had a recollection of all the information being sent at once. He also thought it unlikely that he would have written to the patients without first informing their GPs of that fact as he considered it only fair to make sure that GPs were forewarned before patients began going to see them. GPs were not sent a copy of the circular unless requested.<sup>405</sup> They were not given their patients' test results in these letters.<sup>406</sup>

**33.266** Professor Ludlam thought that the circular would have been sent out with a covering letter, although the Inquiry has been unable to locate a copy of such a letter. When asked for his recollection of what was in the covering letter, Professor Ludlam told the Inquiry that he thought that it would have referred to the meeting and would have said that the circular was being sent out to convey important information about AIDS to patients who had not attended the meeting. He thought that it would have mentioned that some patients had tested positive for HTLV-III in Scotland but that not all patients had been tested and that if patients would like to know the results of their test (which may or may not be available) they should make an appointment to see Professor Ludlam or to discuss the situation with Geraldine Brown.<sup>407</sup>

**33.267** Professor Ludlam thought that the circular, and in particular paragraph 6, combined with what was in his covering letter, was enough to get the message across to patients that they might be positive.<sup>408</sup> Paragraph 6 stated:

---

<sup>398</sup> Advice sheet for adult patients and families [PEN.012.0495]. At the same time a circular was also sent to parents of children with haemophilia. The only difference between these documents was that the latter did not refer to sexual activity. Professor Ludlam – Day 36, pages 47–48

<sup>399</sup> Professor Ludlam – Day 36, page 35

<sup>400</sup> Advice sheet for adult patients and families [PEN.012.0495] at 0496.

<sup>401</sup> Professor Ludlam – Day 36, page 38

<sup>402</sup> Letter from Dr Lowe and Dr Forbes to GRI haemophilia patients dated 8 January 1985 [LOT.003.4244]

<sup>403</sup> Professor Ludlam – Day 36, page 36; Note of a meeting between Professor Ludlam and the Penrose Inquiry legal team [PEN.012.0774] at 0793

<sup>404</sup> Professor Ludlam's letter to GPs dated 31 January 1985 [LOT.002.2489]

<sup>405</sup> Professor Ludlam – Day 36, page 36

<sup>406</sup> Note of a meeting between Professor Ludlam and the Penrose Inquiry legal team [PEN.012.0774] at 0792

<sup>407</sup> Professor Ludlam – Day 36, page 43

<sup>408</sup> Ibid pages 42–43

## 6. What is the virus?

The virus probably responsible is called Human T-cell Lymphotropic Virus (HTLV III). Its main action is to reduce the effectiveness of a particular cell ( $T_4$  cells) in the immune process. Exposure to the virus results in the body making an antibody (HTLV III Ab) to the virus protein and this is now used as a marker of exposure to the virus. These tests are now available and will be carried out on your routine visits to your centre. About half the patients in England and about ten per cent in Scotland have had exposure and are HTLV III Ab-positive.<sup>409</sup>

**33.268** When asked why he did not make the letter more explicit, Professor Ludlam said:

I would have an obligation to inform patients of their antibody result if it was going to make a difference to either the way they lived or treatment that might be available for them. And at that time there was unfortunately no treatment available and there were some patients who clearly didn't want to know, and so, as there was no, in a sense, material gain from knowing, then it was a patient's prerogative not to know.<sup>410</sup>

**33.269** When asked why he did not simply inform all of his patients of their test results, Professor Ludlam explained that it took some time for clinicians themselves to come to terms with the results. That patients had been exposed to the virus was 'a surprise and a shock'. He added that it might have been the case that some patients would not have wanted to know their results and that, following the distribution of the circular, some patients were indeed 'hesitant' about knowing their results. In addition, there was already a great deal of stigma surrounding AIDS and Professor Ludlam believed that patients would have to consider that when deciding whether or not to obtain the results of their tests.<sup>411</sup>

## Communication of results

**33.270** Professor Ludlam thought that it was the beginning of January 1985 before patients began contacting him asking for their results. He described it as an 'ad hoc, unstructured arrangement'. Sometimes patients would come to the clinic for other reasons, for example to collect home treatment, and would ask the nurse if he was available to see them. At other times the patient would come to the clinic and the nurse might initiate a meeting by asking if the patient wanted to see Professor Ludlam.<sup>412</sup> Professor Ludlam told the Inquiry that the physical arrangements at the haemophilia centre at that time were unsatisfactory in terms of conveying results:

It's a time when we were very short of clinic space ... [A]t that time we had a single room with a small partitioned area off in one of the wards which we called our "haemophilia centre", which was for the treatment of acute bleeds, basically.

The patients were seen for their routine reviews in the general medical outpatient department. So I did not have anywhere else to see people with some degree of privacy, and I remember having to borrow rooms in one or two of the other wards [and having] to find out where there was a free room to see someone.

---

<sup>409</sup> Advice sheet for adult patients and families [PEN.012.0495] at 0496

<sup>410</sup> Professor Ludlam – Day 36, page 44

<sup>411</sup> Note of a meeting between Professor Ludlam and the Penrose Inquiry legal team [PEN.012.0774] at 0794

<sup>412</sup> Professor Ludlam – Day 36, pages 58–59

So it was unsatisfactory but I wanted to give the patients a bit of space and time and have a bit of privacy. The facility we had in ward 23, the partition wall between the waiting area and the tiny clinic room, was thin and I don't think there was even room to sit down actually in this little room. We had a couch and a filing cabinet. So I had to find other space. So it was not satisfactory but I had to make do.<sup>413</sup>

**33.271** He said that whether or not he initiated discussion about AIDS with patients attending clinics or encouraged them to ask for their results depended on why he was seeing them in the clinic. If patients came to the clinic with a specific medical issue that needed to be addressed (such as a bleed or a medical problem that required investigation) he would concentrate on that issue because that was what the patient had come for. He said that he would not have raised the topic of AIDS with patients in these circumstances because he felt that it would have been confusing for them.<sup>414</sup>

**33.272** If patients came to the clinic for a routine review appointment and he was having a more general discussion about their health (for example, how they were feeling, whether their clotting factor was working properly, whether they had been off work due to bad bleeds, etc) then he might have asked, as part of that general discussion, what the patient knew, if anything, about AIDS and taken it from there.<sup>415</sup>

**33.273** Professor Ludlam explained that he would not discuss AIDS if the patient had some other preoccupation. At a routine review without any other immediate concerns he would think about raising it with the patient but would not necessarily do so even then.<sup>416</sup> He said that he would raise the matter if he 'thought it appropriate'. He told the Inquiry:

I raised the topic with patients when they came for review, not all patients, not all the time but some of them some of the time.<sup>417</sup>

**33.274** Subsequently, large-scale local testing for HIV was instituted from early in 1985. This is discussed separately below.

### *Follow-up in Glasgow*

**33.275** As noted above, Professor Ludlam's circular was not sent to patients at the GRI. Instead, a letter, signed by Professor Forbes and Professor Lowe and dated 8 January 1985, was sent to all patients registered at the West of Scotland Haemophilia Centre.<sup>418</sup> Professor Lowe described the letter as an 'update' for patients in light of recent developments. He explained that the purpose of the letter was, firstly, to inform patients that there was an apparent HIV problem in the Scottish haemophilia population and, secondly, to invite them to the Haemophilia Centre to discuss the matter with one of the doctors who would then, after obtaining consent, take a fresh blood sample which could be tested for HIV. He did not think that the purpose of the letter was to invite patients to the Haemophilia Centre for Professor Forbes to give them the results of the Gallo research study tests.<sup>419</sup>

---

<sup>413</sup> Ibid pages 57–58

<sup>414</sup> Ibid pages 63–65

<sup>415</sup> Ibid page 66

<sup>416</sup> Ibid

<sup>417</sup> Ibid pages 65

<sup>418</sup> Letter from Dr Lowe and Dr Forbes to GRI haemophilia patients dated 8 January 1985 [LOT.003.4244]; Professor Lowe – Day 40, pages 44–45

<sup>419</sup> Professor Lowe – Day 40, pages 36–40

**33.276** The letter began by setting out the material background:

As you may know, there has been recent publicity in the newspapers and television concerning an increased risk of the disease known as Acquired Immune Deficiency Syndrome (AIDS) in haemophiliacs who have received treatment with clotting factor concentrates.

....

We do not yet have a blood test for the virus particle, but hope to have this within the next few months. However, we and other haemophilia centres do now have a blood test for antibody to the virus. If this antibody test is positive, this means that the person has been exposed at some time to virus particles. A positive test does not mean that the person will develop AIDS. Recent studies in England have found that about half of regularly treated haemophiliacs have positive antibody tests. We have recently tested stored blood samples from many of our patients, of whom about 10% have positive antibody tests.<sup>420</sup>

**33.277** The letter then set out what was to happen next:

Firstly, we enclose an appointment to see you. It is important that we take a blood sample from you for the virus tests, so that we can monitor virus exposure in all our patients who have received factor concentrates. We would also like to perform some skin tests which measure the body's defences against infections. At the same time we will be very happy to give further information and to answer any questions you may have about the virus and the tests.<sup>421</sup>

**33.278** Patients were advised that, if the enclosed appointment was unsuitable, they should contact the haemophilia Sister for an alternative appointment.

### Communication of results

**33.279** Professor Forbes said that his Haemophilia Centre 'always had a very open policy'<sup>422</sup> and that he took the view that his patients should be told about their test results: 'we made a firm decision that we would tell the patients what had been found in the various tests that were done and the implications thereof'.<sup>423</sup> His recollection was that patients were told as soon as practicable: 'we told them as soon as possible and we in fact had to make appointments for many of them especially and bring them in to tell them'.<sup>424</sup> With regard to the initial Gallo tests he stated that the 12 patients who had already tested positive were informed of their primary test results before confirmatory testing by Dr Edward Follett.<sup>425</sup>

**33.280** Professor Lowe recalled that at the time the draft manuscript of the December article in *The Lancet* (with the results of the 12 positive tests) was being discussed, probably around September or October 1984, Professor Forbes said that he would see the patients with positive test results and arrange counselling. Professor Lowe stated that he had 'absolutely no reason' to believe that Professor Forbes did not do so.<sup>426</sup> He described

---

<sup>420</sup> Letter from Dr Lowe and Dr Forbes to GRI haemophilia patients dated 8 January 1985 [LOT.003.4244] (emphasis in the original)

<sup>421</sup> Ibid [LOT.003.4244] at 4244–45 (emphasis in the original)

<sup>422</sup> Professor Forbes' statement in information given to patients [PEN.012.0411] at 0413

<sup>423</sup> Professor Forbes – Day 33, page 131

<sup>424</sup> Ibid page 133

<sup>425</sup> Ibid

<sup>426</sup> Professor Lowe – Day 40, page 52

Professor Forbes as ‘an extremely open person’ who would spend hours with his patients discussing all manner of things and that he could not think of any reason why Professor Forbes would not have been open and honest with patients.<sup>427</sup> Professor Lowe was not involved in communicating the Gallo test results, however, as Professor Forbes felt strongly that, as the Consultant, it was for him to speak to the patients and tell them about the situation.<sup>428</sup>

**33.281** Professor Lowe thought that Professor Forbes had some reservations about the reliability of the Gallo test because it was a research assay and had not yet been licensed for clinical use. He recalled that Professor Forbes thought that the best thing to do was to set up properly approved tests with Dr Follett at the local regional virus laboratory, inform the initial 12 positives of their (provisional, at that stage) results, offer them counselling and arrange for further, confirmatory testing when that became available. Professor Lowe thought that it was around this time that Dr Wilkie was appointed.<sup>429</sup>

**33.282** It is clear that by October 1984, well before the meeting in Edinburgh in December 1984, Professor Forbes had initial positive results on 12 of his patients. It is likely that by then he had made at least preliminary arrangements with Dr Wilkie for counselling patients testing positive for HTLV-III. Professor Forbes was asked whether he knew that he had 12 patients who had tested positive at the time he appointed Dr Wilkie. He replied:

I’m not sure. I don’t remember the chronology of that but I knew that it was going to come that this epidemic would happen in Scottish haemophiliacs, as it did.<sup>430</sup>

**33.283** On Dr Wilkie’s evidence Professor Forbes did know that some of his patients were infected when he approached her.

**33.284** The letter of 8 January 1985 indicated that stored blood samples had already been tested, with about 10% antibody positive results (paragraph 33.276 above). To some extent – which cannot be quantified – patients’ blood samples were also being tested in Dr Follett’s laboratory in January 1985, before the development of a routine requiring prior counselling and consent. The way in which these samples were sent to Dr Follett can only be characterised from the patient’s point of view as clandestine.

**33.285** Equally, there is no reliable evidence that the results of the series of tests performed by Gallo, which from the patient’s point of view were also clearly clandestine, were ever communicated to the patients involved. How far the knowledge of the Gallo results was known within the GRI is not clear. From Professor Lowe’s evidence it appears that circulation of the information was limited, but Professor Forbes clearly knew who had been tested and what the individual results were. In the circumstances, the point of the reference in the letter dated 8 January to recent studies in England showing that about half of regularly treated haemophilia patients had positive antibody tests is not obvious. Indicating that a lower proportion of Glasgow patients was infected minimised the serious implications for the 10% of local patients who had positive antibody tests.<sup>431</sup>

---

<sup>427</sup> Ibid page 52

<sup>428</sup> Ibid pages 43 and 38

<sup>429</sup> Ibid pages 38–40

<sup>430</sup> Professor Forbes – Day 33, page 126

<sup>431</sup> Letter from Dr Lowe and Dr Forbes to GRI haemophilia patients dated 8 January 1985 [LOT.003.4244]

**33.286** Communication of the results of the Gallo test series, available in October 1984, was left in the hands of Professor Forbes. Unfortunately, and as he was well aware, his recollection of the Gallo tests and matters related to them is not good. It seems likely, despite his recollection, that he did not pass the Gallo results on to the patients tested. Professor Lowe mentioned Professor Forbes' reservations about the accuracy of the Gallo tests as it was a research assay, and not yet licensed for clinical use. Dr Froebel also remarked on Professor Forbes' reservations due to the Gallo test's unregulated state. Given the life-changing effects of testing, whether the results were positive or negative, Professor Forbes might well have considered that confirmation of the Gallo tests was required prior to passing on any information to patients about their positive or negative status. His foresight in employing Dr Wilkie as an HIV/AIDS counsellor (his unit being the first in Scotland to do so) suggests that he was sensitive to the extensive ramifications of testing and, in particular, a positive diagnosis.

## **Local testing**

### *Edinburgh*

1985

**33.287** Very early in 1985 it became clear that anti-HTLV-III testing would have to be set up in many centres in the country. Dr John Peutherer, a virologist with whom Professor Ludlam had worked previously, made enquiries about setting up HTLV-III antibody testing in Edinburgh. Professor Ludlam thought that by the spring of 1985 a number of different commercial kits were under evaluation.<sup>432</sup>

**33.288** Local testing was available by the spring of 1985 and was carried out by Dr Peutherer. Professor Ludlam said that patient consent was obtained prior to all local testing if a fresh blood sample was taken.<sup>433</sup> He recalled that most of the patients tested were found to be HTLV-III antibody negative, with between five and 10 found to be antibody-positive.<sup>434</sup>

**33.289** Professor Ludlam also thought that he would probably have sent additional stored samples from those people who had already been tested by Professor Tedder, to confirm the initial result and, for those who had tested positive, to determine their date of seroconversion. He thought that this confirmatory testing had been carried out by Dr Peutherer on all of the results received from Professor Tedder. It appears, therefore, that so far as the original group is concerned (the 50–70 patients who had been tested without their consent), there may have been repeat testing by Dr Peutherer in 1985 by reference to archived material. Professor Ludlam thought that this was probably also done without their consent: the procedure continued under the original regime. He did not think that there was any other testing of patients without consent.<sup>435</sup>

**33.290** Local testing opened up the opportunity for many more individuals to be tested, not just people with haemophilia. The AIDS advisory committee in Edinburgh was established at Professor Ludlam's suggestion and held its first meeting on 19 December 1984.<sup>436</sup> Dr Peutherer told the Inquiry that subsequent testing for HTLV-III infection started

---

<sup>432</sup> Professor Ludlam – Day 36, pages 73–74

<sup>433</sup> Ibid page 90

<sup>434</sup> Ibid page 75

<sup>435</sup> Ibid pages 91–92

<sup>436</sup> Ibid page 74



in 1985 once commercial tests became available. Professor Ludlam did not carry out any HTLV-III testing in his laboratory. All testing for patients from the RIE was carried out by the Hepatitis and HTLV-III/HIV Reference Laboratory within the University of Edinburgh's virus diagnostic service. The tests used were purchased from several companies, including Abbott, Wellcome and Ortho.<sup>437</sup>

**33.291** Professor Ludlam said that early in 1985, when testing became more generally available, there were calls from many different people – particularly surgeons – for screening of all patients. The difficulties around this issue and also, for example, enquiries from insurance companies wanting to know whether someone had been tested, grew very rapidly through 1985 and led to thinking about what is now called pre-test counselling. The whole complexion of testing changed.<sup>438</sup> In 1985 Professor Ludlam drew up some guidelines for testing.<sup>439</sup> He explained:

These were fairly primitive guidelines that – I think they must have been written in 1985, probably the end of 1985, because if I remember correctly ... they don't give a definitive view about the significance of being anti HTLV-III positive.<sup>440</sup>

**33.292** Professor Ludlam thought that he had drafted the guidelines after discussion with colleagues. He said that they were primarily for staff use and were a way of focussing the minds of staff members on the important things to think about:

[T]his evolved, if you like, out of ... our realisation that it was appropriate to get consent and to think about ... whether people want[ed] to know about positive results or ... want[ed] to be tested ....

So the degree of pre-test counselling ... evolved during 1985.<sup>441</sup>

### Discussions with Mrs Geraldine Brown

**33.293** Mrs Brown told the Inquiry that she began working at the Edinburgh Haemophilia Centre in about December 1984 and started seeing patients very shortly thereafter, in January or February 1985.<sup>442</sup> She noted that, at that time, there was no physical haemophilia centre in the way that there is now.<sup>443</sup> Rather, in-patients were seen on the ward and out-patients were seen in the medical out-patients department or in doctors' offices. Mrs Brown told the Inquiry that the arrangement in early 1985 was that she would go to the medical out-patients department and meet with patients after they had been seen at the clinic to introduce herself. If patients were on the ward having treatment she would also go along and introduce herself there. She said that Professor Ludlam also made patients aware that a new social worker was attached to the unit and that she was available to see patients.<sup>444</sup>

---

<sup>437</sup> Dr Peutherer's statement [PEN.012.0857]

<sup>438</sup> Professor Ludlam – Day 36, pages 87–88

<sup>439</sup> Guidelines for counselling pre- and post-HIV testing [PEN.015.0502]

<sup>440</sup> Professor Ludlam – Day 36, page 88

<sup>441</sup> Ibid page 90

<sup>442</sup> Mrs Brown – Day 34, page 39

<sup>443</sup> Ibid page 30; See also Professor Ludlam's note on the development of the Edinburgh Haemophilia and Thrombosis Centre [PEN.012.0386] at 0387, where Professor Ludlam describes the 'haemophilia centre' at that time as comprising a small side room in a ward, a weekly clinic in the Medical Outpatients Department and the haemostasis laboratory. These three sites were spread across the hospital campus. A new Haemophilia Centre, with considerably better facilities, was opened in 1988.

<sup>444</sup> Mrs Brown – Day 34, pages 30–31

**33.294** Mrs Brown told the Inquiry that she often spoke to patients about whether they should ask for their tests results and what the implications were prior to them making a decision. She described some of the difficulties regarding this to the Inquiry:

It was a very different atmosphere then in terms of knowledge and patients were very aware that they were identifiable as a group, haemophiliacs were identifiable as a group ... that they were already seen in the community as people who were potentially infected with HIV.

There was concern [that] the fact that someone ... had been infected with HIV [would interfere with the] provision of services to them ... on a financial level, insurance companies' questions, mortgage lenders' questions. There were concerns about discrimination in terms of the provision of medical services. There was concern that surgeons wouldn't operate on them if they were known to be HIV [positive]. There was a kind of feeling around at the time of this great anxiety about what would happen if people knew you were HIV positive.

There was also, of course, an acknowledgement that there wasn't really any treatment going to be available to patients. So knowing that they were HIV positive, it wasn't like getting another medical diagnosis which would immediately throw in a treatment programme, because at that point there wasn't really anything being offered in terms of treatment, although anyone who was infected with HIV would benefit from being followed up medically. The haemophiliacs were being followed up anyway because they were being seen regularly at the hospital. So people were weighing up the pros and cons really of knowing that they were infected with HIV.

And also, I think, for some people – I think the way you deal with significant medical information about yourself sometimes is you don't want to know. You might just put it aside and prefer to carry on ... as you are.

So people had lots of issues that they discussed really prior to asking for the information.<sup>445</sup>

**33.295** Mrs Brown said that patients began to ask for (and were told) their HIV status during the first three months of 1985. It was a gradual process after that with more and more people asking for their results during the course of the year. She thought that by the end of 1985 most patients would have known their HIV status but that there were one or two patients who had not asked for their results.<sup>446</sup> She said:

I think the point to emphasise is that if people did not know they were infected, it was because they didn't ask. I think it was quite clear to people from the start that this information was available to them and they could have it and I think that in a sense the ball was in their hands, when they were told that a group had been infected. It was quite clear that they did need to make the approach and discuss it.<sup>447</sup>

---

<sup>445</sup> Ibid pages 39–41

<sup>446</sup> Ibid pages 44–45

<sup>447</sup> Ibid page 60

**33.296** Professor Ludlam also thought that the vast majority of his patients were aware of their HTLV-III status by the end of 1985. This included patients who had tested positive and patients who had tested negative. His recollection was that by the end of 1985 there was only a small handful of patients who were known to be anti-HTLV-III positive and who did not know their results. He thought that by the end of 1985 probably only around three to five patients would not have known their HTLV-III status.<sup>448</sup>

**33.297** Those who did not know their results by the end of 1985 fell into two categories: (i) those who were adamant that they did not want to know and (ii) those who did not appreciate that they needed to ask for their results. Professor Ludlam said that he could think of only two individuals in the second category and one individual (the witness pseudonymised as 'Mark', discussed below at paragraph 33.304) who expressly said that he did not want to know.<sup>449</sup>

## 1986

**33.298** Professor Ludlam said that in late 1985 and early 1986 the picture was gradually evolving. By that time it was becoming clearer, firstly, that patients who tested positive for antibodies to HTLV-III probably harboured the virus and, secondly, that the risk of progression to AIDS in patients who were HTLV-III positive was greater than the original estimate of one in 500 or one in 1000. There was greater confidence about what an anti-HTLV-III positive result meant, and conversely there was a bit more confidence that those who were anti-HTLV-III negative did not have the virus.<sup>450</sup> For those who had tested positive, emerging data also suggested the course of the disease might be worse than had previously been thought:

[T]he significance in terms of their prognosis was beginning to look a bit worse. There was still no treatment or no prophylaxis at this stage, nothing that could be done, in a sense, medically to improve their prospects.<sup>451</sup>

**33.299** Professor Ludlam knew the identities of those patients who were HTLV-III antibody positive but who had not received their results at the end of 1985.<sup>452</sup> Weekly multi-disciplinary meetings were held where individual patients were discussed. The meetings were attended by a core group of Professor Ludlam and his registrar; Dr George Masterton, a psychiatrist; Michelle Jones, the Haemophilia Sister; Billie Reynolds, the Staff Nurse; and Geraldine Brown. Professor Ludlam stated:

This was ... a fairly quiescent period at one level because patients were all feeling well. It was a sort of phoney war time, if I can put it that way. All the patients were well and we discussed each week who we had seen, exchanged information that seemed relevant and increasingly worried about the small number of people who ... had tested positive and didn't know.<sup>453</sup>

**33.300** Although the group appears to have been discussing patients who did not know their results during this time, no positive steps were taken to inform those patients. Professor Ludlam told the Inquiry that this approach, of not insisting that patients know their results, did not change at this time.<sup>454</sup>

<sup>448</sup> Professor Ludlam – Day 39, page 135

<sup>449</sup> Ibid pages 135–136

<sup>450</sup> Professor Ludlam – Day 36, page 67. Notwithstanding what is recorded in the transcript, the Inquiry is of the view the 'weren't' recorded at line 23 should be 'were'.

<sup>451</sup> Professor Ludlam – Day 36, page 69

<sup>452</sup> Ibid page 67

<sup>453</sup> Ibid pages 68–69

<sup>454</sup> Ibid page 70

**33.301** The feeling of the group was that those patients who had not asked for their test results did not want to know them:

[T]here was the feeling that ... maybe patients didn't want to know. Maybe once they know they are antibody positive, there is no going back, and if you don't know, then you can believe that you are negative .... It was a very new situation for us and we wanted to be sensitive to the patients because once you have told someone, you can't untell them.<sup>455</sup>

**1987**

**33.302** Professor Ludlam said that his approach of not insisting that patients knew their results changed around the end of 1986/beginning of 1987. As he explained:

[A]t that point ... the possibility of treatment with Zidovudine was being talked about. There was the possibility of prophylaxis against pneumocystis, the awful pentamidine inhalations. At that time ... one or two patients were starting to become clinically unwell, I assume because of the virus.

So a time came when I felt that it really was in the medical interests of the patients to tell them ....

[I]t was a balance and I thought it was becoming more in their interests, medical interests, to know.<sup>456</sup>

**33.303** He began asking patients to come in and see him. He could not recall how strongly he would have put it or how insistent he might have been, but he said that he would have made it very clear that he thought there were good reasons for patients to know their status and that he would like to tell them. He told the Inquiry that he either wrote to them or someone would ring them up and ask them to come in to the clinic.<sup>457</sup>

**Mark**

**Sister Billie Reynolds' evidence**

**33.304** Ms Billie Reynolds worked in nursing posts at the Edinburgh Haemophilia Centre beginning in June 1986. She provided an affidavit in which she challenged some of Professor Ludlam's recollections.<sup>458</sup> With regard to the patient given the pseudonym 'Mark' not finding out his diagnosis with HIV until January 1991, her impression was that Professor Ludlam 'could not face telling Mark his results'. She suggested that this reluctance stemmed from an earlier incident, when Professor Ludlam had given a positive test result to a patient of similar age in about 1986 and it had gone very badly.<sup>459</sup> Initially, she confused Mark with the patient concerned. Her account of events was disputed by Professor Ludlam in a statement provided by him to the Inquiry.<sup>460</sup>

**Professor Ludlam's evidence**

**33.305** Professor Ludlam said that he repeatedly tried to tell Mark the results of his HIV tests and that Mark repeatedly told him that he did not want to know them.

---

<sup>455</sup> Ibid pages 69–70

<sup>456</sup> Ibid pages 70–71

<sup>457</sup> Ibid page 71

<sup>458</sup> Sister Reynolds' affidavit [PEN.018.0810]

<sup>459</sup> Ibid [PEN.018.0810] at 0817

<sup>460</sup> Observations on Affidavit of Billie Reynolds dated 29 November 2011 by Professor Christopher Ludlam [PEN.018.1430]

**33.306** Professor Ludlam said that to begin with he was hesitant to let Mark know of his results because of ‘a number of social reasons’ but felt that a time came when it was important for him to know. He told the Inquiry that he arranged to see Mark sometime in 1986 (he could not recall the date) and said that he had been ‘quite taken aback’ because Mark was ‘quite categorical’ that he did not want to know his results. Professor Ludlam said that he was ‘a bit thrown’ by Mark’s reaction because he had not experienced a patient so determined that he did not want to be told. Professor Ludlam told the Inquiry that he informed Mark that he was telling everyone that they had to be very careful with blood spillages and sex. He was concerned that Mark might sustain injury in consequence of his manual employment.<sup>461</sup> Professor Ludlam explained:

We tried on at least two further occasions to convey this information to him. One was to potentially visit him at home and the other was when he came up to the clinic and he saw one of our very able young doctors and she tried to persuade him, very strongly – this would be about 1988 or 1989 ....

So there were several occasions when we tried very explicitly to explain to him and he adamantly didn’t want to know. And this wasn’t talking about iron levels; this was talking about HTLV-III and AIDS.<sup>462</sup>

**33.307** Professor Ludlam referred to a note from medical records which he thought was dated 13 November 1986:

There is the sheet that was in my private notes, if I can put it that way, that was from 1986 ....

This was a record of my seeing Mark in 1986, wanting to tell him about his result and he not being keen to know – or didn’t want to know the answer. I made a note of that and the advice that I gave to him and I felt it inappropriate to put it in his case notes for some of the reasons we talked about earlier, and I had a confidential file in my room, locked up, in which I kept that information. That information has now been returned to his principal case notes.<sup>463</sup>

### *Glasgow*

**33.308** Subsequent to the original Gallo test series, the local virologist, Dr Follett at Ruchill Hospital, set up a specialist laboratory and thereafter testing of west of Scotland patients was carried out there. Professor Forbes told the Inquiry that he arranged for Dr Follett to confirm the 12 original positive test results. He said that he wanted to confirm the initial results using a slightly different test but that the 12 patients who had already tested positive were informed of their primary test results before confirmatory testing by Dr Follett.<sup>464</sup>

**33.309** Professor Lowe told the Inquiry that it took some months for Dr Follett to get HIV tests up and running in his laboratory. He said that Professor Forbes and Dr Follett were both concerned about the specificity of the early tests: there were lots of false positives and false negatives. Given the increasing concern about the implications of a positive result, they wanted the test to be as accurate as possible. He said that Dr Follett took great care when setting up the test.<sup>465</sup>

---

<sup>461</sup> Professor Ludlam – Day 36, page 102

<sup>462</sup> Ibid page 103

<sup>463</sup> Ibid page 104

<sup>464</sup> Professor Forbes – Day 33, page 133

<sup>465</sup> Professor Lowe – Day 40, page 47

**33.310** Professor Lowe thought that Dr Follett probably carried out HIV tests over the summer of 1985 but he could not be more specific about the date.<sup>466</sup> He recalled that, when patients attended the clinic centre in early 1985, after the 'update letter' but before local testing was available, a lot of time was spent talking to patients about AIDS and telling them that it was hoped that testing would be available in the near future. It was at this time that Dr Wilkie began counselling patients about the significance of HIV testing.<sup>467</sup>

**33.311** Dr Wilkie and her colleagues reported on the research exercise in a paper entitled 'Daily living problems of people with haemophilia and HIV infection: implications for counselling' which was published in 1990.<sup>468</sup> According to the paper patients were told, by letter, at the beginning of 1986 of the forthcoming study and that they would be invited to participate. This date, like many relating to the Glasgow exercise, is problematic. It appears that it may depend on the formal project start date rather than the actual date of the work. However, by way of background the paper stated:

Before the start of the project patients came to the haemophilia clinic at six-monthly intervals for review of their condition and received information about, and were tested for, HIV infection. In addition, many of them had obtained information about AIDS from the news-sheets from The Haemophilia Society, from television and from the press, and had read *AIDS and the Blood* (Jones, 1985) recommended by The Haemophilia Society.<sup>469</sup>

**33.312** Professor Lowe said that he was involved in seeing some of the patients who came for the appointments that had been arranged in the January 1985 letter. When asked what he told the patients he saw during these appointments, Professor Lowe explained that he would go through the letter and discuss the precautions to be taken by patients as this was considered a priority. He would then explain that Professor Forbes was arranging for HIV testing to be performed at the regional virus laboratory and that it was hoped that testing would be in place during 1985. He would tell them that, before such testing was performed, it was important that they had more information about the implications of testing and of both positive and negative test results. Patients would then be seen by Dr Wilkie. Professor Lowe said that blood would not be taken at that time and that he would never have taken a blood sample for HIV testing until the patient had been through the counselling process.<sup>470</sup>

**33.313** Professor Lowe did not know whether he saw any of the patients who had tested positive on the Gallo tests. He said that he never knew the names of those patients.<sup>471</sup> The appointments arranged in January were to discuss the risks, to emphasise the precautions to be taken, to talk about heat treatment and to explain that it was hoped that blood samples would be taken and tested in the future. By the time testing was ready to be carried out by Dr Follett, Professor Lowe considered that the patients had been 'pretty intensively educated and counselled' about HIV testing.<sup>472</sup> It is difficult, however, to imagine a situation in which Professor Lowe could have had such a conversation with a patient who had previously been told that he was HTLV-III positive on the Gallo test without that fact becoming apparent.

---

<sup>466</sup> Ibid pages 46–47

<sup>467</sup> Ibid page 43

<sup>468</sup> Wilkie et al, 'Daily living problems of people with haemophilia and HIV infection: Implications for counselling', *International Journal of Rehabilitation Research*, 1990; 13/1: 15–25 [PEN.018.1228]

<sup>469</sup> Ibid [PEN.018.1228] at 1230

<sup>470</sup> Professor Lowe – Day 40, pages 44–46

<sup>471</sup> Ibid page 46

<sup>472</sup> Ibid page 48

**33.314** In April 1985 a further letter was sent to patients.<sup>473</sup> This was similar to the January 1985 letter but with some updating.<sup>474</sup> The April letter also enclosed Dr Peter Jones' booklet 'AIDS and the Blood' mentioned by Dr Wilkie in her article.<sup>475</sup> The letter and enclosed booklet were sent to all patients who were registered at the haemophilia centre at the time.<sup>476</sup>

**33.315** Professor Lowe told the Inquiry that, from that point, when patients attended the clinic and before any blood samples were taken for testing he would ask them if they had read the January letter, the April letter and the booklet.<sup>477</sup> Professor Lowe said he made sure that all the patients that he saw at the clinic at which time blood was taken were fully informed about HIV testing and its implications.<sup>478</sup>

**33.316** Professor Lowe thought that the great majority of the patients registered at the centre had been tested by Dr Follett over the summer of 1985 and certainly by October 1985.<sup>479</sup>

**33.317** He said that the results went to Professor Forbes and that about a dozen patients tested positive. Professor Lowe recalled Professor Forbes saying that when it came to telling patients results of positive tests they should make 'special arrangements'. Professor Forbes wanted one of the consultants (Professor Lowe or himself) to spend 'a good amount of time' with each patient and fully discuss the implications of their positive test result.<sup>480</sup> It is unclear how the twelve patients who tested positive in the bulk testing exercise described by Dr Froebel (paragraph 33.200) related to the twelve who tested positive in Dr Follett's series; however, it is reasonably clear that it was the patients identified by Dr Follett's study who had received pre-test counselling, and who had given informed consent, who were then informed of their results and counselled by Professor Forbes and Professor Lowe.

**33.318** Professor Lowe told the Inquiry that Professor Forbes' policy was that patients would be told at the next clinic review after a positive test result was discovered.<sup>481</sup> This usually took place within a few weeks of the blood sample being taken but would vary from patient to patient depending on when the results came back. No special arrangements were made for patients who tested negative. Professor Lowe said that, when a patient tested positive, he and Professor Forbes tried to make sure that they had time outwith the usual clinic routine where they could speak with the patient in private and have a long discussion. He said that often Dr Wilkie was present during these meetings and participated in the process of providing information and counselling to patients.<sup>482</sup>

**33.319** Professor Lowe thought that he would have passed positive results on to around half a dozen patients. In 1985 there were 12 HTLV-III antibody positive patients in the region and Professor Lowe thought that he and Professor Forbes had split the responsibility for communicating test results and counselling patients and had informed about half a

---

<sup>473</sup> Letter from Dr Lowe and Dr Forbes to GRI haemophilia patients dated April 1985 [LOT.003.4311]

<sup>474</sup> Professor Lowe – Day 40, pages 50–51

<sup>475</sup> Jones (1985). *Aids and the blood: a practical guide*. Newcastle Haemophilia Reference Centre [SNB.004.6186]

<sup>476</sup> Professor Lowe – Day 40, page 50

<sup>477</sup> *Ibid* page 51

<sup>478</sup> *Ibid* page 56

<sup>479</sup> *Ibid* pages 46–47

<sup>480</sup> *Ibid* page 47

<sup>481</sup> Professor Lowe's statement on information given to patients concerning HIV [PEN.016.1250] at 1256

<sup>482</sup> Professor Lowe – Day 40, pages 57–58

dozen each. He said that none of the patients that he informed expressed any surprise at all at the result.<sup>483</sup>

**33.320** Dr Wilkie told the Inquiry that often she was the person who told the patients that they had tested positive for the virus. She could not recall how many patients she personally delivered results to.<sup>484</sup> Professor Lowe challenged this evidence. He did not think that she would have had responsibility for informing patients of their test results herself but recalled that she would have been sitting with Professor Forbes or himself when the results were passed on.<sup>485</sup> Dr Wilkie said that she didn't have any recollection of sitting in with Professor Lowe; although she may have done so on some occasions, she said it was nearly always with Professor Forbes.<sup>486</sup>

**33.321** When asked to describe how a post-test interview would proceed, Dr Wilkie said that it would normally take place in the clinic rather than in the counselling room. She said that she or Professor Forbes would say that they were there to talk about the results of the HTLV-III tests. Like Professor Lowe, she recalled that patients generally appeared unsurprised at positive test results: usually the patient would say, 'I know doctor that I will be positive'. She said that they would then talk about the implications.<sup>487</sup>

**33.322** Professor Lowe told the Inquiry that when passing on positive test results to patients he would start by reviewing their knowledge about AIDS and HIV testing. He would make sure that they had received full counselling about the test and the implications of a positive or a negative result. He told the Inquiry that he would not have given anybody a positive test result without making sure that they had been through the process of pre-test counselling and fully understood the situation. He would ask the patients if they had been counselled and what information they had been given. He said that all of the patients that he gave positive results to told him that they had been counselled about the test.<sup>488</sup>

**33.323** Professor Lowe said that he told patients that AIDS was caused by a new virus and that a percentage of patients who had a positive antibody test would go on to develop AIDS but that it was not clear what percentage that would be or what the time frame for developing AIDS was. He said that he would reassure the patients that, at that time, the majority of patients found to have a positive antibody test were well and it was hoped that they would remain so. He said that he made sure that they had the current information about the risk of progression to both the milder and the more severe symptoms. He then gave them reading material and suggested that they return within a few days, having thought about the matter, with a list of any questions they wanted to ask.<sup>489</sup>

**33.324** He said that he told patients that he would want to see them more frequently thereafter – initially every couple of months – and that part of their routine examination would now involve monitoring them closely for signs and symptoms of progression to AIDS. They would also be reviewed by the local infectious diseases department at Ruchill Hospital.<sup>490</sup>

---

<sup>483</sup> Ibid page 56–57

<sup>484</sup> Dr Wilkie – Day 32, pages 35–37

<sup>485</sup> Professor Lowe – Day 40, pages 58–9

<sup>486</sup> Dr Wilkie – Day 32, page 37

<sup>487</sup> Ibid pages 36–37

<sup>488</sup> Professor Lowe – Day 40, pages 60–62. See, however, the evidence of 'David' below.

<sup>489</sup> Ibid pages 62–63

<sup>490</sup> Ibid page 63



## David

**33.325** As stated in paragraph 33.217 above, David was told by Professor Lowe that he had acquired HIV on 2 December 1985. The circumstances surrounding his diagnosis are detailed in paragraphs 5.173 to 5.178 of Chapter 5, *An Examination of the Effects of Infection with HIV on the Patients and their Families, Including Treatment*. David was unaware that his blood sample was being tested for HIV and he was very angry that he was tested for HIV without being told or being asked for his consent. When Professor Lowe told him his test result David thought that he spoke to him in a matter of fact way and wished to convey the news and move on.<sup>491</sup> Professor Lowe said that he had looked at David's medical records and that David had been seen by another doctor at the time that blood was taken for HIV testing.<sup>492</sup> He said that, although all of the testing that he performed himself had been preceded by counselling and discussion with the patient, he often saw patients who had been seen by another doctor at the clinic at the time that they had given a sample for testing.<sup>493</sup> In response to David's comments on the manner in which he was informed of his diagnosis with HIV, Professor Lowe stated that telling someone about their diagnosis at this time was very difficult due to the uncertainty at the time about the virus.<sup>494</sup>

## Discussion and conclusions

### *The threat of HIV transmission, haemophilia therapy in Scotland and the provision of information to patients*

#### Practice in Edinburgh and south east Scotland: discussion

**33.326** It is clear from the evidence presented to the Inquiry that Professor Ludlam's practice was that information was provided to his patients largely in response to questions posed by them and as, in his judgement, the occasion demanded it.<sup>495</sup> One could not conclude that any particular proportion of Edinburgh patients was given information until late 1984 at the earliest about the risks of transmission of HTLV-III by blood products. Professor Ludlam acknowledged that there was clearly a risk of the agent that caused AIDS entering the Scottish blood donor population and therefore potentially infecting his patients. From the epidemiology and from what was then known about the agent, however, it had seemed to him that the risk in Scotland was very small. He did not therefore take the initiative to alert patients explicitly to the risk and to any patients who may have asked about the risk he would have said that he thought it was small.<sup>496</sup> Advice was given occasionally and in response to questions or the need to explain the 'AIDS study' (discussed above at paragraphs 33.109 to 33.114) rather than universally. This was consistent with Professor Ludlam's view that there was no risk of transmission of HTLV-III with SNBTS products at the time.

**33.327** This appears to have been Professor Ludlam's position until the point in October 1984 when he received test results from Professor Tedder showing that some of his patients were HTLV-III antibody positive.<sup>497</sup>

---

<sup>491</sup> David's witness statement. See Chapter 5, paragraphs 5.173 and 5.174

<sup>492</sup> Professor Lowe – Day 40, page 55

<sup>493</sup> Ibid pages 55–56

<sup>494</sup> David – Day 30, page 118

<sup>495</sup> See paragraphs 33.10 to 33.17 above

<sup>496</sup> Professor Ludlam – Day 39, pages 22–23

<sup>497</sup> Professor Ludlam's note on long term safety monitoring for transfusion transmitted infections [PEN.012.0351] at 0354

### Practice at the Glasgow Royal Infirmary: discussion

**33.328** The evidence suggests that Professor Forbes would have discussed the threat of AIDS with his patients, whether in relation to product choice or in some other context. He said that he provided his assessment of the risk of AIDS but advised that they continue with their treatment.

**33.329** It is reasonably clear that there was not in force any structured protocol, or series of protocols, for the provision of information about the risks of transmission of HTLV-III by transfusion of blood products. While anxious to emphasise his own relative lack of seniority at the time, Professor Lowe, as an interested observer, was well placed to note practice and to comment on his own approach when dealing with the management of haemophilia patients.

**33.330** Clinical practice during review clinics provided an opportunity to deal with patients' questions, including questions about AIDS. The more significant question, however, relates to providing information about risk when discussing therapy. Professor Lowe's evidence is accepted: patients were told what was known about AIDS when the subject was raised, they were talked through the consequences of stopping treatment and told that, at the end of the day, they had to balance the risks and benefits of treatment. However, the provision of Haemophilia Society publications stressing the advice that patients should continue with concentrate therapy was also a significant element in the provision of information. Apart from 1985, and the fall-out from the discovery of antibodies to HTLV-III in Glasgow patients in 1984, the quantities of concentrate therapy dispensed reflected the practical emphasis on its continued use.

**33.331** It appears that at the GRI, as at the Haemophilia Centre in Edinburgh, during the initial phase of the epidemic AIDS was not discussed systematically with patients as a factor bearing on treatment.

### Practice at Yorkhill: discussion

**33.332** Professor Hann's predecessor at Yorkhill, Dr Michael Willoughby, left before the threat of AIDS in haemophilia patients had become a reality. Dr Willoughby's evidence was that he had no knowledge of the risk of transmission of serious viral disease. The evidence of the witness given the pseudonym 'Christine' is consistent with the impression given by Dr Willoughby: parents were not told by him that there was a risk of transmission of viral infection generally when being advised about treatment. This appears to the Inquiry to reflect the limited understanding of AIDS in 1981 and 1982. The critical period for present purposes began in 1983 when Professor Hann took up his post. While there were obvious differences among the witnesses relating to practice at Yorkhill, Professor Hann's evidence was clear and consistent, and provides a reliable basis for factual conclusions.

**33.333** Professor Hann joined Yorkhill as knowledge about the risk of transmission of a viral agent was first beginning to be disseminated, though his initial exposure to that information came, not in his new capacity as a haemophilia clinician, but in his previous post in London, where he had care of immuno-compromised patients. His position, on an objective view, was different from that of established haemophilia clinicians with a history of prescribing therapeutic products for haemophilia patients. It is therefore of some significance that his first strategic decision was to abandon Dr Willoughby's established practice of using commercial Factor VIII concentrates and adopt the exclusive

use of cryoprecipitate and SNBTS Factor VIII. As shown in Chapter 21, *Haemophilia Therapy – Use of Blood Products*, at paragraph 21.300 and in Figure 21.9, cryoprecipitate accounted for a very small proportion of total therapy. Until 1991, Professor Hann did not use commercial Factor VIII concentrate, with the exception of Dr Willoughby's residue in 1983, and small quantities in 1984 and 1986. Professor Hann's practice reflects consistent confidence in the Scottish product.

**33.334** The routine followed in dealing with patients or their parents during his period included discussions with patients about the relative benefits and risks of treatment options, so far as they were understood. It appears from the evidence as a whole that Professor Hann discussed HIV/AIDS to a greater extent than happened in Edinburgh and the GRI, although his advice, like that of Professors Ludlam and Forbes, was to continue with SNBTS therapy.

***The threat of HIV transmission, haemophilia therapy in Scotland and the provision of information to patients: conclusions***

**33.335** The evidence available to the Inquiry illustrates the independence of clinicians to adopt individual practices in providing information to their patients about the potential risks of transmission of viral infection generally, and of the putative AIDS agent specifically, in the period to 1984. It is also apparent that different views as to the nature and validity of the evidence of a viral aetiology were held by the clinicians at the different centres. There was then no relevant professional standard. As discussed in Chapter 32, *An Investigation into the Systems in Place for Informing Patients about the Risks – Ethical Context*, it would be 1988 before published guidance from the GMC<sup>498</sup> and the BMA<sup>499</sup> was available to the profession. That guidance was developed in the light of experience in the critical years 1983 to 1985. In that period, clinicians were free to develop their approaches on the basis of their individual perceptions of risk, and of the options available to them in treatment, given the fundamental need to treat patients' primary conditions.

**33.336** Professor Lever's observations (at paragraph 33.60 above) define, effectively and forcibly, the problem for clinicians. There was a need for caution in giving information and advice. Raising a fear of virus transmission would have caused distress and concern. If it should prove to have been unnecessary, that would be undesirable. People would 'not necessarily have been very understanding'<sup>500</sup> (a restrained judgment of the position) if it proved to have been a false alarm and, in the meantime, patients had died from lack of treatment for their haemophilia.

**33.337** Most senior clinicians would have been constrained by the knowledge that over the previous decade, as effective therapeutic concentrates had become available which had changed their patients' lives, they had prescribed concentrate therapy with confidence that, overall, the benefits conferred outweighed any disadvantages associated with their use. Professor Hann was an exception: he was new to haemophilia practice at this critical period, starting at Yorkhill in 1983, and had a quite different specialist background. In deciding his own approach to therapy, he proceeded quickly to near exclusive use of SNBTS products and, in becoming familiar with his patients, he was more active in initiating discussion of the options available in treating individual patients.

---

<sup>498</sup> *HIV Infection and AIDS: the Ethical Considerations*, General Medical Council, May 1988 [PEN.016.1165]

<sup>499</sup> British Medical Association, *Philosophy and Practice of Medical Ethics*, 1988, London, Chapter 4: 'Consent to Treatment' [PEN.018.0424]

<sup>500</sup> Professor Lever – Day 26, page 92

**33.338** The period when patients treated with SNBTS Factor VIII concentrate were most exposed to risk of transmission of HIV extended from 1983 to the beginning of 1985. That was the period when information about the risk of transmission and discussion with patients about product selection might, at least hypothetically, have been material to the course of treatment of their primary condition. Some patients have stated that they were not advised of the risk of contracting AIDS from treatment and there is patent concern that this reflected a failure on the part of clinicians to provide information to them.

**33.339** It is clear from the evidence that practice in relation to providing advice and information to patients about the risk of AIDS did vary. Professor Hann's practice at Yorkhill involved the most extensive discussion with patients and he appears to have adopted a proactive approach. Professor Ludlam's practice seems to have involved a more general level of discussion, and a more reactive approach, with information being imparted largely on a 'need to know' basis. His practice can be taken as an example of what happened to a greater, or lesser, extent at other centres. The overall picture that emerges from the evidence discussed in this chapter is that, generally, doctors in Scotland did not initiate discussions with patients about the risk of transmission of an AIDS agent because, for a significant part of the period, they thought that there was not a risk in Scotland at all and, towards the end of the period, they found it very difficult to assess the gravity of the risk that was beginning to be recognised. Nonetheless, if patients did enquire about the risk, the doctors would do their best to inform them, in the light of the then current state of knowledge about AIDS. Some clinicians at least also relied on the ready availability at clinics of publications from the Haemophilia Society.

**33.340** By the spring of 1983, Professor Ludlam had become convinced that there was a syndrome, AIDS, very possibly related to a transmissible agent like a virus, although it appeared to be largely a US phenomenon. He believed that his patients were not at risk from it because he used exclusively Scottish materials. In their case, any immune abnormality was attributed to antigen overload, occasioned by therapy as distinct from an infective agent. His anxiety, and the measures he implemented in consequence of it, to protect his patients from 'foreign' materials when outside Scotland provide eloquent evidence of his views at the time. Until the infectivity of a batch of SNBTS concentrate was discovered in the autumn of 1984, he took the view that his patients should not be exposed to commercial concentrates if that could be avoided.

**33.341** Professor Vivienne Nathanson talked about the uncertainties surrounding the risk of AIDS between 1982 and 1984. She said that all of these uncertainties made it extremely difficult for treating doctors to discuss the risks associated with their treatment because they were unable to categorise the level of that risk.<sup>501</sup> At the beginning of the period the level of uncertainty about the risk was such that it was legitimate for clinicians not to mention it to their patients.<sup>502</sup> The problem facing treating clinicians was that they did not have numerical data and therefore did not know the level of risk. The question at that time was, therefore, whether to wait for it to become clear from the statistics that the risk to patients was so common that they must be told, or to tell patients about the risk, regardless of the likelihood of their infection, because the consequences were so great.<sup>503</sup> She said that it became less acceptable not to warn patients as clinicians began to understand the risks and as it became clearer that the risks were higher than originally thought.

---

<sup>501</sup> Professor Nathanson – Day 37, pages 74–75

<sup>502</sup> Ibid page 77

<sup>503</sup> Ibid pages 79–80

**33.342** Professor Nathanson was not critical of doctors who did not initiate discussions about the risk of AIDS from concentrate therapy in the early 1980s. It is clear that by modern standards a doctor could be criticised for failing to mention a risk to a patient that a particular treatment carries. However in the early 1980s it was commonplace for doctors simply to take decisions for their patients without discussion with them, the so-called 'paternalistic' approach to practice. As the exact extent of the risk was then unknown, a significant number of doctors would not have initiated a discussion about the risk of contracting AIDS by continuing with factor therapy even though by 1984 it was clear that there was a risk of death.

**33.343** Until September 1984 (by which time it was generally accepted that HTLV-III was the agent of transmission of AIDS, and a high prevalence of the HIV virus in UK haemophilia patients had been found) there is no basis in the evidence for any criticism of any Scottish clinicians relating to their approaches to the provision of information and advice concerning the risks of AIDS associated with the continued use of therapeutic materials in the treatment of blood coagulation disorders.

**33.344** There were no specific ethical guidelines for this unprecedented situation. Practice in Edinburgh and Glasgow was tailored to patients' needs as perceived by the various clinicians. Professor Ludlam's provision of information on a reactive basis was, inevitably, a reflection of his personal approach to clinical practice as was Professor Forbes' approach. Relevant to all the clinicians involved was the fact that knowledge of AIDS was limited and, consequently, that there was little that they could tell patients about it with any confidence.

**33.345** The position towards the end of 1984, immediately before Scottish practitioners discovered the results of testing by Professor Tedder and Dr Gallo of samples from their patients, examined below, is that the risk of AIDS was not generally discussed. However, on the evidence of general practice prevailing at the time, particularly from Professor Nathanson, there is no basis for criticism of individual clinicians.

## **The testing of patients' blood samples**

### *Routine blood tests to 1984: discussion and conclusions*

**33.346** Monitoring of patients by blood tests was a routine component of haemophilia care throughout UK haemophilia centres from the 1970s. Dr Winter described the background to this practice. He noted that, shortly after the introduction of factor concentrates in the mid-1970s, it became apparent that nearly all regularly treated patients displayed biochemical abnormalities of liver function of a type that would be compatible with a form of viral hepatitis infection. From that time on, haemophilia clinicians regarded it as their responsibility to monitor their patients regularly for the presence of new viral infections.<sup>504</sup> It was absolutely routine to test haemophilia patients for viruses, whether directly or by means of surrogate indicators of disease, and, because it was seen as being a core part of patient care, it was not considered necessary for doctors to discuss it with patients.

**33.347** Routine testing such as described was an ordinary aspect of diagnosis and of management and did not give rise to controversy at the time. However, in 1983 and early 1984 studies were carried out in Edinburgh and Glasgow that became controversial later. They arose from the discovery, initially in the USA, that haemophilia patients had

---

<sup>504</sup> Dr Winter – Day 16, page 155

developed immune abnormalities which were similar to those found in AIDS patients and reported to be found in some asymptomatic homosexual men. It is appropriate to re-emphasise that, until the immunological studies, the evidence of practice gathered by the Inquiry shows that blood tests for a wide variety of pathogens and for monitoring biometric data were carried out on a routine basis without prior discussion with patients as necessary components of the management of their primary condition.

### *Immunological studies: discussion and conclusions*

**33.348** The evidence suggests that Professor Ludlam may have found it difficult to explain to patients about his immunological studies. Some of his patients may have known that he was carrying out such studies but there was no structured or systematic approach to providing relevant information relating to it, or for obtaining consent for the use of patients' blood. Some patients may have understood from their haematology request forms that their blood was being tested in the 'AIDS study'. However, no reliance could reasonably have been placed on the forms as a means of informing patients of that fact, or of the significance of the studies. Equally, it seems that, at the time and in the retrospective analysis Professor Ludlam required to undertake for this Inquiry, he did not fully appreciate the possible impact on them of the language he used. This is, perhaps, best illustrated by his labelling, in the climate of the time, his immunological investigation as the 'AIDS study'. That choice of words gave rise to a suspicion, harboured by few people, that he had been experimenting on his patients with the AIDS virus. It should be noted that Counsel representing the Patients, Relatives and the Haemophilia Society explicitly acknowledged that there was no factual basis for such a suspicion.<sup>505</sup> Furthermore, it is worth repeating at this juncture, that it is the view of this Inquiry that such a suspicion is without foundation.

**33.349** There was good reason in 1982–83 for Professor Ludlam and Professor Forbes to be concerned about whether their haemophilia patients had been exposed to the transmissible agent then increasingly thought to be responsible for AIDS. The topic had been explored in the United States. The possibility of 'antigen overload' as an explanation of immunological abnormalities had been postulated as an alternative to viral infection. By the spring of 1983 the incidence of similar immune abnormalities in AIDS patients, some asymptomatic homosexual men and some asymptomatic haemophilia patients, was puzzling. It was a subject appropriately demanding investigation.

**33.350** If Professor Ludlam had contemplated the range of possible reactions to this work on the part of patients, he would have been well advised, as he came to recognise, to have devised an alternative shorthand to 'AIDS study' to describe it. Much of the reasoning and explanations tendered in oral and written evidence would not then have been required. For example, the discussion of what patients 'might have understood' from a label on a form accompanying a sample appeared to be unhelpful at the time of the Oral Hearings and has remained so. In the end, discussion of the description, and of possible inferences that might be drawn from the use of the title, provided no help in characterising what was done and in developing views on the appropriateness of that course of action.

**33.351** Several facts are established in relation to Edinburgh:

- Professor Ludlam was aware from international and UK sources that some clinically well haemophilia patients were developing immune abnormalities.

---

<sup>505</sup> Day 39, pages 11–12

- He knew that the pattern of these abnormalities, though less marked in haemophilia patients, bore similarities to those found in some apparently well homosexual men and in AIDS patients.
- The cause was unclear and it was also unclear whether the condition was progressive. It might have been a previously unreported side-effect of therapy or of haemophilia itself.
- On the other hand, the changes might have been related to the prevalence of a blood-borne virus possibly leading to AIDS.
- The condition in his patients could be investigated by the addition to routine haematological lymphocyte counts of a more specific count of CD4 and CD8 lymphocytes, and an assessment of their relative proportions in the patient's blood, using the same blood as taken for standard haematology.
- Professor Ludlam made an arrangement with Dr Steel to have that test carried out on selected samples from patients with severe and moderate haemophilia who had received a lot of concentrate.
- Patients were not told routinely that the study was carried out or that their blood was used, and their consent was not obtained in advance.
- While some patients may have been told, or found out, it could not be concluded on the evidence that the study was known generally or that all patients involved knew of the study or that their blood was used in it.

**33.352** However the study was in the best interest of patients. Finding out whether there was a pattern of immune abnormalities and, if so, its nature and extent could not but have been relevant to patient care whether it was caused by, or associated with, the selection and use of therapeutic products, or involved an agent of transmission of viral infection. The results of the study might be of particular importance in deciding on future therapy. The progressive development of immune abnormalities in patients receiving factor concentrates was a matter of legitimate concern in itself. At this stage, in 1982–83, the common perception in Scotland was that SNBTS Factor products were safe from AIDS and, to the extent it was understood, from an infectious agent associated with AIDS. That was an illusion, as events were soon to prove, but it was deeply embedded in the preference for the domestic product over imported products, especially those imported from the USA.

**33.353** Attempting to differentiate the effects of 'antigen overload' from infection with an AIDS agent would also have been a legitimate concern. That was what lay behind Dr Louis Aledort's studies in America that prompted Professor Ludlam to carry out his own investigations. On any view, the study and the findings potentially had real significance in the context of patient management. If, without virus infection, immune abnormalities developed through the use of concentrates, that would have been important.

**33.354** The question of whether patients should have been informed and whether their consent should have been obtained in advance of the immune studies is more difficult. It cannot be answered by reference to what was found: that was, of necessity, unknown when the material decisions were taken (or, more probably, not taken, since the test was clearly viewed as a simple extension of routine practice). It cannot take into account the emergence of HTLV-III positivity in Scottish patients: that still lay in the future. Similarly,

many of the problems associated with HTLV-III/HIV testing that were to emerge in and after 1985, such as problems relating to employment, to travel and to insurance, were unknown in Scotland in 1983.

**33.355** The matter was taken up with Professor Nathanson, who discussed the distinction between 'monitoring of patients' and 'research'. She said that, in essence, research involves testing a theory about, for example, a causation or the result of a treatment.<sup>506</sup> She said that there is often a very fine line between medical research and treatment. She referred to the old version of the Declaration of Helsinki which talked about 'therapeutic' and 'non-therapeutic' research. Although the phrase 'therapeutic research' is not used today, it was at that time and Professor Nathanson thought that it lay on the fine line between 'monitoring of patients' and 'research' as such.

**33.356** There are times when what a doctor is doing is not part of established therapy (including established protocols for continuing testing or routine tests) but is an aspect of the way in which the doctor is treating that patient, either finding out more information about the patient or seeking a better way to treat their condition. This has always been an area where it is difficult to say whether what the doctor is doing is better characterised as research or as treatment because some such actions straddle that line. Professor Nathanson said that she would characterise the immune function studies carried out by Professor Ludlam between 1983 and 1985 as being 'exactly on this borderline'.<sup>507</sup>

**33.357** When asked whether it would be fair to suggest that something might start out as long-term safety monitoring of patients and metamorphose into what might objectively be regarded as research, Professor Nathanson said:

I think that's absolutely the case. I think this is clearly the issue when you start off with work that is on this borderline, that you start off intending to simply monitor that you are getting the treatment right, that the patient's blood tests are going in the right direction or you are not seeing anything unexpected. You find something unexpected and it morphs into something that is different, and that's a very great difficulty and it's particularly difficult to then stop what you are doing and to redesign the whole thing and to say, 'We will now make this into a formal research protocol.' And I think that that's why, in times when the ethics approval for research was rather less rigid than it is today, that much of this happened. It didn't start off with malign intention, it just metamorphosed in exactly that way.<sup>508</sup>

**33.358** So far as the immunological studies are concerned, classification remains difficult. Viewed as a research project, the testing of those severely and moderately affected haemophilia patients who attended Professor Ludlam's clinic for treatment or review during the period of the AIDS study was not based on the random selection of patients from a wider population. Nor was there a defined research protocol for the study. On the other hand, routine monitoring might have been expected to require that the lymphocyte study should include all patients rather than only those who attended for treatment or review. As already commented, the results might also have been expected to be noted in patients' medical records.

---

<sup>506</sup> This definition of 'research' has to be understood in the context of the discussion of the immune studies: it would now be regarded as out of date more generally. 'Blue Sky' research would not be encompassed by the definition.

<sup>507</sup> Professor Nathanson – Day 37, pages 160–162

<sup>508</sup> Ibid page 166



**33.359** While lacking such a formal structure, there are indications that the intent of the projects was research in a wider sense than the investigation of the individual patient's condition. It might not have met Professor Nathanson's definition of the essence of research. The 'theory under investigation' was, at best, the hypothesis that immune abnormalities found in haemophilia patients had an association with antigen overload rather than a ubiquitous viral agent. It was designed to obtain information, to find out whether there were immune abnormalities in the Edinburgh Haemophilia Centre patients generally and was therefore not focused on individual patient management. It might have been more consistent with the 'monitoring' of patients (as Professor Ludlam described it) rather than a form of unstructured research if all patients had been tested rather than a selection only. The immune studies resulted in published papers rather than in changes in the prescription of therapy. So far as the individual patients were concerned, Professor Ludlam clearly did not know what to do with the information gathered. He did not tell the patients; he could not interpret the results for them. The implications for management of the patients had not been considered at that time: apparently that had not been part of the plan.

**33.360** It is not clear where these exercises would lie relative to the fine line between 'therapeutic' and 'non-therapeutic' research sketched out by Professor Nathanson. They were exploratory exercises aimed at finding out what, if anything, was happening to patients receiving blood product therapy. Professor Nathanson thought that the immune studies lay on the borderline and that is probably where they should be left. Her comment relating to studies that 'morph' into research in the fullest sense of the term is no doubt accurate in the abstract but it is not accurate in relation to the immunological studies in Edinburgh and Glasgow: there is no evidence that the studies changed in content, purpose or direction, which the word 'metamorphose' would suggest. So far as the evidence shows, what changed over time was the perception of the studies which came to reflect ethical rules developed after the work was carried out and reported.

**33.361** In Glasgow and in Edinburgh, the immunological studies are probably best characterised as a preliminary enquiry. They were aimed at finding out whether the patients' lymphocyte 'scores' suggested that something was happening to their immune systems that might be related to therapy. Due to their unstructured, preliminary character, a full research programme following upon them would have been required if reliance was to be based upon their conclusions in instructing any changes in the approach to therapy. Professor Forbes characterised the Glasgow study as an investigation aimed at finding out whether there was any evidence of altered immunological status in patients who had received multiple transfusions with various products. He described the paper as 'very much a preliminary paper'. His team did not know where the results might lead them.

**33.362** If there had been at the time a generally recognised ethical rule that patients should be informed of all research in which they were involved through the use of blood samples, and that their consent should be obtained before use was made of their samples, the conduct of the 'AIDS study', as it was carried out, would have infringed that rule. The Glasgow study, since consent was obtained, would not have done so.

**33.363** However, as indicated earlier in this chapter, and in Chapter 32, *An Investigation into the Systems in Place for Informing Patients about the Risks – Ethical Context*, on the evidence available, from Professor Nathanson in particular so far as general theory is concerned, and from Dr Winter and others from the clinician's point of view, there was not a fixed rule before 1988 that would have required that the patient be informed or that the

patient should consent to the immunological tests. There was no rule that took the decision whether to seek consent for immunological studies out of the clinician's discretion.

**33.364** Professor Nathanson said that even at that time she would have encouraged Professor Ludlam to consider the work as research and follow the research protocols simply because of the benefits that would have brought.<sup>509</sup> However, that plainly fell short of criticism that what had been done breached any ethical rule in force at the time.

**33.365** Professor Nathanson's evidence is accepted. The immune studies were not simply the reflection of the insatiable curiosity of academic doctors confronted with an interesting project and an irresistible urge to research it. Professor Ludlam and Professor Forbes had a legitimate clinical interest in discovering whether concentrate therapy had an impact on patients' immune function. As events were to develop after the AIDS period, the 'purity' of intermediate factor products became an important issue for the SNBTS. In due course, pressure from patients and clinicians grew for the development of 'purer' concentrates, with lower levels of protein impurities than had generally been found in SNBTS intermediate purity products, and in particular SNBTS Factor VIII. A study that focused on the consequences for patients' immune systems of therapy with products of intermediate purity, with a clearly specified aim and supported by a research protocol, could readily have been classified in 1982 as 'therapeutic' research ancillary to patient management and treatment.

**33.366** The immunological studies carried out in Glasgow were not a direct parallel of those conducted in Edinburgh, even though the objective was the same. The study in Glasgow was prompted by the same intelligence that influenced Professor Ludlam and was aimed at finding out whether there was evidence that patients who had received multiple transfusions had developed immune abnormalities. On Professor Forbes' evidence fresh blood samples were required specifically for the study and that necessitated discussion with patients.

**33.367** As observed earlier, Professor Forbes' account of the procedure adopted was imprecise. The impression he gave was of a fairly informal approach to obtaining consent with little information about the purpose of the study imparted to patients. Dr Froebel's published report of the study does not indicate whether the patients gave their consent; it refers to the patients having been selected because of their treatment regime in the recent past.<sup>510</sup> In the absence of any contrary evidence, it is appropriate to proceed on the basis that the patients were asked to participate in the study and gave their consent, albeit informally and with little specification of the purpose and significance of the study.

**33.368** Like Professor Ludlam, Professor Forbes obtained results but did not know what to do with them in the context of patient management. He did not go back to the patients with their results because he did not know the implications of the findings. There was no follow-up to the results, so far as the specific patients were concerned. In the event, what he actually told his patients and how well informed they were about his immunological investigations are open questions. His approach can properly be described as paternalistic, in the sense previously defined, leaving patients with the impression that he was doing something for their own good but avoiding overloading them with information about it.

---

<sup>509</sup> Ibid page 162

<sup>510</sup> Froebel et al, 'Immunological abnormalities in haemophilia: are they caused by American factor VIII concentrate?', *British Medical Journal*, 1983; 287 [LIT.001.0215]

**33.369** The 'skin tests' carried out in Edinburgh and Glasgow illustrate that clinicians did draw a line and seek ethical approval where they perceived that the work involved amounted to research. The investigation for the 'skin tests' was invasive: it was intended to test immune response by causing physical changes in the patient's skin.

**33.370** Professor Ludlam viewed his skin test programme in 1984 as a research project requiring ethical approval. He took a different view of the immunological studies he carried out on stored samples. They did not require fresh blood samples to be taken, and were, in that sense, not invasive. That was a matter of judgment on which he was entitled to take a view at the time. There was little difference between them: they had the same objective, involved patients' immune functions and they both provided general information. The more invasive exercise received ethical consent when Professor Ludlam sought it. It is very difficult to see anything of substance turning on the failure to seek ethical consent for the immunological studies.

**33.371** In retrospect, aspects of the conceptualisation and implementation of the 'AIDS study' could have been handled better, but it is not possible to say that there was any breach of any ethical rule prevalent or recognised at the time the studies were carried out.

#### *Publication of patients' information: discussion and conclusions*

**33.372** Professor Nathanson explained that in contemporary practice where data is extracted from the files of a limited number of patients, where the researchers know the identity of the research subjects and especially if they comprise a small, defined and potentially identifiable group, the researcher is obliged to obtain the consent of the patient(s) to the inclusion of their data in the research. The GMC considers such cases in its supplementary guidance on research ethics, which makes it clear that identifiable data requires either patient consent or, where that cannot be obtained, separate independent permission to use such data.<sup>511</sup>

**33.373** She said that the main thing that most patients worry about in research publications is whether they can be identified from the description in the article. Today in almost all publications, patients are given a guarantee that the information will be aggregated or presented in such a way that they cannot be identified from it. This fits with the valid consent model and patient-centred practice. Patients are given the choice of either being in the research exercise or not. Another key component of research ethics is that a doctor should also make sure that patients understand that refusal to be part of the research will not change their access to healthcare.<sup>512</sup>

**33.374** Professor Nathanson also discussed 'anonymisation' and 'pseudonymisation'. Anonymisation is the practice of making sure that whatever is done with the information used in the research, such as actual files about individual patients, is treated in such a way that all identifiers are removed. Pseudonymisation involves the use of false personal information to conceal an identity. With anonymisation doctors have to be very careful that they are not presenting information which, even though they have removed the patient's name and date of birth, has enough detail to allow the patient to be identified. Nowadays the biggest research studies use fully anonymised data. Often they use aggregated data, which might look at information extracted from, for example, the population of 5 million in Scotland.<sup>513</sup>

---

<sup>511</sup> Professor Nathanson's first report to the Inquiry [PEN.012.0330] at 0340

<sup>512</sup> Professor Nathanson – Day 37, page 131

<sup>513</sup> Professor Nathanson – Day 37, pages 131–133; Professor Nathanson's first report to the Inquiry [PEN.012.0330] at 0340

**33.375** She said that the fact that the results were published made very little difference to any ethical concerns around the immune studies. She recognised that the use of patient information in medical journals, anonymised but without formal consent to inclusion in a published study, was fairly common in the 1980s. The important point about publication at that time was that it required consent if there was any likelihood of individuals being identified.<sup>514</sup> All three of the articles mentioned were fully anonymised.

**33.376** The publication in *The Lancet* of the results of the immunological studies from Edinburgh and Glasgow did not infringe any ethical rule recognised in 1983. On Professor Nathanson's evidence, they would not infringe current rules. The data were fully anonymised and there was no likelihood of individuals being identified. As Professor Nathanson said in this context, publication made very little difference in this case. It does not affect the legitimacy of either of the studies.

**33.377** While the feelings of the patients on finding out that they were part of such studies without their knowledge are easily understandable, in the result there was no breach of any ethical rule or principle associated with the publication of the results of the immune studies.

### *Testing for anti-HTLV-III: discussion and conclusions*

#### Glasgow

**33.378** The evidence of the timing of events in Glasgow is confused and in some respects contradictory. Dr Froebel's evidence is accepted and is generally to be preferred to competing accounts. It relates most naturally to the reports, from Montagnier in France and Gallo in the US, claiming that a virus had been isolated from patients with AIDS and indicating that both laboratories were working on an antibody (ELISA) assay, a blood test that would show exposure to the virus (though attributing the date of spring 1984 to each, as Dr Froebel did, was incorrect). Her narrative of the assembly of samples and their dispatch to Dr Gallo has circumstantial detail that supports its accuracy. She cannot have written to Professor Montagnier and Dr Gallo before 4 May 1984 when *Science* published the articles on Gallo's research. The samples that were tested were recorded in the subsequent paper published in *The Lancet* as having been taken between December 1983 and July 1984. The samples therefore cannot have been sent prior to July 1984. The HTLV-III antibody testing of the Glasgow samples in Dr Gallo's laboratory must have been carried out thereafter.

**33.379** The only evidence suggesting that Professor Forbes had knowledge of HTLV-III antibody test results for some patients before the report of the bulk shipment of named samples to Dr Gallo, was provided by Dr Wilkie, and concerned the kits. She made no reference to the Gallo tests. Whilst trying her best to assist the Inquiry she had, as she acknowledged, difficulty in recollecting certain matters including dates. In relation to the test kits, she said that she and Professor Forbes conversed on this matter once and then never again. Many matters referred to by her in relation to the kits would fit equally well in the context of the Gallo tests. Her description of Professor Forbes' agitation would fit his likely state on discovering from the Gallo test results that 16% of his patients had tested positive. Like the putative kits described by her, the Gallo test originated in the USA and was unlicensed. On the basis of either the Gallo results or the kit results, Professor Forbes would be concerned to find out what his patients knew about HTLV-III, whether they

---

<sup>514</sup> Professor Nathanson – Day 37, pages 162–163

thought they might be affected and whether they would like to be tested for the virus. Neither Professor Lowe nor Dr Froebel referred to any test kits, and Dr Froebel stated that she expected the Gallo tests to be negative and was shocked by the positive results. She and Professor Forbes were collaborating and it is difficult to think of any reason why he would keep any pre-existing positive results from her. Furthermore, positive HTLV-III test results from patients at the GRI would, in all probability, have significance for the SNBTS and the PFC. Dr Wilkie described Professor Forbes as 'a very ethical man with far-reaching ideas'. Professor Lowe said he was 'an extremely open person who would spend hours with his patients, discussing all manner of things'. The weight of the evidence on this matter suggests that the first HTLV-III testing of GRI patients was by Dr Gallo.

**33.380** It appears likely that when those first test results came to hand they would have caused the agitation Dr Wilkie described and provided the incentive she needed to abandon her own lines of research and agree to assist Professor Forbes. Her evidence that the reason Professor Forbes had contacted her was agitation about the test results and that had prompted him to ask for her help, is accepted.

**33.381** The Inquiry endeavoured to ascertain the likely date upon which the Gallo test results first became available at the GRI. On 29 October 1984, Dr Froebel wrote to Dr Perry that, after checking records, she and her colleagues now thought that seropositivity for HTLV-III was strongly associated with the patients having received commercial concentrate mostly before 1981. Dr Gallo's results were clearly available before 29 October 1984. On 29 November 1984, a meeting of haemophilia directors and SNBTS representatives was held. Paragraph 4 of the minutes notes:

Dr Forbes described the findings relating to HTLV-III antibody sero-conversion in a comparative study of haemophilia patients in Glasgow and Denmark. This study would shortly be published in the *Lancet*.<sup>515</sup>

**33.382** The exact date that Professor Forbes received the results from the USA is not known but it must have been some time before this meeting since in the interval Dr Melbye became involved in the joint exercise with Glasgow, research was completed, and the joint paper was prepared, submitted for publication, reviewed and finally approved for publication all before December 1984. The article was published in *The Lancet* of 22/29 December 1984.<sup>516</sup> It contains data on a patient who died in late October, but that could have been added in the review process. Professor Lowe is recorded as one of the authors of the article. He said that he was not involved in collecting blood samples from patients or sending them for HTLV-III testing.<sup>517</sup> His involvement was limited to a critical review of the draft paper, probably around about September or October 1984.<sup>518</sup>

**33.383** On the evidence as a whole, it seems highly likely that Professor Forbes had the results of Dr Gallo's tests by late summer or early autumn 1984, in time for the work leading to the article in *The Lancet*. He may have had them by August or September. A date in October is less likely, notwithstanding the reference to the October death, given the spread of authors between Scotland, Denmark and United States, and the confirmatory tests referred to in the article.

---

<sup>515</sup> Minutes of meeting of Haemophilia Directors and SNBTS representatives held on 29 November 1984 [SNF.001.0255]

<sup>516</sup> Melbye et al, 'HTLV-III seropositivity in European haemophiliacs exposed to Factor VIII concentrate imported from the USA', *The Lancet*, 22/29 December 1984 [LIT.001.1702]

<sup>517</sup> Professor Lowe – Day 40, page 26

<sup>518</sup> *Ibid* page 53

## Edinburgh

**33.384** The timing of some events in Edinburgh is also open to doubt. On Professor Tedder's evidence, Professor Ludlam made an initial approach in August 1984. That would have been before the publication in the Cheingsong-Popov article of the results of the Tedder/Weiss research project in September. Since the approach was made on the basis of personal connection that is not at all unlikely, but at the time of the initial approach, on Professor Ludlam's evidence, Professor Tedder was already inundated with requests from various sources for HTLV-III testing, a situation more likely to relate to publication in September. The critical issue is related to the submission of the first particular group of samples that resulted in the positive diagnosis of infection. That places the event in October 1984 and for practical purposes, on the evidence as a whole, Professor Ludlam's timing is accepted.

## The ethical considerations

**33.385** From the accounts of the way in which events unfolded, already dealt with at length, it is clear that in both Edinburgh and Glasgow, the initial samples of sera for testing were selected from store and submitted without prior consent of the patients, though the samples were identified as belonging to identified individuals. The wide context is relevant.

**33.386** In Professor Nathanson's opinion, the use of stored blood or tissue samples for research would have been contrary to the spirit of the Declaration of Helsinki if consent had not been obtained. However, if doctors were not using the information for research but rather as a part of the continuing monitoring of the patient that would have been legitimate. She noted that there is 'a very fine line' between the two uses of samples.<sup>519</sup> This appears to be the difficult line between 'therapeutic' and 'non-therapeutic' research already discussed.

**33.387** In her view it was clear that the spirit of the Declaration of Helsinki dictated that, if doctors had been in any doubt, they should have erred on the side of thinking that there was a need for a research protocol and gone through the relevant processes.

**33.388** However, she said that although conducting research without consent might be contrary to the spirit of the Declaration, particularly as that is understood today, in practice it did occur quite widely in the early 1980s. Doctors often regarded what might now be considered to be research as part of continuing care, or a 'check and balance' on the quality of care a patient received. Although Professor Nathanson said that she would be critical of a doctor who had used stored samples without the patient's consent, she recognised that this was, in fact, common practice in the 1980s. As she put it: 'I would say it was not ... the gold standard but it was a common fault and it was commonly done'.<sup>520</sup>

**33.389** Throughout the United Kingdom, and across Scotland, there were haemophilia clinicians who used stored samples for testing without patient consent in the course of day-to-day monitoring of patients' progression.<sup>521</sup>

**33.390** Having regard to the discussions that led to the 1988 GMC guidance, and notwithstanding Professor Nathanson's opinion of what the spirit of the Declaration of

---

<sup>519</sup> Professor Nathanson – Day 37, pages 136–137

<sup>520</sup> Ibid pages 137–138

<sup>521</sup> Dr Tait – Day 14, page 65

Helsinki required, it is not possible to hold that there was an accepted or established rule of ethical practice that required patient consent for the submission of stored samples for testing in all circumstances in 1984. There are, however, substantial questions relating to the particular case of conducting HTLV-III/HIV studies on stored, and named, samples without consent of the patients involved. AIDS was already understood as a devastating disease in 1984 and the possibility of infection with an agent that might lead to the development of an AIDS disease, however remote, was a matter of real concern to patients and their families.

### *Communication of the results of HTLV-III testing: discussion and conclusions*

#### **Edinburgh**

**33.391** So far as concerns intimation to patients, the response to the findings was slow. After the initial flurry of telephone calls and memoranda at the end of October, nothing had been resolved in Edinburgh by the date of the meeting of Scottish Haemophilia Directors, SNBTS representatives and SHHD personnel convened on 29 November 1984. The position in Glasgow was the same. The meeting of the Haemophilia Reference Centre Directors at the BPL, Elstree, on 10 December 1984 left matters concerning whether and how patients with positive results should be informed in the hands of individual Haemophilia Directors with no real guidance on how to handle the situation. The approach in Edinburgh changed to crisis management with the threat of publication in *The Yorkshire Post* received by Professor Ludlam on 11 December.

**33.392** At the present time, when protocols for managing relations with the media are rather better developed, the course adopted by Professor Ludlam may seem inapposite, even unwise. It should, however, be considered in the light of the circumstances then prevailing. The day after the long and difficult meeting on 10 December, he was contacted by a *Yorkshire Post* reporter who informed him that he knew about the Edinburgh seroconversions, wanted to publish that information and would like to meet him. The following day they met and Professor Ludlam begged the reporter not to publish, explaining that this was no way for the patients to receive such news. Negotiating hard, he managed to extract one week's grace. Later that same day he wrote the invitations to the meeting, thinking such a gathering would be the quickest, most open way to start to inform all the patients. Professor Ludlam said in his evidence that had *The Yorkshire Post* not intervened, he would have found a different way of advising the patients. In retrospect, and as he acknowledged, it is plain that a public meeting was not the best way either to disseminate important personal information or to provide sensitive advice. However, the evidence does not disclose any objection to the course of action that he took, and it was reported to Scottish Office officials at the time.

**33.393** On the evidence gathered by the Inquiry it is clear that Edinburgh-registered patients and their families were invited to the meeting of 19 December 1984. Professor Ludlam concluded that some of those attending must have come from Glasgow as he did not recognise them. However, he also stated that he would have sent out invitations to the east coast haemophilia centres at Aberdeen and Inverness. The patients he did not recognise could have come from the other east coast centres. Unfortunately, the evidence in relation to Glasgow produces a less clear picture than that relating to Edinburgh, in part due to Professor Forbes' difficulties with his memory. Professor Ludlam believed that Professor Forbes had sent invitations to the meeting to his GRI patients. *The Yorkshire Post*, in its near contemporaneous account, stated that news of the positive testing was

broken 'to haemophiliacs from Edinburgh and Glasgow'. Information for that article came from Professor Ludlam and that account would be consistent with his belief at the time. Dr Bell's memorandum, dated 12 December 1984, suggested that 'the haemophilia consultants' were going to call a meeting of haemophilia patients. On the other hand, Professor Forbes (who chaired the meeting) had no recollection of any Glasgow patients attending. Neither Professor Hann nor Dr Pettigrew appears to have sent out invitations. On balance, it seems likely that for some reason west of Scotland patients were not invited to the Edinburgh meeting and did not attend it.

**33.394** After the meeting different courses of action were followed in Edinburgh and Glasgow and, as appears from the letter sent to patients by Professor Forbes and Professor Lowe on 8 January 1985, communication with Glasgow patients did not include any reference to the meeting. The tone of the letter was 'prospective': it proposed a fresh course of action that had no reference to an earlier meeting. It appears likely that Professor Forbes had already decided to pursue his own course by the time of the meeting and that he proceeded to implement his plan of action without reference to Professor Ludlam.

**33.395** The invitation to attend the meeting suggested something like a general information session. It was, unfortunately, ill-adapted to inform patients and their families that, among the recipients of the letter, there were individuals who were already known to have been infected with HTLV-III. Yet, on Professor Ludlam's evidence, one of the two objectives of the meeting was to inform those who attended that some patients were positive for the antibody. Patients would not have been prepared for information to that effect. The evidence of what transpired at the meeting has been set out fairly fully. It is not clear that specific information was given about the particular centres at which the 'Scottish' patients who had been infected were treated. Since Professor Ludlam had anticipated that Glasgow and west of Scotland patients would have been invited as well as those in other regions, the information was unhelpful and could have left patients in confusion about what they might be told at the meeting.

**33.396** For the reasons already discussed, the article published in *The Yorkshire Post* on 20 December 1984 cannot be treated as a wholly reliable account of what transpired at the meeting. In any event, it is not clear from its content what precise information was imparted to patients on that occasion. The article published in *The Edinburgh Evening News* on 21 December was brief and lacked specification of what had transpired at the meeting, commenting only that '[t]he situation was explained to haemophiliacs at a meeting with medical experts in Edinburgh this week'.<sup>522</sup>

**33.397** Plainly, the most reliable evidence in relation to the meeting is Witness A's note. It suggests, amongst other things, that practical information was imparted about how to avoid transmitting the virus together with additional information about HTLV-III and AIDS. From its terms, Professor Ludlam also seems to have indicated that he was prepared to inform his patients if they had the antibody to the virus. Mrs Brown believed he had communicated at the meeting that there was an infected group in Edinburgh, those present might be in that group and if they wanted to know if they were infected or not, they had to ask.

**33.398** The notes of Witness A and Geraldine Brown's evidence both suggest that at the meeting Professor Ludlam did communicate that he was offering to inform any of

---

<sup>522</sup> 'Plea to donors in AIDS alert', *The Edinburgh Evening News*, 21 December 1984 [PEN.016.1294]



his patients who asked him, whether or not they had the antibody. Frances' evidence of her father's position shows that some patients did take this on board. He sought and received his results on 21 December. However, the limitations of the meeting, and the scope for confusion that it generated, is attested to by the fact that two of Dr Alison Richardson's patients, both of whom had tested positive, left the meeting believing that they were negative. They believed that if they had been positive they would have been told that at the meeting. Professor Ludlam said that he was devastated on first hearing the news that some of his patients had tested positive. In all the circumstances, it is not surprising that haemophilia patients and their relatives, hearing the same news, should find it difficult to take in any information subsequently imparted. On any view, the meeting was an inappropriate means of conveying such news and any advice consequent upon it, although the Inquiry recognises that the media pressure probably left little room for choice in how to proceed.

**33.399** Given the obvious limitations of the meeting some follow-up was clearly required. It is unfortunate that the covering letter Professor Ludlam sent with the circular on AIDS has not been recovered. His evidence that it would have mentioned that some patients 'in Scotland' had tested positive is consistent with other evidence of the degree of specification in his public statements, as is the invitation to his patients to make an appointment to discuss their position. That evidence is accepted.

**33.400** It is clear, however, that Professor Ludlam's patients were not invited on an individual basis to attend the Edinburgh clinic. Whether patients had tested positive or negative for the antibody, Professor Ludlam had information about their health that they might have chosen to know. He could not have insisted on informing them but he could have followed the course adopted in Glasgow, at least from the summer of 1985, and sent an appointment to each patient inviting them to come individually for an interview. Such an invitation would have focused the recipient's attention on this important issue. In the climate of the time, some of them might have decided to remain in ignorance, since testing in itself, regardless of the result, might bring about adverse financial consequences. However, such a decision should have been theirs. That there was no treatment at the time would have been, no doubt, a factor in the patient's decision whether or not to discover if they had been tested. It is a matter of regret that Professor Ludlam did not issue such individual invitations. As a result, information reached his patients on a piecemeal basis over a long period of time and some were left ill-informed.

## Mark

**33.401** Mark's case is perplexing. Ms Reynolds' evidence cannot be accepted as it has no adequate time reference and is in too general terms to have dealt with the long period of time that passed before Mark was told of his diagnosis. During much of that time, Mark was seen by another doctor. Professor Ludlam explained that he felt that it was important for Mark to know of his diagnosis on a number of grounds. He spoke of an initial unsuccessful attempt to tell him in 1986, detailed in his notes, together with two further attempts. One was, potentially, to visit his home and the other was when he was seen by, as Professor Ludlam put it, 'one of our very able young doctors'. That doctor was Bernadette Auger. Dr Auger's note dated 20 March 1989 is a clear, contemporaneous and full account of her consultation with Mark and is accepted as accurate, true and reliable.<sup>523</sup>

---

<sup>523</sup> See Chapter 5, *An Examination of the Effects of Infection with HIV on the Patients and their Families, Including Treatment*, at paragraph 5.249

It cannot be reconciled with Mark's evidence and especially the frequent repetition of the recollection that he always said: '[t]ell me if there's anything wrong', in resisting detailed information about test results. It appears that Mark did resist information about his test results more generally and that that was understood by the clinicians treating him.

**33.402** There was considerable discussion with Professor Nathanson about this situation. The developing knowledge about AIDS was relevant. In 1984 the implications of a positive diagnosis were unclear. As Professor Nathanson explained, by 1988 it had become clear that positive antibody status usually meant that the patient had the virus and that the prognosis was very poor. From 1984 to about 1988 there was effectively no treatment for the condition. However, from about 1987–88 doctors were aware that an HIV positive patient was susceptible to certain AIDS-related conditions which had to be treated quickly and aggressively with antimicrobials.<sup>524</sup> In particular it was important to treat a patient quickly with pentamidine if they developed PCP.<sup>525</sup>

**33.403** Professor Nathanson's general evidence has been set out at length. So far as it bears on Mark's case, it can be summarised:

- A doctor could not force a patient to know the results of tests.
- A patient who refused to learn his results should be advised to act as if positive, so as to protect others.
- As means of helping infected patients developed – specifically with the introduction of antiretroviral medication in this case – the doctor would increase pressure on the patient to know the results.
- A point could be reached at which the doctor might consider forcing the knowledge on the patient because of the advantage of obtaining treatment.
- Before 1988 a doctor could not be criticised for not forcing patients to hear the results of tests.

**33.404** Applying the ethical rules and guidelines, as outlined by Professor Nathanson, it is not possible to find that Professor Ludlam was in breach. It is fortunate that in Mark's case his contemporaneous medical records assist in determining what probably happened over two decades ago. Conversations, at such a distance in time, are unlikely to be remembered accurately by their participants although the gist may remain clear to them. It is, of course, difficult to explain the difference between Mark's evidence and that of the practitioners treating him. It is trite that the message spoken is not always the message heard. For obvious reasons, medical practitioners would be particularly concerned to advise those testing positive of their results. Mark does not dispute that he was seen on a number of occasions where reference was made to his test result. It may be that he assumed that if he was positive the result would simply be passed on to him. That was not the policy at the RIE until treatment considerations arose. Whilst being offered a test result on a number of occasions might alert some to the probability that the result was positive, it would not do so with others. There is no doubt from his evidence, and that of Professor Ludlam, that when Mark received his diagnosis, he was surprised. He does not seem to have assumed from the attempts to tell him his result that it was, in all probability, because it was positive. Mark's evidence that he was 'stunned' on hearing the news of his diagnosis, is accepted.

---

<sup>524</sup> Professor Nathanson – Day 37, page 123

<sup>525</sup> Ibid pages 174–175

## Glasgow

**33.405** It is not possible to reconcile the several sources of evidence of practice at the GRI, from Professor Forbes, Professor Lowe and Dr Wilkie. Specific difficulties with their evidence have been noted above. How and when patients were told the results of anti-HTLV-III testing is unclear.

**33.406** Dr Follett had clearly been carrying out some HTLV-III tests as early as January 1985. The notes in David's case are unequivocal: he was tested and found HTLV-III negative on 25 January 1985. That was before any counselling protocol had been considered, much less implemented, and in particular was probably before Dr Wilkie became actively engaged in advising haemophilia patients about HTLV-III infection.

**33.407** The circular letter dated 8 January 1985 which was sent to all patients registered at the West of Scotland Haemophilia Centre at the GRI contained no indication that the individuals found positive had been, or indeed would be, informed of the positive findings in their cases. On the contrary, the clear indication was of a new initiative to investigate virus exposure and monitor all patients who had received concentrate therapy.

**33.408** From its terms, the letter of 8 January 1985 sent to patients registered at the Glasgow Centre was not addressed to people who were expected to have had prior knowledge of the results from the tests carried out by Dr Gallo or who had attended the meeting on 19 December 1984. Nor did it indicate that among the patients addressed were some for whom test results were available. The opening paragraph, referring to newspaper and television reports, would not be appropriate in a letter addressed to individuals who had been invited to a meeting at which Professor Forbes and Professor Ludlam had spoken on the topic of AIDS. The invitation to attend and have a test which 'we ... now' had available, despite the prior knowledge that 10% of patients had already been found antibody positive, may appear obscure unless the 'we' is taken as meaning Glasgow. The original testing was done in the USA. In any event, whatever reservations may exist in relation to the wording of this letter, it is clear from its terms that the recipient of it would not be aware after reading it that he had been tested and could obtain his results from the centre.

**33.409** There is no contemporaneous documentation to corroborate Professor Forbes' recollection of communicating the results of the Gallo tests 'as soon as possible' after November 1984. Whilst Professor Lowe, who has a good recollection of events, made it plain that it was his colleague's clear intention to do so, he also indicated that Professor Forbes had reservations about the accuracy of the Gallo test. Professor Forbes said in his evidence that he considered that confirmatory testing of the Gallo results was necessary. Neither Professor Lowe's evidence nor Dr Wilkie's suggest that either of them dealt with any patients who had received their Gallo test result. There can be no doubt, in the climate of AIDS fear then extant, that any patient advised of a positive result would be likely to consider it something akin to a death sentence. The catalyst for the appointment of Dr Wilkie, a social scientist, appears to have been the obtaining by Professor Forbes of the positive test results, suggesting that he was alive to the possible social and economic consequences of a positive diagnosis. Undoubtedly, Dr Wilkie will have further refined Professor Forbes's understanding of the likely impact of a positive result. Other documentation suggests that HTLV-III test results were communicated at the earliest after March 1985 and, in some cases, after 1986. In the circumstances, it seems probable that

Professor Forbes changed his mind and decided not to pass on the results obtained by Dr Gallo's unlicensed tests until they had been confirmed by Dr Follett. Whilst that sequence of events may not accord with Professor Forbes' memory, it would be consistent with his colleagues' high opinion of him and understandable in the circumstances then prevailing.

### David

**33.410** Professor Lowe's evidence, and that of Dr Wilkie, suggested that the policy at the GRI was that patients should not have their blood tested for HTLV-III before they had received counselling about the implications of the test. Regrettably, this does not appear to have happened in David's case, and his evidence in this matter is accepted. It seems, from the medical records, that when he was seen in January 1985 he was negative for the virus and was provided with Haemophilia Society leaflets. Dr Wilkie only began interviewing patients in the late summer of 1985. When David was seen on 8 November 1985 it was by an unknown doctor, who appears to have taken blood and submitted it for testing without either obtaining consent for the test or providing counselling. Consequently, when Professor Lowe saw David on 2 December 1985, his patient had not been prepared for receipt of his results. In the circumstances, it is entirely understandable that David should have felt angry. His reaction confirms the wisdom of the counselling programme pioneered at the GRI, but suggests that it did not always proceed as intended.

**33.411** David's evidence about the manner in which Professor Lowe told him his diagnosis gives one patient's perspective of receiving such information from a clinician. It is, perhaps, illustrative of the difference which may sometimes exist between how a clinician believes he is conveying such a diagnosis and how the patient perceives he has been told of the diagnosis. A number of factors, in addition to the clinician's manner, will affect this perception. Breaking bad news is never easy, and Professor Lowe candidly admitted that he found providing such a diagnosis a difficult task to perform.

### *General comments*

**33.412** Until the events of 1982–84, and the questions relating to providing information to patients in 1985 and later, which raise specific issues, routine testing of patients' blood ancillary to diagnosis and the prescription of proper care and management was standard practice. Consent was not normally sought for specific investigations, as distinct from the physical act of taking blood which could clearly not take place without the patient's consent, either express or implicit, in the act of extending an arm for preparation by ligature, puncture and for the withdrawal of blood. Dr Winter's written evidence to the Archer Inquiry (see paragraphs 33.176 to 33.180 above) is accepted. For a considerable period before 1988, clinicians saw it as part of their responsibility to their patients to monitor for infections. It was perceived to be a core part of patient care and not something to be discussed with patients.

**33.413** It is an almost inevitable consequence of the paternalistic attitudes in the early 1980s together with the relative ignorance of the significance of the AIDS virus at that time, that in the absence of appropriate professional guidance some clinicians would consider AIDS-related investigations to have the same character as established investigatory/monitoring tests for which no specific consent required to be sought. The rate at which doctors realised that this new infection required a different response, particularly in regard to the provision of information and the obtaining of consent for testing, would vary within the profession. Such realisation of the need for a change of approach would depend upon many things including experience and attitude.

**33.414** As events were to prove, but unknown to clinicians generally until 1984, AIDS transmitted by an infective agent was a material risk associated with all forms of factor therapy in the early 1980s. The commercial pharmaceutical industry responded to the risk by introducing early forms of heat-treated products in 1984, although evidence of their effectiveness was lacking at that stage. Selection of products for therapeutic use had become more problematical. It is from mid-1984 and into 1985 that issues relating to the provision of information about the products offered and about the risks associated with them became real, ultimately giving rise to a need for informed consent to treatment on the part of the patient.

**33.415** There is a distinction between the risk of transmission of AIDS and the risk of transmission of NANB Hepatitis which it is important to note. AIDS was a new disease. With the exception of those patients being introduced to factor therapy for the first time, most coagulation disorder patients at risk of NANB Hepatitis would have been exposed to the infective agent (usually the Hepatitis C virus, as events were to show) before it was realised that the risk of transmission was virtually universal from first treatment with factor concentrates, of whatever origin. When that was appreciated, there was little that could be done to protect established patients. AIDS presented a new and distinct risk to long-established patients as well as to previously untreated patients. When the risk became real, it was greater for patients with severe coagulation disorders, for whom effective therapy required heavier concentrate usage. It was also greater for those using commercial concentrates. Since a majority of those established on concentrate therapy in the early 80s were patients with severe coagulation disorders, there was a risk that a very significant proportion of patients would contract AIDS. The risk was higher in England and Wales due to their greater reliance on commercial concentrates.

**33.416** A very significant number of patients did develop AIDS. This was not anticipated, however, and was not generally understood until late 1984 or later. Some clinicians in England and Wales did change from concentrate therapy to the use of cryoprecipitate in 1982 and 1983 but that was by no means general. The priority remained the provision of effective treatment for haemophilia and other coagulation disorders. That is the practical context in which the ethics of clinical practice must be considered.

***Scottish practice: the ethics of providing information about HIV/AIDS, risk from treatment and seeking consent***

**33.417** It is clear from Professor Nathanson's evidence that today failure to discuss treatment with patients and to obtain their consent to treatment would be unacceptable. That appears from the General Medical Council booklet *Consent: patients and doctors making decisions together* discussed in Chapter 32, *An Investigation into the Systems in Place for Informing Patients about the Risks – Ethical Context*.<sup>526</sup>

**33.418** In contrast to her evidence on practice in relation to HCV, there was little controversy about Professor Nathanson's evidence relating to the ethical principles and rules applicable to clinical practice in respect of HIV/AIDS in relation to the late 1980s.

**33.419** In respect of the provision of information relating to tests, again, context is important. As described by Professor Ludlam and Professor Forbes, routine blood tests were long-standing aspects of the treatment, or management, of the patient as an individual

---

<sup>526</sup> *Consent: patients and doctors making decisions together*, GMC, 2008 [PEN.018.0430]

and provided information of immediate clinical importance to the patient. However, it is also apparent that in any teaching hospital with a research agenda, the accumulation of data from testing individuals would inevitably have wider significance, increasing general knowledge of the index condition and the direct effects and side-effects of any treatment that followed. It would not be unreasonable to expect the individual patient to understand that his data contributed to the general store of knowledge from which all other patients in the care of the one clinician or clinical team would take benefit and to expect that he would similarly benefit from advances in knowledge achieved from the management and investigation of other patients.

**33.420** It is really inconceivable that it would be otherwise. Ordinary clinical practice, as described by Professor Ludlam, involved discussions in the course of ward rounds with junior doctors and students. Research projects were discussed, and patients were asked to cooperate by participating, in the ordinary course of events. In the real world of medical wards in teaching hospitals, patients are not insensitive to what happens around them. While his research interests, or those of his colleagues in Glasgow, may not have been understood, that they had research interests would have been known to regular patients and, through them, to the close community of coagulation disorder patients attending the hospitals as a whole.

**33.421** It follows that a clinician intending to carry out a particular testing programme should have been conscious of the need to structure the approach adopted and, in particular, the information given to patients about the tests and any consent sought for the tests to be carried out, so as to reflect the likelihood that some information at least would become widely known among patients, as well as having a wider professional application. So far as the evidence shows, the issues around the approach to testing arose first in Edinburgh and Glasgow in relation to the immunological studies carried out on haemophilia patients in 1983.

**33.422** As set out in paragraphs 33.173 to 33.174 above, the considered view of the UKHCDO in December 1984 was (a) that testing of patients should proceed; (b) that it was for individual clinicians to decide, having regard to the circumstances, whether an individual testing anti-HTLV-III positive should be informed of the result; and (c) that advice should be given to patients about the risks associated with sexual transmission and steps to be taken to protect spouses and other partners. There was no stipulation in Professor Bloom's advice of 14 December 1984 for patient consent to testing. Indeed it can be inferred that consent was not considered to be required since disclosure of the result was discretionary and that is inconsistent with a principle of patient involvement in the decision to carry out a test in the first place. This is significant in considering the steps taken in Edinburgh and Glasgow, since the advice of the Reference Centre Directors is a clear expression of the ethical stance of this professional group at a critical time in the evolving picture. It is important to bear it in mind in considering Professor Nathanson's evidence.

**33.423** Professor Nathanson explained that in order to carry out an HIV test in accordance with BMA and GMC guidance current from 1988 it is necessary to (i) obtain a patient's valid consent and (ii) ensure that the results are offered to patients. She said that in current practice clinicians are expected to offer 'pre-test counselling' to patients before HIV testing. This will include full information about the test and the implications of a positive result. The practical result of following this procedure is that, if a patient tests positive, they will already know the implications of the diagnosis. Pre-test counselling

helps to remove some of the shock and surprise that a patient might experience on being told of a positive diagnosis.<sup>527</sup>

**33.424** It is clear that the practice described by Professors Ludlam and Forbes of taking an apparently routine blood sample from a patient on an apparently routine visit, storing it in the deep freeze and later sending it for an HTLV-III antibody test without informing the patient would not be acceptable today. It is also clear, however, that standards were different in 1984.

**33.425** As Professor Nathanson noted:

When the first diagnostic test for HIV disease (in fact a test for antibodies for what was then called HTLV III) became available in 1984 there was considerable debate over whether those for whom a test might be considered clinically relevant needed to be asked for consent to the test.<sup>528</sup>

**33.426** In the early days of testing many believed that HTLV-III antibody tests could and should be carried out without consent and that taking blood for the test at the same time as other routine medical tests would mean that necessarily implied consent had been given.<sup>529</sup>

**33.427** Professor Nathanson expressed the view that, while testing for HTLV-III antibody without consent was not the 'gold standard' of medical practice, it was common practice in the early 1980s. She said that she would not be critical of clinicians who had not conducted their practices in accordance with the 1988 guidance before that date. She explained that, until the GMC guidance was published, much of the advice on consent concerned consent to treatment rather than consent to testing. The advice published by the GMC in 1988 helped to close the argument about consent for testing.<sup>530</sup> She explained:

The question is: does that mean that anything that the doctor wants to test that blood for, you have given necessarily implied consent for? And I would say that in the mid 1980s that was the issue about which people were discussing, and I think we really came to the conclusions that you might say that there were certain tests that were so routine, that are so often done, that you were necessarily consenting to them without being given the details.

....

But it was felt [by the date of publication of the GMC 1988 guidance] that a test for HIV was sufficiently different because of the clinical uncertainty, what did a result mean, and because of the social consequences, that you needed to get a specific consent to say that.<sup>531</sup>

**33.428** Professor Nathanson said that the current approach to HIV testing has not changed much since the 1988 guidance, which applies to consent to testing as much as it does to treatment. In contemporary practice clinicians are expected to offer full information to patients about all tests they intend to perform. To supplement the basic guidance set out in *Good Medical Practice*, the GMC produces a booklet on consent. 'Good medical

---

<sup>527</sup> Professor Nathanson – Day 37, pages 37–39

<sup>528</sup> Professor Nathanson's first report to the Inquiry [PEN.012.0330] at 0336

<sup>529</sup> Ibid [PEN.012.0330] at 0336

<sup>530</sup> Professor Nathanson – Day 37, pages 92–93

<sup>531</sup> Ibid pages 90–91

practice' is not a body of formal rules, however, but rather a set of principles and values on which good medical practice is founded. The supplement, *Consent: patients and doctors making decisions together* (May 2008) provides more specific advice.<sup>532</sup> The clear advice is that testing for HIV now requires specific consent.

**33.429** However, Professor Nathanson explained that the 1988 guidance was the first time that the GMC was explicit on the topic. In the late 1970s, it would have been extremely rare to tell patients everything about their care. The 1988 guidance was part of the 'evolution towards patient-centred care'.<sup>533</sup> She said that between 1984 and the 1988 guidance, not fully informing the patient 'wasn't best practice but it was understandable and widespread and something that was becoming less understandable and less widespread, if you like, diminishing'.<sup>534</sup>

### *Glasgow and Edinburgh compared*

**33.430** At the end of 1984, Professors Forbes and Ludlam found themselves in the position of having HTLV-III test results for some of their patients. Those tested were unaware of the tests and, in many cases, unaware that they were even at risk of infection. Obviously, no pre-test counselling had been carried out. The initial attempt to communicate the existence of such results to east of Scotland patients at the meeting was largely ineffectual. Attempting to communicate such sensitive and life-shattering information by such means was ill advised. The response in the west of Scotland was more conventional and, in the long run, seems to have been more effective.

**33.431** At the end of 1984 there was no consensus amongst haemophilia clinicians in relation to the communication of HTLV-III test results to patients. There were effectively three schools of thought on this matter:

1. All patients should be told their test results regardless of their wishes.
2. Patients should not be told their results and should all assume that they are positive.
3. Patients should only be told their results if they asked for them.

**33.432** Professor Nathanson recognised that the situation was 'extraordinarily difficult' and that many doctors did not communicate results of HIV tests.<sup>535</sup> She explained, however, that in 1984 the 'gold standard' for a clinician in that position was to offer the information to their patients. In Professor Nathanson's view, Professor Ludlam's approach of offering his patients information rather than simply telling them their results, and thus forcing them to know their antibody status, was reasonable. It would not have been up to the 'gold standard' for Professor Ludlam to have either withheld the test results from patients or to have told the patients their results without ascertaining whether or not they actually wanted to know them. Professor Ludlam's approach of not telling patients their test results unless they asked for them was consistent with the UKHCDO advice and it is clear that many doctors at that time considered that testing for HIV was simply an extension of the monitoring of patients which was already being done.

**33.433** Professor Nathanson said that she would be critical of a clinician who had test results for his patients but did not make it clear to them that results for them were available.

---

<sup>532</sup> *Consent: patients and doctors making decisions together*, GMC, 2008 [PEN.018.0430]

<sup>533</sup> Professor Nathanson – Day 37, pages 113–114

<sup>534</sup> *Ibid* page 118

<sup>535</sup> *Ibid* page 125



She felt that the way to do that was by writing to them. While this is more of a practical consideration than an ethical question, in her view a clinician who has decided to offer his patients information about their test results (and many did not at that time), in order to do so properly had to tell the patient clearly that information about them was available. When asked about how to approach communicating results she said:

I think that really depends upon how often you see the patient and what the relationship is with the patient. That would be equally true today in the sense of communicating results. The clear issue is of course to make sure that the patient knows, or is given the availability of that knowledge, as early as possible.

In 1984 that would almost certainly have meant writing to patients and saying, "We have information available, please make an appointment to come and see me if you want to know that information." If you have patients that have routine appointments within the next few weeks, you could probably not write to that group but you must make sure that they are seen, and if by any chance they don't come to those appointments, then make sure they get an offer of another appointment quickly.<sup>536</sup>

**33.434** Professor Ludlam was told by the reporter from *The Yorkshire Post* that he intended to publish the details of the positive test results in the Edinburgh haemophilia population. The Inquiry has not heard evidence from the reporter concerned. It is almost certainly the case that information was leaked to the newspaper by a person to whom it had been imparted on a confidential basis. The motives behind the decision by the newspaper to prepare and publish a report are not known. But the involvement of the paper was the immediate cause of hasty resort to a public meeting. This was an unsuitable mechanism for release of such sensitive information about the health of patients.

**33.435** Dr Wilkie described, graphically, attitudes to HIV-positive individuals at about that time. She explained that they were viewed as 'lepers', or 'dirty patients' and subjected to humiliating, and unnecessary, precautions in order to ensure that they did not infect others.<sup>537</sup> Out of fear of such consequences, sufferers routinely concealed their diagnoses. However, unlike the other groups particularly at risk of the infection such as IV drug users or homosexuals, haemophilia sufferers tended to be known in the communities in which they lived, their condition unconcealed from family, friends, workmates and acquaintances. Having begged the reporter to delay publication, and been allowed one week, Professor Ludlam wrote invitations to the meeting that same day. As a vehicle for the transmission of sensitive information, the meeting's shortcomings do not require to be re-rehearsed here. Considering the need to get information to as many patients as possible, imparted by him personally and as quickly as possible, it was the option he chose. It would not have been, he explained to the Inquiry, his 'first choice, given a completely blank sheet and without other constraints'.<sup>538</sup>

**33.436** It is clear from the evidence that Professor Ludlam attempted to prompt his patients into inquiring about their test results by means of the meeting, the circular and the covering letter. If they attended the RIE, he decided, depending upon the circumstances of

---

<sup>536</sup> Ibid page 128

<sup>537</sup> Dr Wilkie – Day 32, pages 64–67

<sup>538</sup> Professor Ludlam – Day 35, page 116

their visit, whether to initiate a conversation about AIDS or encourage them to seek their results. His approach was based, in part, on his awareness of the consequences for them of knowing that they had been tested, and the significance of a positive or a negative result. It is clear that he considered two matters of particular relevance in making that decision. Firstly, the fact that no treatment for the condition then existed and, secondly, the fact that all haemophiliacs were being advised to adopt precautions as if they were infected. If a patient did not attend the RIE no communication was sent to them as a further prompt.

**33.437** Despite the meeting of 19 December, the circular and these discussions, Professor Ludlam did not make it *sufficiently* clear to all of his patients that they had to ask him if they wanted to know their results. He could have made appointments for every patient who used factor concentrates to be seen by him, by Mrs Brown or by both. He could have sent out appointments with the circular in the way Professor Forbes did with his letters of January and April 1985. He could have started with the 40-50 patients who had already been tested. He could have met with patients in early 1985 and made sure that they were individually fully aware of the situation, that he had HTLV-III test results for them, where that was the case, and that he would give them the results if they asked for them. He could have been more explicit about this without insisting that they knew their test results. If Professor Ludlam had done something along these lines, it is likely that by the end of 1985 all patients would have known their HTLV-III status except for patients who did not want to know.

**33.438** In the result, some patients were angry that they had not been told of their diagnosis sooner or at all, and some were glad that they remained in ignorance for so long. As might be expected, as his knowledge of the virus and its effects increased and the possibility of treatment emerged, Professor Ludlam became increasingly proactive in his approach. To modern sensibilities, paternalism and the 'Doctor knows best' approach are anathema but in considering judgements made in the early and mid 80s, it has to be taken into account. A quite different approach would be taken nowadays but that is in large part because of the effect that the emergence of the AIDS virus has had on medical ethics.

**33.439** The position in the west of Scotland is complicated by the inconsistencies in the evidence relating to it, and Professor Forbes' memory difficulties. On balance, it is concluded that the only testing carried out prior to that executed by Dr Follett was that done in the USA by Dr Gallo. Further, it is concluded that, despite his recollection to the contrary, Professor Forbes did not pass on the results of the Gallo tests to his patients before confirmatory testing was undertaken by Dr Follett. It is clear that it was his intention to pass them on, Professor Lowe attested to that fact, but the evidence suggests that Professor Forbes must have changed his mind and the reservations he expressed about the reliability of the research assay provide both an explanation and a justification for that course of action. It cannot be concluded that that practice, in itself, involved any breach of the norms of ethical behaviour of the time.

**33.440** It should be noted that with the emergence of AIDS, an entirely new disease, almost all haemophilia clinicians found themselves in an extraordinarily difficult situation. Due to the chronic nature of haemophilia, those clinicians had known and treated many of their patients since childhood. They had seen many of those patients' lives transformed

by the introduction of concentrates, and rejoiced with their patients. As knowledge of the AIDS virus increased, so did the realisation amongst those clinicians that the treatment they had prescribed to alleviate their patients' primary condition, had also transmitted a potentially fatal viral infection. In the early days, they knew almost nothing about the disease and its natural history and could themselves only pass on the little they knew. As more was learnt about the virus, they endeavoured to alter their practice in accordance with that knowledge. They had received no guidance or training for the unprecedented circumstances in which they found themselves.

**33.441** Whilst initially the medical profession knew little about AIDS, those they were treating knew less and depended upon the professionals for guidance. In a paternalistic age, those providing such guidance aim to reassure and to comfort the patient, on the basis that 'Doctor knows best'. Equally, those receiving such guidance do not tend to question it, feeling entitled to rely upon it. Inevitably, if that guidance proves wrong and patients suffer, or die, in consequence of it, some of those patients may, entirely understandably, feel both angry and betrayed. If a new, potentially fatal disease like AIDS were to emerge today it is likely that patients would be made aware of the medical profession's ignorance of it and share all the uncertainties and anxieties consequent upon that. Unfortunately, patients would, in all likelihood, still suffer and die. Anger against the disease and all of its consequences would probably be felt. But there would be no sense of betrayal. On the evidence, in relation to the procedures adopted for testing patients' samples for HTLV-III and the communication of test results, there was no breach in Edinburgh or Glasgow of any rule or principle of ethical conduct then applicable. In the circumstances, where many patients died, and many continue to suffer today, some crumb of comfort may be gained from the fact that due to HIV/AIDS and its fallout, all patients must now be treated in a patient-centred way and the last vestiges of paternalism have largely been swept away. Being informed is now the patient's prerogative.



## CHAPTER 34

### AN INVESTIGATION INTO THE SYSTEMS IN PLACE FOR INFORMING THE PATIENTS ABOUT THE RISKS – HEPATITIS C

#### Introduction

**34.1** The discussion in Chapter 33, *An Investigation into the Systems in Place for Informing the Patients about the Risks – HIV/AIDS*, sets the scene for this chapter. The previous chapter dealt with relationships between doctors and patients, from the beginning of the AIDS epidemic in 1982 to about 1985, with particular reference to HIV/AIDS. In that period, it became clear that NHS blood disorder patients had acquired the HIV virus and the focus in clinical and ethical practice shifted towards the management and care of patients infected, or suspected to be infected, with that condition. The lessons learned in that context were available to instruct doctors in the management and care of patients, as it came to be understood that non-A, non-B Hepatitis (NANB Hepatitis) was a potentially more serious disease than had generally been thought up to the end of 1985. In that period NANB Hepatitis was not entirely overlooked, even at the height of the AIDS epidemic. For the most part, however, it was a secondary consideration in an environment dominated by the threat of AIDS.

**34.2** Developing knowledge of viral hepatitis has been traced in Chapters 14–16, *Knowledge of Hepatitis 1 to 3*. This forms the background to the discussion that follows.

#### Scope of the chapter

**34.3** This chapter deals with the evidence on the information and advice given to patients, and where appropriate to their parents, in Scotland in the course of the reference period with regard to NANB Hepatitis/Hepatitis C. More specifically it considers:

- Questions relating to the choice of therapeutic products in treating blood coagulation disorders and, in particular, understanding the risks of contracting NANB Hepatitis, from 1974 onwards.
- The information given to patients about those risks.
- The investigation and management of patients' conditions with regard to symptoms of NANB Hepatitis/Hepatitis C.
- The understanding of risks associated with HCV once tests for infection had become available, including pre-test counselling.
- The communication of results to patients who were found to be infected with HCV.
- Practices at centres in Edinburgh, Glasgow and Dundee are examined in some detail as these developed over the reference period. Practitioners from these centres were able to give evidence to the Inquiry in relation to practices there.

#### Background

**34.4** The information available to doctors on which to base their advice to patients, having regard both to what was generally accepted in the medical profession and what was in the public domain, varied widely both over time and across the UK and other western countries. In Chapter 32, *An Investigation into the Systems in Place for Informing Patients about the Risks – Ethical Context*, Dr Charles Hay's evidence was relied upon as illustrating

best clinical practice. That was appropriate since in some respects his practice reflected at an early stage an understanding of NANB Hepatitis that was not shared generally and involved a more demanding level of communication of NANB Hepatitis infection than would have been practised elsewhere. In this chapter it is appropriate to take note of distinctions between Sheffield, one of the places where he worked, and other centres.

**34.5** As noted in Chapter 21, *Haemophilia Therapy – Use of Blood Products* paragraphs 21.161–21.171, on 26 April 2011 the Inquiry viewed two *World in Action* documentaries called ‘Blood Money’ which were first transmitted in 1975.<sup>1</sup> The programmes dealt with blood products and the transmission of viral infections in haemophilia patients receiving replacement therapy with factor concentrates. The programmes did not deal with the risks of transmission associated with transfusion of whole blood or blood components in general medical and surgical practice. In relation to HBV, which was then understood to be the main pathogen threatening recipients, the programmes were explicit reminders, if reminders were needed, that the risk of transmission of viral hepatitis was inherent in factor replacement therapy.

**34.6** In one respect at least, patients with haemophilia or other blood coagulation disorders, or the patients’ parents, were in a better position to inform themselves of risk than others receiving transfusions. It was clear from what patients and their parents said in the television documentary that in the 1970s many haemophilia patients were aware that there was a risk of contracting hepatitis from the use of factor concentrates. In the later years of the decade, there was published material on the risk of transmission that was available to members of the Haemophilia Society. David Watters, General Secretary of the Society between 1986 and 1994 (and Coordinator for five years before that), explained that this risk was discussed in Haemophilia Society Newsletters from 1978.<sup>2</sup> It is clear from the evidence of clinicians noted later in this chapter that the Society’s leaflets were in circulation in haemophilia centres. There was a body of shared information, often backed by expert authors and commentators, available to patients and haemophilia clinicians alike.

**34.7** The natural history of NANB Hepatitis was not well understood, however, until the second half of the 1980s, at the earliest.<sup>3</sup> In the mid-1970s discussions of viral hepatitis almost certainly referred to the then well-known risk of contracting Hepatitis B. By 1975, screening for Hepatitis B Virus (HBV) in blood donations had become standard practice in the USA and in Europe, though high sensitivity in screening tests was not achieved until the end of the 1970s. Progressively, there was increasing confidence in the effectiveness of the methods used to identify infected blood and to exclude it from therapeutic use.

**34.8** The extent of the problem of transfusion-associated transmission of NANB Hepatitis did not begin to become apparent until about 1978.<sup>4</sup> Even then it was not generally thought to present a risk of comparable order to the risks associated with bleeding in coagulation disorder patients. Until the later 1980s there was no general consensus in the medical profession that NANB Hepatitis infection was associated with serious liver disease. Even at that point, some commentators thought that the condition was not a matter of serious clinical concern.

---

<sup>1</sup> *Blood Money*, *World in Action*, Transcripts of episodes broadcast on 1 and 8 December 1975 [PEN.013.1400]

<sup>2</sup> Mr Watters – Day 87, pages 39–40. See also Haemophilia Society Bulletin, 1977, No. 3 [PEN.018.1262] and Haemophilia Society Report, ‘Haemophilia Today’, 1978 [PEN.018.1336]

<sup>3</sup> See Chapter 16, *Knowledge of Viral Hepatitis 3 – 1986 Onwards*

<sup>4</sup> See Chapter 15, *Knowledge of Viral Hepatitis 2 – 1975 to 1985*

**34.9** For the purposes of this chapter, it is interesting to compare the treatment of NANB Hepatitis in successive editions from around this period, of Dr Peter Jones' (Newcastle Haemophilia Reference Centre) book, *Living with Haemophilia*. The book is a guide that was widely distributed among patients and their families. The first edition, published in 1974, discussed 'serum hepatitis' briefly and described its transmission by the 'Australia', or 'hepatitis-associated', antigen. It was presented as a rare but important side-effect of blood transfusion. The second edition was published in 1984. The book now dealt with Hepatitis B extensively, less so with Hepatitis A, and only briefly with NANB Hepatitis. It identified hepatitis generally, inflammation of the liver, as one of the most important side-effects of blood transfusion. It commented that, 'if the infection is marked enough jaundice may result', and continued:

We know that many liver infections are not severe enough to result in the appearance of jaundice; they show themselves as mild, transient periods of feeling unwell, or only as changes in liver function measured in the laboratory. One of the reasons for following up people with haemophilia carefully is to monitor these changes.<sup>5</sup>

**34.10** The second edition of the book noted the three types of viral hepatitis then known and said:

Hepatitis non-A, non-B results from infection with one of at least three viruses, none of which has ... been positively identified in the laboratory ....<sup>6</sup>

**34.11** It commented on the NANB Hepatitis viruses:

The incubation periods for these viruses appear to be short, in some cases only a matter of days. There is evidence that haemophiliacs have multiple episodes of NANB Hepatitis, most going unnoticed, although the first attack is sometimes accompanied by the appearance of jaundice. The NANB agents are important because, as with hepatitis B, the infection they cause can lead on to chronic liver disease. No way of protecting recipients from NANB Hepatitis is known.<sup>7</sup>

**34.12** The third edition (1990) introduced the term 'transaminitis' for the 'condition', identified by changes in liver function measured in the laboratory.<sup>8</sup> The comment on NANB Hepatitis was in substantially the same terms as the 1984 edition, but added that donor testing for Hepatitis C was just being introduced.<sup>9</sup> Dr Jones did not equate 'transaminitis' with NANB Hepatitis or otherwise suggest that liver function test biometrics were monitored as specific indications of infection with NANB Hepatitis.

**34.13** There were two parallel trends: increasing confidence in the effective screening of donations to exclude blood infected with Hepatitis B and slow, and late, developing knowledge of the serious risks associated with NANB Hepatitis. Dr Jones' comments in the 2nd edition of his book indicate that by 1984 he was taking a more serious view of NANB Hepatitis than he had in the 1974 edition. These books form important background material in considering the provision of information and advice to patients who, generally, had underlying blood coagulation deficiencies that exposed them to the risk of serious, and in some case life threatening, episodes of haemorrhage.

---

<sup>5</sup> Jones, P. *Living with Haemophilia*, 2<sup>nd</sup> ed, 1984, MTP Press, Lancaster [PEN.018.0754] at 0756

<sup>6</sup> Ibid [PEN.018.0754] at 0757

<sup>7</sup> Ibid [PEN.018.0754] at 0758

<sup>8</sup> Jones, P. *Living with Haemophilia*, 3<sup>rd</sup> ed, 1990, MTP Press, Lancaster, [PEN.018.0761] at 0763

<sup>9</sup> Ibid [PEN.018.0761] at 0765

**34.14** In their 1974 report, the UK Medical Research Council (MRC) Working Party on Post-Transfusion Hepatitis included in their definition of 'hepatitis' a finding of enzyme elevation in association with other clinical indications of hepatitis, typically jaundice.<sup>10</sup> Since this was a definition of 'hepatitis' generally, it was as applicable to the postulated NANB Hepatitis as it was to Hepatitis A and B.

**34.15** In August 1975, Dr John Craske of the Public Health Laboratory, Dorset, published data on an outbreak of hepatitis following the infusion of commercial Factor VIII in the Bournemouth Haemophilia Centre.<sup>11</sup> The criteria for diagnosis were jaundice or raised transaminase levels associated with compatible history and clinical signs of infection.<sup>12</sup> With this publication, NANB Hepatitis had been recognised and reported from a UK haemophilia centre.

**34.16** In 1978 doctors at the Royal Hallamshire Hospital, Sheffield, published the results of liver biopsies carried out on haemophilia patients with persistent abnormal liver function test results.<sup>13</sup> A wide spectrum of chronic liver disease was found that bore no relationship to clinical history or biochemical findings using tests available at the time. They concluded that a large proportion of haemophilia patients receiving treatment with Factor VIII had chronic liver disease and that NANB Hepatitis may well have been an important factor. This was supported by observations in half of the cohort of patients studied. The paper did not say that abnormal liver function amounted to a diagnosis of NANB Hepatitis but it provided evidence that a clinical history of hepatitis was not essential for proof of infection.

**34.17** On 4 July 1981, an editorial in the *British Medical Journal (BMJ)* stated that a NANB Hepatitis diagnosis was usually inferred from abnormalities in the results of hepatic biochemical tests rather than from clinical evidence.<sup>14</sup> It referred to the biopsy-based research at Sheffield as indicating that changes in liver architecture were consistent with previous viral assault. The editorial also referred to Scottish research by Stirling et al. That research looked at Edinburgh patients treated with SNBTS Factor VIII who, followed over a five year period, had no symptoms or other objective clinical evidence of liver disease but did have ALT abnormalities. The authors suggested that, 'Possible causes include repeated infection with as yet unidentified non-A, non-B hepatitis viruses'.<sup>15</sup>

**34.18** The next stage was the research initiated by Dr Hay following his return to Sheffield in 1983 that resulted in publication in 1985 of the provocatively entitled article, 'Progressive Liver Disease in Haemophilia: An Understated Problem?'.<sup>16</sup> In the interval between 1978 and 1985 Dr Hay and his Sheffield colleagues were in the vanguard in recognising NANB Hepatitis as a potentially serious condition and in reporting it in the

<sup>10</sup> Medical Research Council Working party on Post-Transfusion Hepatitis, 'Post-transfusion hepatitis in a London hospital: results of a two-year prospective study', *Journal of Hygiene*, 1974; 73:173–188 [LIT.001.0116]

<sup>11</sup> Craske et al, 'An outbreak of hepatitis associated with intravenous injection of Factor VIII concentrate', *The Lancet*, 2 August 1975; 221–223 [LIT.001.0360]

<sup>12</sup> Other clinical signs of infection included pyrexia and urticaria which had occasionally occurred with cryoprecipitate. The article commented that these signs did not occur with concentrates.

<sup>13</sup> Preston et al, 'Percutaneous liver biopsy and chronic liver disease in haemophiliacs', *The Lancet*, 19 September 1978; 592–594 [LIT.001.0387] Details are given in the Preliminary Report, paragraph 6.71. Professor Thomas identified this as Dr Triger's work: Day 52, page 1292.

<sup>14</sup> 'Post-transfusion hepatitis' *British Medical Journal*, 1981; 283 [LIT.001.0227]

<sup>15</sup> Stirling, Beckett and Percy-Robb, 'Liver function in Edinburgh haemophiliacs: a five year follow up', *Journal of Clinical Pathology* 1981; 34:17–20 [LIT.001.0748]

<sup>16</sup> Hay et al, 'Progressive liver disease in haemophilia: an understated problem?' *The Lancet*, 1985; 1:1495–98. [LIT.001.0335] In oral evidence (Day 8, page 4) Dr Hay noted that the article title was a 'poke' at another paper, published the previous year, which had suggested NANB Hepatitis might be an over-stated problem: Stevens et al, 'Liver disease in haemophiliacs: an overstated problem?', *British Journal of Haematology*, 1983; 55:649–655 [LIT.001.0008]



absence of objective clinical evidence before liver biopsy was widely practised, particularly on haemophilia patients. His evidence of what patients would have been told about the condition distinguishes him from others who continued to follow the MRC definition of hepatitis.

**34.19** Dr Hay said that in the mid- to late 1970s very little would have been said to patients about the risk of viral infection. From the late 1970s most regularly reviewed patients would have had liver function tests conducted and he expected that most of those affected would have been told that they had NANB Hepatitis, but that it was probably nothing to worry about.<sup>17</sup> His evidence about a diagnosis of NANB Hepatitis prior to 1983 is unlikely to have reflected universal practice, however, given the general adherence to the MRC definition of ‘hepatitis’, but the advice that NANB Hepatitis was probably nothing to worry about would have been consistent with the prevailing view, which continued into the mid-1980s. Professor Sherlock’s discussion of viral hepatitis in the 1981 edition of her standard textbook, *Diseases of the Liver and Biliary System*, indicated that the clinical course of NANB Hepatitis often involved a mild chronic hepatitis, but that the prognosis, while still uncertain, was probably benign.<sup>18</sup>

**34.20** In the mid-1980s it began to be recognised, first by hepatologists and some other specialists and later by the medical profession more generally, that infection with NANB Hepatitis could potentially be associated with more serious liver disease than had previously been thought. The risk of acquiring NANB Hepatitis had become the predominant concern in respect of the transmission of viral hepatitis following the transfusion of blood or blood products. The view of relative risk highlighted in the *World in Action* programmes had become more significant although, ironically, by that time the risk of transfusion-acquired Hepatitis B (the ‘hepatitis’ of the 1975 documentary) had become negligible.

**34.21** By the end of 1983, it was understood by haemophilia doctors that all factor concentrates, NHS or imported, carried a risk of transmission of NANB Hepatitis. Dr Craske’s 1982–1983 Annual Report for the UKHCDO’s Hepatitis Working Party, produced on 28 September 1983, noted that a prospective study begun in 1981 had confirmed that there was a near 100% risk of contracting NANB Hepatitis from Factor VIII concentrates on first exposure, whatever their source.<sup>19</sup> A report of that study, published on 10 December 1983, indicated that the diagnosis was based on elevated AST and ALT measurements and the absence of markers of other viral infections and clinical evidence of any other cause.<sup>20</sup> An editorial in the *BMJ* by Dr Jones noted that most post-transfusion hepatitis was now NANB.<sup>21</sup> However, he did not expressly link diagnosis to liver function test results, noting that abnormal results were found in most severely affected haemophilia patients who had repeated transfusions. There were conflicting views of the implications for patients of the changes in liver function then being observed. Dr Jones considered that most observed changes in liver function represented chronic persistent hepatitis rather than the more serious chronic active hepatitis.<sup>22</sup>

<sup>17</sup> Dr Hay’s report on communication to patients about hepatitis [PEN.018.0961] at 0987

<sup>18</sup> See Chapter 15, *Knowledge of Viral Hepatitis 2 – 1975 to 1985*

<sup>19</sup> UK Haemophilia Hepatitis Working Party, Annual Report for the Year 1982-83 [SNF.001.0948]; see Chapter 15, *Knowledge of Viral Hepatitis 2, 1975 – 1985*, paragraph 15.122

<sup>20</sup> Fletcher et al, ‘Non-A non-B hepatitis after transfusion of factor VIII in infrequently treated patients’, *British Medical Journal*, 1983; 287:1754–57 [LIT.001.0239]

<sup>21</sup> Jones, ‘Acquired immunodeficiency syndrome, hepatitis and haemophilia’, *British Medical Journal*, 1983; 287:1737-1738 [LIT.001.0243]; see Chapter 15, *Knowledge of Viral Hepatitis 2 – 1975 to 1985*, paragraph 15.127

<sup>22</sup> See Chapter 13, *Knowledge of Viral Hepatitis Now*, paragraph 13.43 for discussion of the difference between these two forms of hepatitis.

**34.22** Other elements were to enter the wider picture, as noted in Chapter 33, *An Investigation into the Systems in Place for Informing the Patients about the Risks – HIV/AIDS*. The 'Tarzanoid' approach to imported US concentrates in about 1983 described by Dr Winter, reflected patients' views that Factor VIII concentrate of ('good') British origin was to be preferred over ('bad') commercial products. Dr Winter thought that patients were fully aware that they risked contracting hepatitis if they used US concentrates, as exemplified in the 1975 television programmes.

**34.23** As the threat of AIDS came to be understood in and after 1983, the selection of products for therapeutic use became more problematical.<sup>23</sup> However, while the AIDS epidemic raised awareness of the risks of transmission of virus infection generally, it has to be borne in mind that understanding of the natural history of NANB Hepatitis had not matured. It is appropriate to consider in stages the provision of information and warnings to patients about NANB Hepatitis, as knowledge increased over this complex period. The first step is to examine what was said about viral hepatitis until 1983.

**34.24** As is apparent from the discussion of practice in the three major centres in the Royal Infirmary of Edinburgh (RIE), the Glasgow Royal Infirmary (GRI) and The Royal Hospital for Sick Children, Yorkhill, Glasgow (Yorkhill), that product selection varied considerably between 1975 and 1985 and the response of individual clinicians to the perceived risks, and communication of those risks, must be considered in that context.

**34.25** The data on product use accumulated by the UKHCDO has been set out in Chapter 21, *Haemophilia Therapy – Use of Blood Products*. In Scotland, with the exception of the two major regions centred around Glasgow and Edinburgh, there was little variation and, with the exception of a high use of FEIBA<sup>24</sup> in Aberdeen for particular patients, there was little use of commercial concentrates.

**34.26** The risk of transmission of NANB Hepatitis was related to the prevalence of infection in the donor population. As discussed in Chapter 3, *Statistics*, estimating that value from time to time was difficult and there are questions whether a reliable pattern was established. However, there are some acceptable indicators of the general picture:

- There was a statistically valid basis for estimating prevalence in September 1991.
- Prevalence of NANBH infection in the donor population was negligible in 1970.
- The introduction of self-deferral policies related to HIV/AIDS in 1984 is assumed to have had an immediate impact on prevalence in 1984 and a continuing impact from then until 1991.
- While calculating actual and estimated prevalence values remains problematical, it is likely that historic peak prevalence was reached in 1983, followed by a fall in 1984 and a gradual progression to September 1991 values thereafter.

**34.27** While none of this was, or could have been, known at the time, it appears that the risk of transmission of NANB Hepatitis was greatest for those treated first in the period up to 1983, fell significantly for those treated first in 1984 and grew gradually thereafter although by September 1991 it had not quite reached the estimated 1983 levels. The 100% prevalence of infection in haemophilia patients treated with concentrates found by Dr Craske at the end of 1983, coincides with the end of the period of highest exposure to

---

<sup>23</sup> See Chapter 15, *Knowledge of Viral Hepatitis 2, 1975 to 1985*, paragraphs 15.121–15.128

<sup>24</sup> FEIBA is a 'bypassing agent' used in the treatment of patients who develop inhibitors, or antibodies, to Factor VIII concentrates.

risk. The information and advice that could have been given in the 1970s and early 1980s would not have pitched the level of risk at or even close to 100%, until the studies were published and the results validated for the UK generally and for Scotland in particular. In 1980 and 1985 respectively there were 408 and 443 Haemophilia A patients registered with Scottish centres. The vast majority of those would have been exposed to the virus by the end of 1983.

## The evidence of patients and clinicians

### *Practice in Edinburgh and south east Scotland*

#### The evidence of patients treated in Edinburgh

**34.28** The witness given the pseudonym 'Mark' was treated in Edinburgh during the late 1970s and early 1980s and was introduced to home therapy in August 1981. Professor Christopher Ludlam wrote to Mark's local doctor on 13 August reporting his advice on the new treatment regime.<sup>25</sup> Mark recalled the risk of infection with hepatitis (and HTLV-III) being discussed at his clinic appointments, usually at the end of the appointment.<sup>26</sup> He described going down to England to stay with his grandparents and being given letters which he could hand over should he need to attend a hospital in England. The letters stated that he was to be treated with local Factor VIII only.<sup>27</sup> He told the Inquiry that he thought that there was more risk associated with commercial factor products<sup>28</sup> and that receiving only Factor VIII produced from voluntary Scottish donors was safer and carried less risk than the commercial products.<sup>29</sup> At Mark's regular clinic appointments blood samples would be taken and results from previous tests discussed. Mark knew that one of the tests was for hepatitis.<sup>30</sup> Although Mark believed that he was first made aware that he had Hepatitis C in 1997, his medical records disclose that, in December 1993, Professor Ludlam's clinical assistant had a long discussion with Mark about Hepatitis C after he was found to be antibody positive. The records also state that Mark was given an information leaflet about the virus and invited to attend a joint clinic.<sup>31</sup>

**34.29** 'James', the father of the witness given the pseudonym 'Frances', was aware of the risks of transmission of Hepatitis B when he was a patient of Dr Davies. In his case, Dr Davies agreed to experiment with early prophylactic treatment and recorded at the time, in April 1971, that the patient appreciated that there was a small risk of serum hepatitis from the transfusions.<sup>32</sup> At that stage, Hepatitis B was clearly the candidate virus. In a letter to the patient dated 9 July 1982, Professor Ludlam wrote:

Following our telephone conversation I enclose 2 letters. I hope they are satisfactory for your needs. I understand that you would like some factor VIII to take with you to [America]. If supplies permit we will try and let you have 40 bottles on [date]. Please could you phone in a day or two in advance to make arrangements to collect the factor VIII. If possible, whilst in [America] could you try and avoid the use of commercial factor VIII concentrates, as they may well give you hepatitis. I would suggest that you try and obtain cryoprecipitate for

<sup>25</sup> From medical records recovered in respect of witness Mark.

<sup>26</sup> Mark – Day 32, pages 25–26

<sup>27</sup> Ibid, pages 19–22

<sup>28</sup> Ibid, page 19

<sup>29</sup> Ibid, Page 19

<sup>30</sup> See Chapter 5, *An Examination of the Effects of Infection with HIV on Patients and their Families, Including Treatment*, paragraph 5.248

<sup>31</sup> Ibid paragraph 5.263

<sup>32</sup> Ibid.

minor bleeds. Obviously, if you have a major bleed, then you will have to take the advice of the local [hospital] staff at the haemophilia centre and possibly have commercial factor VIII.<sup>33</sup>

In 1988 James, who had already been diagnosed with HIV, was referred by Professor Ludlam to Dr Niall Finlayson, Consultant Physician at the Gastrointestinal and Liver Service at the Royal Infirmary of Edinburgh as he was mildly jaundiced and his liver was enlarged.<sup>34</sup> Dr Finlayson diagnosed James with chronic liver disease and thought that this was probably caused by chronic non-A non-B Hepatitis virus from blood products. James died in 1990.

**34.30** The witness given the pseudonym 'Elaine' told the Inquiry that her husband, Brian, was warned in general terms about the risk of a hepatitis virus.<sup>35</sup> As detailed in paragraph 5.235 of Chapter 5 it is likely that Brian was unaware before his death on 8 February 1992 (as a result of HIV) that he had acquired Hepatitis C. A blood test dated 13 January 1992 confirmed that he was positive for the virus. His wife, Elaine, did not find out her husband's diagnosis with Hepatitis C until 2002 when she went to her GP for testing after receiving information from the Haemophilia Society that patients who were HIV-positive were also very likely to be infected with Hepatitis C. She was concerned that she might have contracted the virus from her husband and have suffered, untreated, from the effects of it until 2002.

**34.31** The husband of witness 'Laura', who has Haemophilia A and who transmitted Hepatitis C to Laura, was a patient of Professor Ludlam.<sup>36</sup> In 1993, he received a letter from the Haemophilia Centre in Edinburgh advising him that he might have been infected with a virus. He then attended the hospital for tests and, at a follow-up appointment, was told that he had acquired Hepatitis C. Laura's husband could not recall what was discussed at these appointments. Laura was tested by her GP for the virus, at her own instigation.

### The evidence of clinicians: the use of blood products

**34.32** In Edinburgh and the south east of Scotland, practice until 1980 reflected the policies of the Director, Dr Howard Davies. He used SNBTS material, cryoprecipitate and concentrates, almost exclusively throughout his period as Director. The pattern changed with the appointment of Dr (later Professor) Ludlam. There was a dramatic increase in the use of therapeutic products generally in 1980, and for the first time in the region that included, in 1980 and 1981, a significant amount of commercial Factor VIII concentrate. Thereafter use of commercial concentrate was relatively low, but sustained, until the late 1980s when transmission of hepatitis infection had ceased to be a material issue.

**34.33** As Professor Ludlam understood the position, Dr Davies was very open with his patients about their situations. The patients he 'inherited' in 1980 had been looked after, as he put it, 'extremely well and obsessively'.<sup>37</sup> They were very well-informed.<sup>38</sup> Professor Ludlam said that there was a lot of discussion in Dr Davies' period about how many different sorts of hepatitis viruses there might be and that Dr Davies felt that it was better for patients, if they were going to get hepatitis, to get 'the local type of hepatitis'

---

<sup>33</sup> Excerpt from medical records recovered in respect of Frances' father

<sup>34</sup> See Chapter 5, *An Examination of the Effects of Infection with HIV on Patients and their Families, Including Treatment*.

<sup>35</sup> Elaine – Day 31, page 20

<sup>36</sup> See Chapter 5, *An Examination of the Effects of Infection with HIV on Patients and their Families, Including Treatment*.

<sup>37</sup> Professor Ludlam – Day 35, page 10

<sup>38</sup> Ibid, page 11

because some of them might have immunity to it anyway having acquired the virus from the community, as happened with Hepatitis A for example.<sup>39</sup>

**34.34** Having regard only to the pattern of use, Dr Davies' period was stable. Professor Ludlam's change of practice suggests that in 1980 and 1981 there was a new focus for clinicians and patients, with the emergence of new treatments and the way in which they were used, which might have included a review of practice relating to the provision of information, advice and warnings relating to risk.

**34.35** From the record of products administered, Professor Ludlam's period in office began with fairly radical change. The use of SNBTS Factor VIII rose from 210,486 to 1,644,750 units. Use of cryoprecipitate rose from 694,190 to 1,212,470 units. In addition, 164,000 units of commercial product were administered. Over the next two or three years, most patients were put on home treatment with factor concentrates. By 1983 most patients with Haemophilia A registered with the Centre were being treated with SNBTS Factor VIII, though some received cryoprecipitate and some received commercial concentrates.<sup>40</sup>

**34.36** Cryoprecipitate was used where clinically possible to treat patients who had either never or only infrequently been treated with concentrates, particularly people with mild or moderate Haemophilia A who were unlikely to require frequent treatment. Commercial concentrates were used where clinically indicated. Haemophilia B patients were treated with SNBTS Factor IX concentrate.

#### The evidence of clinicians: information about the risk of infection with NANB Hepatitis/Hepatitis C

**34.37** Professor Ludlam provided the Inquiry with a statement on this topic.<sup>41</sup> In it he referred to a document entitled the 'Collective Response' of which he was one of the principal authors.<sup>42</sup> In his statement he said that the Collective Response reflected much of the practice in Edinburgh (and elsewhere).<sup>43</sup>

**34.38** The Collective Response was prepared by current and recent haemophilia clinicians to set out the history of haemophilia care in Scotland. Professor Gordon Lowe explained that there had been discussions amongst past and present haemophilia doctors in their regular meetings at the Central Legal Office. It had been suggested by the legal team representing haemophilia clinicians that such a document might be a useful supplement to the various individual witness statements produced for the Inquiry, especially as it could encompass the views of people with relevant knowledge who were unable, or not required, to give statements in their own right. The document was drafted mainly by Professors Lowe and Ludlam, with the assistance of Dr Brenda Gibson, the Director of Haemophilia Care at Yorkhill Hospital during the period dealt with in the Collective Response.<sup>44</sup>

**34.39** The Collective Response was written in sections. Professor Ludlam had already drafted a number of these as he had been involved in collating information over the years for various purposes. Around half of the completed document had been drafted by him from the perspective of the Edinburgh Haemophilia Centre.<sup>45</sup> Added to this was a section

<sup>39</sup> Ibid, page 10

<sup>40</sup> Chapter 21, *Haemophilia Therapy – Use of Blood Products*, Table 21.3

<sup>41</sup> Professor Ludlam's statement on Topic C5 [PEN.018.0832]

<sup>42</sup> Collective Response on behalf of past and present Haemophilia Centre staff in Scotland on Topic C5 [PEN.018.0649]

<sup>43</sup> Professor Ludlam's statement on Topic C5 [PEN.018.0832]

<sup>44</sup> Professor Lowe – Day 80, pages 2–3

<sup>45</sup> Ibid, page 3

drafted by Professor Lowe and Dr Gibson giving their perspective on equivalent practices in the west of Scotland (GRI and Yorkhill). The entire document, as it then stood,<sup>46</sup> was sent to past and present Haemophilia Directors in Inverness, Dundee and Aberdeen to give them the opportunity to comment on its contents.<sup>47</sup> In the view of Professor Lowe, the revisions to the Collective Response at this stage were minor and there were 'relatively few changes' after he, Professor Ludlam and Dr Gibson had completed their drafts.<sup>48</sup> At the conclusion of the Collective Response there was a list of doctors and nurses who 'endorsed' its contents.<sup>49</sup> Professor Lowe ran through this list in oral evidence and gave a brief explanation of each individual's role.<sup>50</sup>

**34.40** While the Collective Response was well-intentioned, not much weight could be given to it as evidence. Whether there was a general practice in Scotland is a question for the Inquiry, and not for the haemophilia clinicians, or for a sub-group of them. As the evidence was to unfold, it became clear that there was considerable variation in practice. However, Professor Ludlam was entitled to adopt the statement as reflecting practice in Edinburgh. He clearly wrote much of the document on the basis of his personal experience.

**34.41** The Collective Response noted a problem that was common in Scotland and is accepted as accurate in this respect. Most patients with haemophilia who acquired NANB Hepatitis infection would have done so at the time of their first treatment with pooled factor concentrates or during their first several treatments with cryoprecipitate or fresh frozen plasma in the period following diagnosis. Many patients received their first treatment or treatments at a hospital that did not have a haemophilia centre.<sup>51</sup> In the south east of Scotland patients were treated at a number of district hospitals and in small hospitals in Edinburgh.<sup>52</sup> Local physicians may not have referred patients to haemophilia centres for many years and, when they did so, their referral letters would not usually state what information had been given to patients prior to their first treatment. In many cases, the information given in haemophilia centres would therefore have been given after the patient's first exposure to, and infection with, NANB Hepatitis/HCV.

**34.42** In Edinburgh, haemophilia care was provided by a multi-disciplinary team that, from 1982, included a Haemophilia Sister who played a major part in interacting with patients on a day-to-day basis, especially in the early 1980s when very many patients still had to attend hospital in Edinburgh for treatment of acute bleeds.<sup>53</sup> Professor Ludlam said:

It was our policy to inform patients (and parents of children) of all the risks of haemophilia as well as its treatment, including hepatitis because virtually all recipients of blood products were likely to be at risk or suffer from, this complication .... This would have included the complications of haemophilia itself and of its treatment. Discussion of hepatitis, like inhibitors, would be important topics. Information leaflets and contact with the Haemophilia Society was encouraged.<sup>54</sup>

<sup>46</sup> Professor Lowe thought that at this stage of drafting the contents of the Collective Response were divided equally between Edinburgh and Glasgow opinion; see Day 80, page 4

<sup>47</sup> Professor Lowe – Day 80, page 10

<sup>48</sup> Ibid, pages 4–5

<sup>49</sup> Collective Response on behalf of past and present Haemophilia Centre staff in Scotland on Topic C5 [PEN.018.0649] at 0666

<sup>50</sup> Professor Lowe – Day 80, pages 6–7

<sup>51</sup> Collective Response on behalf of past and present Haemophilia Centre staff in Scotland on Topic C5 [PEN.018.0649] at 0650

<sup>52</sup> Professor Ludlam's statement on Topic C5 [PEN.018.0832] at 0833

<sup>53</sup> Ibid [PEN.018.0832] at 0833

<sup>54</sup> Ibid [PEN.018.0832] at 0833–34

**34.43** The Collective Response stated:

The risks of haemophilia and of its treatment, including hepatitis, were well explained by staff and regularly reinforced by haemophilia nurse specialists and doctors.

....

Such education started when patients were first referred to a Haemophilia Centre, and continued thereafter, e.g. at emergency attendance for treatment of acute bleeding episodes, clinic reviews, and enquiries by telephone, in writing or in person.<sup>55</sup>

**34.44** From 1983 it was known that patients receiving clotting factor concentrates were at high risk of NANB Hepatitis infection.<sup>56</sup> The UKHCDO recommended the use of cryoprecipitate for patients with Factor VIII deficiencies and no, or limited, previous exposure to concentrates.<sup>57</sup> Professor Ludlam said that in the early 1980s he would have explained that he was administering cryoprecipitate to children to try to reduce the risk of contracting hepatitis, and avoiding the use of commercial concentrates because of the perceived increased risk of hepatitis in comparison to NHS concentrates.<sup>58</sup>

**34.45** Professor Ludlam said that it was well known amongst patients in the early 1980s that there was a risk of hepatitis from treatment with factor concentrates and cryoprecipitate. Like others, he observed that in the 1970s and 1980s there was literature available from the Haemophilia Society that commented on the risks. Patients on home treatment or their parents signed consent forms in which the risk of infection was specifically mentioned.<sup>59</sup> The consent form was, however, very general in its terms, referring only to 'the risk of an allergic reaction ... and ... the problems associated with any transfusion, such as the risk of introducing infection or air into my vein'.<sup>60</sup>

**34.46** Although Professor Ludlam said that he discussed the risk of hepatitis with some patients (if a patient became jaundiced then he discussed that with them and explained how it would have arisen, for example), he was unable to recall specifically whether or not he routinely discussed this issue with patients on an individual basis in the early 1980s.<sup>61</sup> While members of the multidisciplinary team may have implemented the general policy regarding the provision of information, it appears that Professor Ludlam himself would not have done so as a matter of course. He said that a lot of information provided to people with chronic disorders who are seen very frequently, is done on a 'need to know' basis as the need arises in their clinical care.<sup>62</sup> It seems that his practice was to give information as the occasion demanded, rather than as an aspect of programmed communication of information. He said that he probably would not himself have raised with his patients the topic of the different kinds of treatment that they could be prescribed, in the context of the emerging risk of NANB Hepatitis.<sup>63</sup>

---

<sup>55</sup> Collective Response on behalf of past and present Haemophilia Centre staff in Scotland on Topic C5 [PEN.018.0649] at 0651

<sup>56</sup> See Chapter 15, *Knowledge of Viral Hepatitis 2 – 1975 to 1985*, paragraph 15.122

<sup>57</sup> Collective Response on behalf of past and present Haemophilia Centre staff in Scotland on Topic C5 [PEN.018.0649] at 0654

<sup>58</sup> Professor Ludlam's statement on Topic C5 [PEN.018.0832] at 0834

<sup>59</sup> Note of a Meeting between Professor Ludlam and the Penrose Inquiry legal team [PEN.012.0774]

<sup>60</sup> Day 35, pages 14–16

<sup>61</sup> Note of a Meeting between Professor Ludlam and the Penrose Inquiry legal team [PEN.012.0774]

<sup>62</sup> Day 35, pages 11–12

<sup>63</sup> Day 39, pages 21–22

**34.47** Professor Ludlam explained that when patients first attended the Haemophilia Centre – usually having been referred by another hospital – it could be a stressful time, with the parents of children trying to assimilate a great deal of new information while also dealing with an upset child. He commented that these circumstances would not be conducive to the parents remembering everything that they had been told at that first attendance. These sessions were therefore followed up at an early stage by giving patients, and their parents, booklets about haemophilia, including information about hepatitis.<sup>64</sup> Patients and their families were also encouraged to make contact with the Haemophilia Society.<sup>65</sup>

**34.48** The impression of a continuous educational process as described in the Collective Response, making use of every contact to provide information, was not sustained in oral evidence. Advice was given occasionally rather than universally, and the oral evidence of patients referred to above is consistent with Professor Ludlam’s description of his practice: information was provided as he thought the occasion demanded, rather than in a structured and regular manner and this appears to have continued throughout the 1980s and into the 1990s.

**34.49** Much of the circumstantial detail provided by Professor Ludlam supports this approach. Many of the patients had male relatives with haemophilia and they, or their parents, were aware of the risks of hepatitis from information circulating in the family. Severely affected boys on home treatment and their mothers were vaccinated against Hepatitis B and, when it became available in 1992, Hepatitis A. They were educated on the risk of hepatitis, and how to handle needle-stick injuries and blood spills. The patients had regular four-monthly liver function tests before a test for HCV became available.<sup>66</sup> The provision of information as the occasion demanded was clearly proportionate to need.

**34.50** Professor Ludlam told the Inquiry that, because he was so keen for Edinburgh patients not to be exposed to commercial concentrates if possible, he gave them a small card to carry when travelling which said: ‘this patient has only been treated with NHS concentrate. If possible please treat with cryoprecipitate or NHS concentrate’.<sup>67</sup> It was explained to them that the reason for this measure was to minimise their risk of contracting hepatitis from commercial concentrate. As it transpired, there was no material difference in the risk of acquiring NANB Hepatitis between UK public sector products and commercial US products, but this was not appreciated until the end of 1983. However, during 1982 and 1983, this ‘NHS concentrate only’ policy may have protected some NHS patients from acquiring HIV from commercial product.

**34.51** Both medical and nursing staff took precautions to prevent infection during treatment. They wore disposable gloves and carefully disposed of needles, syringes, intravenous lines and blood or blood product packs.<sup>68</sup> This was obvious to patients.

**34.52** Professor Ludlam said that his patients knew that he had an interest in using liver function tests to monitor the risk of hepatitis, and that test results would often be discussed with patients when they came back for review appointments.<sup>69</sup> He also commented that

---

<sup>64</sup> Professor Ludlam’s statement on Topic C5 [PEN.018.0832] at 0834

<sup>65</sup> Ibid [PEN.018.0832] at 0833–34

<sup>66</sup> Collective Response on behalf of past and present Haemophilia Centre staff in Scotland on Topic C5 [PEN.018.0649] at 0652

<sup>67</sup> Professor Ludlam’s statement on Topic C5 [PEN.018.0832] at 0838

<sup>68</sup> Professor Lowe’s statement on Topic C5 [PEN.018.0839] at 0839

<sup>69</sup> Day 35, page 9



some patients were generous enough to make themselves available for teaching students. Some patients were in the hospital quite frequently early in the reference period, because of the limited treatment that was available, and they often allowed him to bring medical students to see them. The doctors would have quite full discussions about the risks of treatment. He thought that his views would have been known to and accepted by the patients.<sup>70</sup>

**34.53** Professor Ludlam told the Inquiry that haemophilia patients in Edinburgh were kept up to date with developments during the 1980s when it came to be realised that NANB Hepatitis was more progressive than previously thought, and also later following the identification of HCV and the development of specific tests for the virus.<sup>71</sup> He said that patients and their families were aware of concerns about hepatitis because of frequent discussions at review clinics between clinicians and patients about the results of their liver function tests. He also thought patients were aware that the Haemophilia Centre was retaining blood samples for future virological testing.

**34.54** A few documents reflected this understanding. On 27 January 1986, Professor Ludlam wrote to patients enrolled at the Edinburgh centre.<sup>72</sup> The letter stated that Factor VIII and Factor IX might cause hepatitis in individuals with haemophilia ‘as you will know’, and was very occasionally transmitted to other members of the family. He wanted to investigate the position in local families. The letter noted that blood samples provided by family members were held in storage and asked patients to request the approval of the individuals in question for the use of these samples in the proposed study.

**34.55** Following the publication of a paper by Hoofnagle and others in 1986,<sup>73</sup> which established that Interferon could be successfully used to treat NANB Hepatitis, patients were informed of this development and studies were commenced to assess the use of Interferon.<sup>74</sup> As a result, from 1988 a few patients in Edinburgh with symptoms of NANB Hepatitis received treatment using Interferon.<sup>75</sup>

**34.56** From 1988 patients not previously exposed to concentrates were given information on virally-inactivated SNBTS concentrates and invited to participate in a clinical trial.<sup>76</sup>

**34.57** In the early 1990s an HCV patient information sheet and investigation check-list was developed for patients whose blood tests showed that they were HCV-positive.<sup>77</sup> The document, entitled ‘Hepatitis C Liver Disease and its Treatment’ stated that the patient’s blood results showed that they had HCV. It stated that the virus may cause inflammation of the liver, ‘known as hepatitis’, and that in some individuals the inflammation may become chronic, giving rise to long-term damage which may in some cases be severe. The document then set out the investigations required to determine the patient’s suitability for Interferon treatment and described the treatment and possible side-effects. It commented on the risk of sexual transmission and offered consultation to the sexual partners of infected individuals. It also contained advice on the use of alcohol.

<sup>70</sup> Day 39, page 21

<sup>71</sup> Professor Ludlam’s statement on Topic C5 [PEN.018.0832] at 0836–37

<sup>72</sup> Letter to patients, dated 27 January 1986 [PEN.018.0787]

<sup>73</sup> Hoofnagle et al, ‘Treatment of Chronic Non-A, Non-B Hepatitis with recombinant human alpha interferon’, *The New England Journal of Medicine*; 1986, 315:1575 [LIT.001.3806]

<sup>74</sup> Professor Ludlam’s statement on Topic C5 [PEN.018.0832] at 0837

<sup>75</sup> Professor Ludlam’s response to questions from the Inquiry on information to patients [PEN.018.1246] at 1247

<sup>76</sup> Collective Response on behalf of past and present Haemophilia Centre staff in Scotland on Topic C5 [PEN.018.0649] at 0654

<sup>77</sup> Patient information sheet [PEN.018.0807]

**34.58** Professor Ludlam said:

The information given to patients with non-A non-B hepatitis was continually updated with the developments in knowledge and practice. For example in the late 1970s and early 1980s it was a puzzling condition of uncertain aetiology but not known to be serious. At this stage there was no evidence that it might be sexually transmitted. It became clearer in the mid-1980s that it was a potentially serious and progressive condition although it has taken many further years of study to begin to obtain a reasonably reliable estimate of the risk of cirrhosis, liver failure and hepatoma development. Once it became clear that it was progressive and after Hoofnagle's paper in 1986, patients were informed of this and we consequently initiated studies to use interferon treatment.<sup>78</sup>

**34.59** The patient information sheet illustrated a further development in this approach.

**34.60** In general terms, Professor Ludlam thought there had been 'a very open policy of giving patients the most up to date information about hepatitis, their individual results and our assessment of their clinical situation'.<sup>79</sup>

**The evidence of clinicians: testing**

**34.61** Professor Ludlam explained that the Edinburgh Haemophilia Centre carried out 'anonymous' testing of stored samples when an HCV test became available. This was an early, insensitive test. The results revealed that 85% of those tested were HCV antibody-positive.<sup>80</sup> He published a small study of this group in a letter to *The Lancet* in September 1989.<sup>81</sup> Samples from 61 patients were tested: 48 had received non-heated factor concentrates before 1985 and 41 of these tested positive for anti-HCV. It is implicit in the report that the treatment histories of all 61 patients were known.

**34.62** Between 1990 and 1992 Professor Ludlam and colleagues assessed a series of different antibody detection methods. A paper submitted for publication in October 1991 reported a study of tests on stored sera from 85 randomly chosen haemophilia patients attending the Edinburgh Centre.<sup>82</sup> Of 78 patients previously exposed to non-virally-inactivated concentrates, 68 were confirmed positive by Chiron RIBA. Of the remaining 10, some were positive on some of the other tests applied. In addition, a virology colleague, Professor Simmonds, developed a polymerase chain reaction (PCR) assay to detect HCV viral RNA.<sup>83</sup> A study using this assay was carried out with 21 haemophilia patients and 27 intravenous drug users. From the results found and reported, Professor Ludlam said that it was clear that the first generation of the antibody test did not have sufficient sensitivity to 'identify all previously or currently HCV-infected individuals'.<sup>84</sup>

---

<sup>78</sup> Professor Ludlam's statement on Topic C5 [PEN.018.0832] at 0837

<sup>79</sup> Ibid [PEN.018.0832] at 0837

<sup>80</sup> Ibid [PEN.018.0832] at 0835

<sup>81</sup> Ludlam et al, 'Antibodies to Hepatitis C virus in haemophilia', *The Lancet*; 2 September 1989; ii, 560–561 [LIT.001.3859]

<sup>82</sup> Watson et al, 'Use of several second generation serological assays to determine the true prevalence of Hepatitis C virus infection in haemophiliacs treated with non-virus inactivated factor VIII and IX concentrates', *British Journal of Haematology*, 1992; 80:514–518 [SNB.004.6000]

<sup>83</sup> Simmonds et al, 'Hepatitis C quantification and sequencing in blood products haemophiliacs, and drug users', *The Lancet*, 1990; 336:1439–72 [LIT.001.0287]

<sup>84</sup> Professor Ludlam's statement on Topic C5 [PEN.018.0832] at 0835

**34.63** By 1992 ‘reliable and sensitive’ assays for detection of the Hepatitis C antibody and virus were available. In his statement, Professor Ludlam said that ‘it was at this point that we felt confident to provide the results of these tests to patients’. It seems, therefore, that patients were tested for research purposes during the period 1989–92 but not given the results of the tests.<sup>85</sup>

**34.64** The process adopted for the first round of testing (in 1989) involved the selection of three sets of patients, grouped according to their treatment histories. The samples were labelled only according to these groupings and, when the results were received, the patients could not have been given their individual results. The use of an anonymous process was due, Professor Ludlam said, to his concerns about the reliability of the test.

**34.65** He explained that in 1992 in all cases, including cases in which stored samples had been tested during the initial studies to validate the techniques, a fresh sample was sought from the patient after ‘explanation and consent’:

The patients being told that we considered that we had a sensitive and specific test for both the antibody and virus which was responsible for the majority of cases of non-A non-B hepatitis. The result would be essential in deciding who might benefit from anti-viral therapy, e.g., it might be appropriate to offer therapy to PCR positive, rather than PCR negative, individuals. The patient would be given the result at the next clinic visit (or earlier if specifically requested). In most instances there was no need for the patient to receive the result urgently. The HCV tests were offered to all patients who we identified as having been exposed to blood or blood products.<sup>86</sup>

### **The evidence of clinicians: communicating test results to patients**

**34.66** Professor Ludlam stated that the information given to patients with non-A non-B Hepatitis was continually updated with the developments in knowledge and practice. He stated that once it became clear in the mid-1980s that the disease was progressive, patients were informed of this and studies were initiated on the use of Interferon treatment.<sup>87</sup> A Hepatitis C Patient Information sheet and an Investigation Checklist were developed in the early 1990s. Leaflets from the Haemophilia Society and the British Liver Trust were readily available in the Haemophilia Centre.<sup>88</sup>

### ***The practice at the Glasgow Royal Infirmary***

#### **The evidence of a patient who was treated in the Glasgow Royal Infirmary**

**34.67** David was treated with Factor IX in both Yorkhill and the GRI. He said he remembered Hepatitis A being mentioned to him during routine screening for this virus in 1984, but stated that he was not warned of the risk of infection with any other virus from his treatment for haemophilia.<sup>89</sup> His medical records showed that, in 1983 while he was being treated at Glasgow Royal Infirmary, David was found to have abnormal liver function test results. NANB Hepatitis was thought to be the cause of these results. David has no recollection of these test results being mentioned to him. David found out from Professor Lowe in 1991 that he had tested positive for the antibody to the Hepatitis C virus.<sup>90</sup> He

---

<sup>85</sup> Ibid [PEN.018.0832] at 0835

<sup>86</sup> Ibid [PEN.018.0832] at 0835–36

<sup>87</sup> Ibid [PEN.018.0832] at 0837

<sup>88</sup> Ibid [PEN.018.0832] at 0838

<sup>89</sup> Paragraph 5.171 of Chapter 5

<sup>90</sup> Paragraph 5.186 of Chapter 5

said that Professor Lowe did not tell him much about the severity of the virus, its health implications or the risk of secondary infection. Professor Lowe told him that they would continue to monitor his liver function at his routine haemophilia clinic appointments.

### The evidence of clinicians: the use of blood products and information about the risk of infection with NANB Hepatitis/Hepatitis C

**34.68** For most of the reference period, Professor Charles Forbes was the Haemophilia Director at the GRI and he was in control of policy and practice in the Haemophilia Centre. Professor Lowe joined the Infirmiry staff in November 1974. He was a Registrar and Senior Registrar from 1976 to 1985<sup>91</sup> and then Co-director of the Centre from 1988 to 2009.<sup>92</sup>

**34.69** Professor Forbes said that in the 1970s to early 1980s, when, as he remembered it, the usual policy for haemophilia bleeding was the use of pooled cryoprecipitate, clinicians were all aware of the potential problems associated with giving material of human blood origin to individuals. They monitored patients for changes in liver function, using what at that time were probably the best and only available tests.<sup>93</sup> Changes in liver enzymes were a good indicator of infection.<sup>94</sup>

**34.70** Professor Forbes said that it would have been very reasonable to have discussed with patients the risks of contracting hepatitis, and that would have been the Centre's policy at that time. He said that patients at the GRI Centre would certainly have been told that there was a possibility of hepatitis resulting from the use of concentrates or cryoprecipitate, and that they would be followed up after receiving blood products of any type. It is worth noting that in an article in the Haemophilia Society Bulletin 1 of 1980, Professor Forbes mentioned Hepatitis B as a 'serious side effect' of treatment with concentrates, but made no mention of NANB Hepatitis.<sup>95</sup>

**34.71** Professor Lowe gave both written and oral evidence to the Inquiry on this topic and was one of the principal authors of the Collective Response. He said that he had discussed his recollection of events for the purposes of that document with Professor Ludlam and Dr Gibson. He agreed that it was possible his recollection of events had been influenced by other people's recall of the same events but said that his own statement,<sup>96</sup> submitted as a separate document, reflected his personal experience and was probably a better reflection of his own recollection of events concerning NANB Hepatitis and HCV, than his contribution to the Collective Response.<sup>97</sup> That is clearly correct, and it is inappropriate generally to rely on the Collective Response in relation to practice at the GRI.

**34.72** One point already mentioned is material, however. The Collective Response emphasised that the problem arising from treatment of patients at local hospitals, before reference to haemophilia centres, was particularly significant in the west of Scotland.<sup>98</sup> In view of the territorial extent of the region, that clearly must have been the case.

<sup>91</sup> Professor Lowe, in oral evidence, corrected a typographical error in his statement. He was a 'trainee' doctor from 1976 to the end of 1985, and not 1987. He became a consultant in 1985. Prior to that he was a Registrar and then a Senior Registrar and medically qualified to treat patients. Day 80, page 15

<sup>92</sup> Professor Lowe's statement on Topic C5 [PEN.018.0839] at 0839

<sup>93</sup> As stated in paragraphs 21.313–21.320 of Chapter 21, *Haemophilia Therapy – Use of Blood Products*. Professor Forbes' recollection about the pattern of use of therapeutic materials did not accord with the UKHCDO statistics on the administration of blood products at the GRI.

<sup>94</sup> Professor Forbes' statement on information given to patients [PEN.012.0411]

<sup>95</sup> Forbes, 'Innovations for haemophiliacs', *The Bulletin*, 1980; 1, The Haemophilia Society [PEN.018.0676]

<sup>96</sup> Professor Lowe's statement on Topic C5 [PEN.018.0839]

<sup>97</sup> Professor Lowe – Day 80, pages 9–10

<sup>98</sup> Collective Response on behalf of past and present Haemophilia Centre staff in Scotland on Topic C5 [PEN.018.0649] at 0650

**34.73** Professor Lowe told the Inquiry that, when he began working in the University Medical Unit at the GRI at the end of 1974, the first thing he noticed was big red signs labelled 'Hepatitis'. Every room in the Haemophilia Centre had such a sign. From his first day at the unit he observed that patients were being tested for Hepatitis B and that liver function tests were being carried out. There was an emphasis right from the start on reminding patients to be careful with needles and blood and on the disposal of all equipment.<sup>99</sup>

**34.74** Management of haemophilia in the mid-1970s included routine monitoring (usually annually at clinic reviews) for complications of the disease and of its treatment (including hepatitis). Routine blood tests included:

- Full blood count including haemoglobin, differential white cell count (an assessment of the different types of white cells) and platelet count.
- Assessment of blood chemistry including liver function tests – to assess possible presence and degree of hepatitis.
- Assessment of clotting factor function – for example, Factor VIII level and the presence of any Factor VIII inhibitor.
- Taking samples for virology, specifically for Hepatitis B antibody and antigen.<sup>100</sup>

**34.75** Professor Lowe recalled sitting in on haemophilia review clinics listening to the Consultants telling patients that they were going to take blood tests to check for hepatitis, which was a risk associated with blood product therapy. He said that the majority of patients who attended the Haemophilia Centre had been treated since childhood and knew what the tests were for and that none of it was a surprise to patients.<sup>101</sup> In addition, the Haemophilia Society issued a lot of booklets and pamphlets over the years which included information on the risks of hepatitis.<sup>102</sup>

**34.76** Professor Lowe gave evidence that haemophilia patients (and, in the case of children, their families) at the GRI were routinely advised by medical and nursing staff of the risk of infection by the blood-borne hepatitis viruses (HBV and NANB Hepatitis), both before and after their treatment with blood products. Furthermore, he thought that the risk of infection would have been apparent to patients from several of the routine practices at the GRI:

- Both medical and nursing staff took obvious precautions to prevent infection during treatment. They would wear disposable gloves and carefully dispose of needles, syringes, intravenous lines and blood or blood product packs.<sup>103</sup>
- Patients or their parents were provided with, or given access to, educational and information leaflets, such as those issued by the UK Haemophilia Society.<sup>104</sup> Professor Lowe considered that the Haemophilia Society was generally well-informed and was aware of the risks of hepatitis as knowledge developed. The Society issued regular

---

<sup>99</sup> Professor Lowe – Day 39, pages 160–1

<sup>100</sup> Collective Response on behalf of past and present Haemophilia Centre staff in Scotland on Topic C5 [PEN.018.0649] at 0660

<sup>101</sup> Professor Lowe – Day 39, page 163. The patients at the Royal Infirmary were usually older children and adults who had previously been patients at Yorkhill during their earlier years.

<sup>102</sup> Professor Lowe – Day 39, page 164

<sup>103</sup> Professor Lowe's statement on Topic C5 [PEN.018.0839] at 0839

<sup>104</sup> Ibid [PEN.018.0839] at 0839

information leaflets and other publications to its members. It also produced other, more occasional, publications for patients and their relatives and these were displayed in the waiting area and treatment rooms of the Haemophilia Centre at the GRI.<sup>105</sup>

- Patients, or their parents, who requested further information about NHS or commercial clotting factor concentrates were given the information leaflets provided along with the concentrates themselves. These package inserts included details on the possibility that they might transmit hepatitis.<sup>106</sup>
- A vaccination against HBV was introduced in the UK in 1985 and was offered to patients who lacked natural immunity. Patients were told that the vaccination was protective against HBV only, and not against threats from other hepatitis viruses, such as NANB Hepatitis. Similar advice was given when the HAV vaccine was offered to patients from 1992. The parents of children with haemophilia were also offered vaccinations and advised on the risks of hepatitis from blood spills and needle-stick injuries.<sup>107</sup>
- A journal article published in 1983 made it clear that patients treated with clotting factor concentrates had a high risk of developing NANB Hepatitis.<sup>108</sup> As a result the UKHCDO recommended that cryoprecipitate be preferred to clotting factor concentrate for patients with mild haemophilia who had no, or limited previous exposure,<sup>109</sup> before 1988.<sup>110</sup>
- From 1988, patients who had not been previously treated with concentrates were given information on, and invited to participate in, a clinical trial of virally-inactivated SNBTS clotting factor concentrates, to demonstrate that it would not infect them with NANB Hepatitis.<sup>111</sup>
- When recombinant factor concentrates (artificially synthesised clotting factors free from the risk of transmission of viruses from blood donors) were licensed in the UK in 1995, haemophilia directors ensured they were made available for treatment of patients with haemophilia in Scotland. The first priority was patients not previously exposed to clotting factor concentrates.<sup>112</sup>

**34.77** Professor Lowe stated that it was considered important to regularly monitor liver function and keep patients abreast of changing information about the disease.<sup>113</sup> The message to patients at the GRI prior to 1985 about how concerned they should be about this condition was:

[W]e would say that, "Non-A non-B Hepatitis is a concern. We need to monitor you for it. We will explain what we are doing collectively to minimise the risks through safer products and immunisation, and regular medical review is important and it gives us a chance to continue to update you on the significance."<sup>114</sup>

<sup>105</sup> Ibid [PEN.018.0839] at 0842

<sup>106</sup> Ibid [PEN.018.0839] at 0839. See, however, paragraphs 34.163–34.169 below.

<sup>107</sup> Professor Lowe's statement on Topic C5 [PEN.018.0839] at 0840

<sup>108</sup> Fletcher et al, 'Non-A non-B hepatitis after transfusion of factor VIII in infrequently treated patients', *British Medical Journal*, 1983; 287:1754 [LIT.001.0239]

<sup>109</sup> Professor Lowe's statement on Topic C5 [PEN.018.0839] at 0840; Letter from Professor Bloom and Dr Rizza to Haemophilia Centre Directors, dated 24 June 1983 [SGH.002.2175] and UKHCDO AIDS Advisory Document, dated 14 December 1984 [SGF.001.2388]

<sup>110</sup> Professor Lowe's statement on Topic C5 [PEN.018.0839] at 0840; *Recommendations on choice of therapeutic products...* UKHCDO, 16 May 1988 [SNB.001.5606]

<sup>111</sup> Professor Lowe's statement on Topic C5 [PEN.018.0839] at 0840

<sup>112</sup> Ibid [PEN.018.0839] at 0840

<sup>113</sup> Professor Lowe – Day 80, pages 21–22

<sup>114</sup> Ibid, page 23

**34.78** From 1985 it was known that the asymptomatic stage of NANB Hepatitis infection could progress to serious liver disease and this was communicated to patients or their parents at their clinic reviews.<sup>115</sup> Professor Lowe recalled that by this time every haemophilia centre in the UK was seeing one or two patients who had clear clinical evidence of liver disease. There was a hepatitis working group monitoring these studies and passing on reports to doctors and to the Haemophilia Society.

**34.79** The Haemophilia Centre at the GRI was amongst those seeing a small number of patients with clinical liver disease and all patients in receipt of blood products were being more closely monitored as a result. Previously, patients with cirrhosis seen in the haemophilia unit at the GRI had been those infected with Hepatitis B or who were heavy alcohol users; in 1987 the centre in which Professor Lowe worked saw its first patient with early cirrhosis caused by NANB Hepatitis.

**34.80** The message to patients at this point was similar to that given before 1985; but they were now advised that it appeared that a number of patients might progress to serious liver disease.<sup>116</sup> When talking to patients in his clinic, Professor Lowe found it helpful to give them a rough percentage of people who might expect to be affected. He stated that between 1985 and 1987 he would have advised all of his patients that those with NANB Hepatitis had a 25% risk<sup>117</sup> of progressing to cirrhosis as a result of their infection.<sup>118</sup>

**34.81** At routine clinic sessions, Professor Lowe would enquire about a patient's recent health and ask if they had noticed any change in their well-being. Any incidence of jaundice would naturally be of concern but Professor Lowe would also routinely carry out a physical examination of his patients' abdomens to feel the condition of their liver and spleen. Blood samples would be taken for liver function tests and, if the results from a previous test had been abnormal, he would discuss the likely cause of that abnormality with the patient at their next review. In the absence of any other explanation, he would advise that the most likely diagnosis was NANB Hepatitis, which he would then discuss with the patient. Professor Lowe also said that, even for patients with normal liver function test results, the state of knowledge of the severity of NANB Hepatitis, as understood at that time, would be communicated to everyone at clinic reviews.<sup>119</sup> From 1985 patients (or their parents) were also told that it was hoped that concentrates could be successfully virally inactivated in the future and that this would reduce or remove the risk of transmission of NANB Hepatitis.<sup>120</sup>

**34.82** Professor Lowe recalled that a few years later, around 1988–89, patients reviewed in his clinic were told the estimation of risk of cirrhosis following NANB Hepatitis infection had increased from 25% to 33%. He was of the view that his medical colleagues in the Haemophilia Unit at the GRI would be passing on the same information to patients.<sup>121</sup> There would be regular meetings within the haemophilia centre to ensure the clinicians and nurses<sup>122</sup> shared information, and were able to pass consistent advice to their

---

<sup>115</sup> Professor Lowe's statement on Topic C5 [PEN.018.0839] at 0841; Day 80, pages 17-18

<sup>116</sup> Professor Lowe – Day 80, page 26

<sup>117</sup> This percentage figure was taken, by Professor Lowe, from liver biopsy studies.

<sup>118</sup> Professor Lowe – Day 80, pages 28–29

<sup>119</sup> Professor Lowe – Day 80, page 20

<sup>120</sup> Professor Lowe's statement on Topic C5 [PEN.018.0839] at 0841

<sup>121</sup> Professor Lowe – Day 80, pages 31–32

<sup>122</sup> Ibid, page 48

patients.<sup>123</sup> It was helpful to the Centre that Dr Forbes, their Director, was at that time also the Chairman of the UKHCDO. Professor Lowe was asked what the Centre's policy about hepatitis was at this time. He explained that it was:

To tell patients about it and to explain ... that all patients should be asked about symptoms of liver disease, examined for liver disease, have blood tests taken for liver disease and to explain to them often at the time that you were discussing blood tests, you would say, "I want to check you out for Hepatitis B and non-A non-B, and the current situation with these problems in haemophiliacs in the United Kingdom is this, and this is why it's important that we do this", and, "Keep coming to the clinics and we will keep monitoring you for the complications".<sup>124</sup>

**34.83** Professor Lowe also recalled that it was around this time that the risk of progression to liver cancer in those with NANB Hepatitis was becoming clearer, and that this was also discussed with patients at review appointments:

Yes, I think it would be about that time that liver cancer was being reported, associated with Hepatitis C, in the early 1990s.

So we would talk about cirrhosis, what was cirrhosis and what would the symptoms be, and what would the prognosis be for somebody who developed cirrhosis and what treatment would be given, and then to say that particularly patients who have developed cirrhosis – the liver as part of a cirrhotic process, it's prone to forming tumours .... "We will carry on examining you, doing the blood tests, and we may start doing liver scans but .... Once we get the tests to see if you carry the virus or not, if you do carry the virus, we will then be referring you to [the] liver clinic for more detailed information from the liver doctors, the experts ...." As we had already done for HIV a few years previously.

We said, "We will continue to follow you up and give you whatever advice and support we can as haemophilia doctors and nurses, but it's time for the specialists to start taking over your liver disease and they will give you full information about the up-to-date prognosis, estimates and further tests, like genotype and scanning. And the good news is that we have antiviral treatment starting to be developed .... The hope is that it will work in some people with Hepatitis C."

"So again, this is part of a journey, where we are all learning about the virus, we are all learning about the tests, the prognosis and the treatment, and we will keep you informed as much as we can."<sup>125</sup>

**34.84** Professor Lowe stated that before the identification of HCV and the introduction of a specific test at the end of 1991, informed advice on the possible sexual transmission of NANB Hepatitis could not be given as not enough was known about the disease.<sup>126</sup> After that date, and as evidence of low rates of sexual transmission became clearer, the risk of sexual transmission of HCV was discussed with infected patients at their routine appointments at the GRI.<sup>127</sup>

---

<sup>123</sup> Ibid, page 36

<sup>124</sup> Ibid, pages 37–38.

<sup>125</sup> Ibid, Pages 104–105

<sup>126</sup> Professor Lowe's statement on Topic C5 [PEN.018.0839] at 0847

<sup>127</sup> Ibid [PEN.018.0839] at 0844



**34.85** In oral evidence, Professor Lowe agreed that the best method for a clinician to give information to a patient about treatment and prognosis was through direct, face-to-face communication. However, he noted research which had demonstrated that patients often do not take in all of the information they are given in an interview with their doctor or nurse and suggested that direct, face-to-face communication could be usefully supported by information leaflets.<sup>128</sup>

**34.86** Professor Lowe added that any full, written protocol for use by doctors in haemophilia reviews would have been difficult to formulate. It would have had to be ‘a pretty long-winded protocol and ... so general as to probably be counter productive’. He thought that the best way to cover the wide range of issues that arose in a haemophilia review appointment was to lead by example, with real patients, showing the range of subjects that might be covered, and how to interact with patients.<sup>129</sup>

### The evidence of clinicians: testing

**34.87** Professor Lowe could not recall if there were written policies or protocols relating to hepatitis testing in place at the Glasgow Haemophilia Centre in the 1970s and 1980s. He could, however, recall that the GRI produced written policies from around the 1990s, following the introduction of a specific screening test for HCV, which included HCV testing as part of liver function monitoring, along with vaccinations for Hepatitis A and B.<sup>130</sup> Following advice from the UKHCDO, from late 1991 the co-directors of the GRI Haemophilia Centre added HCV testing to routine surveillance for liver disease in haemophilia patients.<sup>131</sup> By then, second generation test kits of improved specificity and sensitivity were available from the Regional Virus Laboratory at Ruchill Hospital, Glasgow.

**34.88** In the period 1990–95, patients were asked to give fresh blood samples at their clinic appointments. Professor Lowe and his colleagues would explain that, in addition to the routine blood tests patients were aware of, there was now a test for the recently discovered Hepatitis C virus. He would add further that, now that the virus had been discovered, it was possible that anti-viral treatment might become available for the patients found to carry the virus.<sup>132</sup>

**34.89** Professor Lowe was asked to consider the report written for the Inquiry by Dr Hay. He considered that Dr Hay’s description of his practice as a haemophilia clinician dealing with patients with NANB Hepatitis/HCV infection was entirely in keeping with both his own practice in the GRI, and practice in haemophilia centres in Scotland, in the early 1990s generally. As he understood it, ‘practice was to inform patients about hepatitis C tests and outline what was known about HCV; and to inform the patient and their general practitioner of the results’. This had been the practice for HBV as knowledge about that condition increased and it was the opinion of haemophilia directors in the early 1990s that the practice should continue when dealing with patients with HCV.<sup>133</sup>

**34.90** Professor Lowe also agreed with Dr Hay’s view that there could be no useful comparison between procedures for HIV testing after 1985, and HCV testing in the 1990s, and expressed his disagreement with Professor Nathanson’s view (as he understood it when

---

<sup>128</sup> Professor Lowe – Day 80, page 44

<sup>129</sup> Ibid, pages 72–73

<sup>130</sup> Professor Lowe’s response to questions from the Inquiry concerning written protocols for testing [PEN.017.2663]

<sup>131</sup> Professor Lowe’s statement on Topic C5 [PEN.018.0839] at 0848; Day 80, page 55

<sup>132</sup> Professor Lowe – Day 80, pages 61–62

<sup>133</sup> Professor Lowe’s response to questions from the Inquiry about the reports of Dr Hay and Dr Nathanson [PEN.018.1240]

giving evidence) that ‘best practice’ HCV pre-test counselling was comparable to that considered appropriate for HIV testing.<sup>134</sup> He noted that, at a meeting of the Haemophilia Directors of Scotland and Northern Ireland on 6 February 1990,<sup>135</sup> it was reported that the UKHCDO and Haemophilia Centre Directors were advised by their medical defence societies that HCV testing could be undertaken on the same basis as other liver function tests, and that ‘HIV-type counselling’ was not necessary.<sup>136</sup> Professor Lowe also recalled that Dr Iain Simpson, Chief Executive of the Medical and Dental Defence Union of Scotland, had attended a meeting of the UK Regional Haemophilia Centre Directors. Professor Lowe said that when asked whether haemophilia clinicians had to go to the lengths of the HIV pre-test counselling prior to taking a blood sample for an HCV test, Dr Simpson’s opinion had been that ‘if patients are well used to being regularly monitored for post-transfusion hepatitis, and Hepatitis C is being added to all these other tests ... he could see no special case’.<sup>137</sup>

**34.91** Professor Lowe explained that he decided against giving HIV-style pre-test counselling to his patients in the early 1990s, because of the consensus that emerged after the lengthy discussions at the UKHCDO meetings, and because of Dr Simpson’s advice. Patients were not tested without their knowledge or consent, however. Professor Lowe stated that ‘we gave pre-test information about the test’, although the type of pre-test counselling thought suitable for HIV testing was not considered an appropriate model for the equivalent HCV test.<sup>138</sup>

**34.92** In his statement, Professor Lowe noted that patients were ‘routinely informed that HCV tests were being carried out’, although the Haemophilia Centre at the GRI did not call patients in especially to be told about the new HCV test. However, it was the practice there that every patient, even those very mildly affected, was seen at least annually for a review and more severely affected patients would typically have been seen earlier as they were reviewed more frequently. At review they would be told about the new HCV test once it had become available; they would then have been tested for the virus. Most patients were tested between late 1991 and late 1992.<sup>139</sup>

**34.93** He said that explanations were given before blood was taken.<sup>140</sup> Professor Lowe’s recollection was that, at the stage at which blood was to be taken, he would explain to his patients that a new test had become available for the most common cause of NANB Hepatitis:

“We are now coming to the routine blood tests and we would like to” – or we would want to – “this is now our policy,” at which point patients could say, “Well, I don’t want the test”. If they wanted. I can’t remember anybody saying no ... they already knew that they were being screened for non-A non-B hepatitis ....<sup>141</sup>

<sup>134</sup> Ibid [PEN.018.1240]

<sup>135</sup> Notes of meeting of Haemophilia Directors for Scotland and Northern Ireland, 26 February 1990 [PEN.018.0793] at 0794

<sup>136</sup> Professor Lowe’s statement on Topic C5 [PEN.018.0839] at 0849

<sup>137</sup> Professor Lowe – Day 80, page 76

<sup>138</sup> Ibid, page 65

<sup>139</sup> Ibid, page 66

<sup>140</sup> Ibid, page 65

<sup>141</sup> Ibid, page 64

**34.94** Patients who had received pooled blood products would be told to be prepared for a positive test result, as research had shown the majority of these patients had been exposed to the virus. At that stage, although the test could establish whether the patient had been infected and had developed antibodies, it would not indicate if they still had the virus that could lead to chronic liver disease.<sup>142</sup>

**34.95** Professor Lowe went on to explain that, if a patient had a positive HCV test result, they would be sent notification of an early appointment for a clinic review, so that they would know within the following few weeks, or at most few months, about their test result and its implications.<sup>143</sup> The Centre would aim to see the patient for a half-hour appointment in a private room in the clinic to enable them to have a full discussion of the implications of a positive test result.<sup>144</sup>

**34.96** Professor Lowe explained what he would say to a patient who had received a positive HCV antibody test result. He noted that the information available to clinicians improved over time as more came to be understood about the disease. In 1991 he was only able to tell a patient that they had been exposed to HCV at some point, but not when. At that time, a doctor could not advise if having the antibody meant the patient was immune from HCV infection in the future. Most importantly he could not tell the patient if they were still carrying the virus and what the chances were of the virus causing future problems with the liver, although different tests were being developed in the hope of answering those questions. Professor Lowe would emphasise the importance for the patient of continuing to attend the clinic for regular reviews and monitoring. Even if the HCV test was negative, he would still advise his patient that the test would be repeated annually as there were concerns about the accuracy of the first-generation tests. Patients were advised to take the same precautions with regard to sexual intercourse and blood spills that had been recommended since 1985.<sup>145</sup>

**34.97** With regard to prognosis, if the later PCR tests demonstrated the patient was a carrier of the virus, they would have to be carefully monitored for liver disease and consideration of antiviral treatment.

**34.98** As knowledge of the risks of transmission improved, haemophilia patients at the GRI who tested positive for HCV were advised that, as the virus could in rare cases be transmitted sexually, they should use barrier contraception and discuss the risks with their partner who could be tested for HCV by their GP.

**34.99** Patients were also informed that treatment in the form of Interferon was being developed and becoming available, and that liver transplant was ultimately an option if required. Patients with a positive test result would also be referred to a liver clinic for monitoring of their HCV.<sup>146</sup>

**34.100** Professor Lowe was referred in oral testimony to the supplementary statement from Professor Nathanson discussed in Chapter 32, *An Investigation into the Systems In Place for Informing Patients about the Risks – Ethical Context*, and in particular her views on the correct approach to testing for HCV between 1991 and 2000.<sup>147</sup> He agreed that

---

<sup>142</sup> Ibid, page 69

<sup>143</sup> Ibid, page 93

<sup>144</sup> Ibid, page 94

<sup>145</sup> Ibid, pages 98-102

<sup>146</sup> Professor Lowe's statement on Topic C5 [PEN.018.0839] at 0850-51

<sup>147</sup> Dr Nathanson's supplementary statement [PEN.018.0419] at 0421

Professor Nathanson appeared to be suggesting that, from 1997, best practice for HCV testing was to discuss the implications of the test and to give the patient time to consider whether to go ahead with it, as would happen with HIV pre-test counselling.

**34.101** He did not think that the timing and context of what Professor Nathanson told the Inquiry applied to what he was doing at his haemophilia centre in 1991, however. He had tested all his haemophilia patients before 1997. He disagreed with what Professor Nathanson told the Inquiry about appropriate practice in 1991, but by 1997 he agreed that the best practice was to give HIV-style counselling for HCV testing. He was asked why he thought a different approach was required in 1997:

I think one factor has been increasing knowledge of the severity of Hepatitis C. In 1991 we were keen to find out which patients had been exposed to it so that that could clarify advice given to patients and for management. It was hoped, I think, initially, that rather like Hepatitis B before it, the majority of patients would have cleared the virus and only a minority would then progress to liver disease. And I think the part of the change in opinion, which Dr Nathanson has considered, is that during the 1990s, we now know that only about a third at most of patients clear the Hepatitis C virus and two thirds are carrying it, and we also know that the proportion of patients developing serious liver disease is increasing. So I think there is a change in the perception of the severity in Hepatitis C.<sup>148</sup>

**34.102** Professor Lowe was then referred to the report written by Dr Charles Hay.<sup>149</sup> Professor Lowe noted the view of Dr Hay that there was no comparison between HIV pre-test counselling and HCV testing. He explained that hepatologists in Glasgow would not routinely give detailed counselling to patients when investigating them for liver disease: there could be a difference in approach between testing for HCV at the Haemophilia Centre and testing by a liver specialist. He thought that Dr Hay described a realistic approach in his report for the Inquiry, one that mirrored the practice at the Haemophilia Centre at the GRI at the material time.<sup>150</sup>

**34.103** Professor Lowe was asked to comment on some patients' and relatives' recollections that they were not told that they were being tested for HCV, and were not immediately told the results of their tests or the implications of the diagnosis. He was of the view that doctors and nurses did discuss hepatitis with their patients, particularly in the 1990s after testing for HCV became available. He identified several deficiencies in early knowledge about HCV which made it difficult to inform HCV-positive patients of the meaning of their diagnosis, including the long time lag until becoming ill, the uncertainty of the accuracy of early test results and the uncertainty whether those who tested positive might remain asymptomatic carriers of the disease. He noted that conversations with patients over the 1990s changed as more became known about the natural history of HCV, and it became apparent that it was considerably more serious than originally thought for some patients. He thought that patients may have been reassured by early conversations.<sup>151</sup>

---

<sup>148</sup> Professor Lowe – Day 80, page 87

<sup>149</sup> Dr Hay's report on communication to patients about hepatitis [PEN.018.0961] at 0991

<sup>150</sup> Professor Lowe – Day 80, page 90

<sup>151</sup> Ibid, pages 111-112

**34.104** He also commented briefly on studies that have established that many patients do not recall what they have been told in an interview with their doctor. His view was that the policy in the GRI was always to have very open discussions with patients and to be available to them for their questions. He thought that, overall, he and his colleagues did their best to communicate adequately with their patients and assumed they had achieved that goal.<sup>152</sup>

**34.105** Professor Lowe was referred to Professor Nathanson's suggestion that the way to deal with the phenomenon of some patients not absorbing bad news is to repeat the message and reinforce it at subsequent meetings. It was suggested to him that an explanation for the many patients who claimed not to have been given information was that this had not been done at the GRI. He was reluctant to accept that clinicians at the GRI may not have reinforced the details of the diagnosis at subsequent meetings with their patients. He was adamant that he and the Haemophilia Sister took significant steps to ensure that they were available for the patients to speak to and seek advice from.<sup>153</sup>

#### *Royal Hospital for Sick Children in Glasgow (Yorkhill)*

The evidence of parents of patients who were treated at Yorkhill Hospital, Glasgow

**34.106** Neither 'Christine' nor her husband were warned that their son, John, was at risk of infection with Hepatitis C from his treatment for haemophilia.<sup>154</sup> She was not warned that there was an increased risk from prophylactic treatment as opposed to treatment in response to bleeds. John was treated at Yorkhill Hospital until 1991 when his care was transferred to the Glasgow Royal Infirmary. The referral letter noted that John was positive for the antibody to the Hepatitis C virus.<sup>155</sup> According to Christine this result was not conveyed to either John or herself. She found out that John had Hepatitis C only after his death in March 1995, when she asked a nurse. The nurse replied 'Oh yes, all of our boys have got it'.<sup>156</sup>

**34.107** 'Alex' was first treated in 1986 when he was about six months old. Alex's father said that he remembered his son's first treatment very well. He recalled a doctor coming into the ward to see them and saying that they needed to treat Alex with Factor VIII as this was all they could do for haemophilia. At that time Alex's parents did not know what haemophilia was. The doctor told them that they would give Alex a dose of Factor VIII, and that Alex would probably need to take Factor VIII for the rest of his life.

**34.108** Alex's parents knew that the blood tests he underwent at each clinic appointment included a liver function test. At some point they were told that Alex was being tested for 'non-A non-B' but they did not know what that was.<sup>157</sup> They were not told the results of this test. Alex's mother was told that Alex had Hepatitis C in about 1993 at one of Alex's review appointments at Yorkhill Hospital. Alex's father stated that Alex's mother was not given any advice about the virus at that time. Neither of them knew then what Hepatitis C was.<sup>158</sup>

<sup>152</sup> Ibid, pages 113-114

<sup>153</sup> Ibid, pages 114-115

<sup>154</sup> See Chapter 5, *An Examination of the Effects of Infection with HIV on the Patients and their Families, Including Treatment*, at paragraph 5.9

<sup>155</sup> Ibid, at paragraph 5.37

<sup>156</sup> Ibid 5.37

<sup>157</sup> See Chapter 6, *An Examination of the Effects of Infection with Hepatitis C on the Patients and their Families, Including Treatment*, at paragraph 6.321

<sup>158</sup> Day 81, page 43

### The evidence of clinicians: the use of blood products and information about the risk of infection with NANB Hepatitis/Hepatitis C

**34.109** Dr Michael Willoughby was appointed Consultant Haematologist at Yorkhill Hospital in late 1973. He resigned in 1982 and took up an appointment in Australia. He was not traced by the Inquiry until October 2012, after the public hearings had concluded. He provided the Inquiry with two written reports.<sup>159</sup>

**34.110** Dr Willoughby's initial remit on joining Yorkhill was to set up a department able to carry out the haematology tests necessary to diagnose and manage blood disorders. His main focus in practice was on the management of childhood leukaemia.<sup>160</sup> Treatment of those conditions and related clinical trials were his main professional interests. Over the years he became increasingly involved with the clinical management of blood disorders, including haemophilia, but Dr Willoughby said that there was no question of him establishing a Haemophilia Centre at Yorkhill in his time there.<sup>161</sup> Children with all types of blood disorders from the west of Scotland were referred to Yorkhill.

**34.111** Dr Willoughby wrote a well-regarded textbook, *Paediatric Haematology*, published in 1977. Hereditary coagulation disorders and developments in their treatment up to the time of writing were discussed and set in the context of a busy haematology department caring for children with a wide range of illnesses.

**34.112** In relation to treatment of haemophilia Dr Willoughby received advice from Dr Forbes. In the late 1970s, he heard of the success of home therapy and decided to introduce it for patients attending at Yorkhill. Dr Willoughby used the commercial Factor VIII concentrate, Hemofil, for this purpose on the view that it was easier for the parents of children to use. It could be reconstituted more easily than other concentrates, was administered in low volumes and was injected using a slender scalp-vein intravenous needle.

**34.113** Dr Willoughby ordered the commercial concentrate through the hospital pharmacy. He considered the additional expense incurred over the use of SNBTS products to be justified for his young patients because of the advantages it offered in administration.<sup>162</sup>

**34.114** Dr Willoughby's narrative of his practice in introducing parents to home therapy dealt exclusively with the practical procedures involved. Parents were warned of possible reactions to Hemofil and were prescribed chlorphenamine for use if there were adverse, allergic-type reactions, although he could not remember that being a problem with Hemofil.<sup>163</sup> Cryoprecipitate was not suitable for home treatment of his patients because of the difficulties associated with its administration. He understood that all concentrates, whether SNBTS or commercial, carried a high risk of transmission of NANB Hepatitis. He commented on the introduction of home treatment:

I think it would be fair to say that in most patients their quality of life improved to an unrecognisable degree, with a number playing football at school. I personally thought it was proving one of the best things we had set up, and I think the others involved felt the same.

---

<sup>159</sup> Dr Willoughby's first statement on the use of blood product concentrates [PEN.019.1265]; Questions from the Inquiry to Dr Willoughby [PEN.019.1272]; Dr Willoughby's second statement [PEN.019.1272]

<sup>160</sup> Dr Willoughby's first statement on the use of blood product concentrates [PEN.019.1265] at 1265–66

<sup>161</sup> Dr Willoughby's second statement [PEN.019.1272] at 1273

<sup>162</sup> Dr Willoughby's first statement on the use of blood product concentrates [PEN.019.1265] at 1266

<sup>163</sup> Dr Willoughby's second statement [PEN.019.1272] at 1274

We had no idea that we were exposing these patients to serious viral diseases. I believe that problem only started coming to light in around 1983, after I had left the U.K.<sup>164</sup>

**34.115** In relation to the risk of transmission of viral hepatitis, he agreed generally with his successor, Professor Ian Hann: NANB Hepatitis was not seen as outweighing the risk of serious bleeding. It was known that all concentrates, commercial and NHS, carried a very high, virtually total, risk of transmitting hepatitis but Dr Willoughby felt that the risk never justified giving up the use of concentrates.<sup>165</sup> The risk of transmission of Hepatitis B was well known, but thought to be in the past, and NANB Hepatitis was generally thought to be a less serious condition.

**34.116** Dr Willoughby left Scotland before the risk of transmission of HIV had become a reality and before the potentially serious consequences of NANB Hepatitis became apparent. His narrative of practice did not include the provision of information about the risk of transmission of viral hepatitis. It appears to be clear that he implemented the Yorkhill home treatment policy on the advice of Professor Forbes and found that it yielded the anticipated benefits in improving children's lives. With 'no idea'<sup>166</sup> that treatment was exposing patients to serious viral diseases, it also appears to be clear that he would not have discussed such an issue with the parents of his patients.

**34.117** Dr Anna Pettigrew, who worked with Dr Willoughby from 1980, had no recollection of discussing with Dr Willoughby the risks associated with treatment. They were aware of the risk of Hepatitis B but she thought that, probably until 1983, they were not really aware of any other risks; it was known that there was a possibility of another form of hepatitis that could affect haemophilia patients, '[b]ut the main concern at that time was Hepatitis B.' However, she thought that the benefits of treatment generally and home treatment in particular were quite obvious.<sup>167</sup>

**34.118** It appears that during Dr Willoughby's tenure there was not a systematic approach to providing information about the risks of transmission of viral hepatitis associated with therapeutic products at Yorkhill: there was no perception of a need for it at that time. As indicated by the scope of his textbook, Dr Willoughby was a paediatric haematologist, not a haemophilia specialist, and depended on Professor Forbes for advice on haemophilia.

**34.119** Professor Hann moved to Yorkhill at the beginning of 1983 and brought a fresh perspective to practice at the hospital. With experience of treating childhood leukaemia, he already had experience of dealing with patients, and parents of patients, confronting a potentially fatal disease. It appears to be clear that his decisions on therapy were influenced primarily by his response to the threat of AIDS and have been dealt with in that context.<sup>168</sup> He quickly abandoned the use of commercial products at Yorkhill, preferring cryoprecipitate or NHS Factor VIII concentrate. However, that decision does not appear on the evidence to have been prompted by a view relating to the risk of transmission of viral hepatitis. By the time NANB Hepatitis was recognised as a potentially serious disease, in late 1985, Professor Hann's practice was firmly based on the use of SNBTS products, using cryoprecipitate and Factor VIII as the situation demanded.

---

<sup>164</sup> Dr Willoughby's first statement on the use of blood product concentrates [PEN.019.1265] at 1267

<sup>165</sup> Dr Willoughby's second statement [PEN.019.1272] at 1274

<sup>166</sup> Dr Willoughby's first statement on the use of blood product concentrates [PEN.019.1265] at 1267

<sup>167</sup> Dr Pettigrew – Day 20, pages 19-20

<sup>168</sup> See Chapter 33, *An Investigation into the Systems in Place for Informing the Patients about the Risks – HIV/AIDS*, paragraphs 33.34–33.42

**34.120** Professor Brenda Gibson was appointed Paediatric Haematologist at Yorkhill in 1984 and became the Haemophilia Director there in 1988. She was the third principal author of the Collective Response. She also provided the Inquiry with a written statement.<sup>169</sup>

**34.121** Professor Gibson recalled that the parents of patients at Yorkhill would receive advice on the benefits and risks of treatment and were 'routinely informed of the risk of hepatitis (B and non-A, non-B)'. The risks of hepatitis would be explained by both medical staff and the haemophilia nurse specialist. Parents of children who administered factor concentrate at home were educated to take precautions to avoid transmission of infection and the risk of hepatitis.<sup>170</sup>

**34.122** Clinicians also relied on other sources of information from outside the hospital, such as that provided by the Haemophilia Society. The families of patients were encouraged to read the book *Living with Haemophilia* written by Dr Peter Jones, the Haemophilia Director in Newcastle-upon-Tyne, discussed above at paragraphs 34.9–34.13. Dr Gibson also referred in her statement to the large number of the mothers of Yorkhill patients who had male relatives with haemophilia and could gather information from them on the risks of hepatitis. Many of the families who attended Yorkhill with their sons would become friends and would share information.<sup>171</sup>

**34.123** Professor Gibson also noted that parents who administered factor concentrates to their children at home would be able to read the information leaflets provided in the box with the concentrates. This information would include the risk of possible transmission of hepatitis.<sup>172</sup> (See paragraphs 34.163–34.169 below for further discussion on SNBTS package inserts at this time.)

**34.124** From 1983 there was evidence that patients receiving factor concentrate had a high risk of developing NANB Hepatitis from initial exposure. As a result the UKHCDO, and others, recommended that 'boys who had never received clotting factor concentrate ... should receive cryoprecipitate in preference'.<sup>173</sup>

**34.125** Professor Gibson went on to add that the information from 1985 onwards about the increased severity of NANB Hepatitis came from studies of adult patients and, as a result, the significance of the virus for children was unclear. From 1985 onwards patients and their parents could be told that it was hoped viral inactivation of factor concentrates would be successful in reducing or eliminating the risk of transmission of NANB Hepatitis.<sup>174</sup> She went on to tell the Inquiry that children would have been the first beneficiaries of virally inactivated concentrate and that 'the advantages, primarily the reduction in risk of viral transmission, would have been explained to parents'.<sup>175</sup>

---

<sup>169</sup> Professor Gibson's statement on topic C5 [PEN.018.0824]

<sup>170</sup> Ibid [PEN.018.0824] at 0824

<sup>171</sup> Ibid [PEN.018.0824] at 0825

<sup>172</sup> Ibid [PEN.018.0824] at 0825. However note the comment of Dr Perry at paragraph 34.168 that the Product Information Leaflets were intended for prescribing doctors and not patients. It was not until 1994 that information leaflets for patients became mandatory

<sup>173</sup> Dr Gibson's statement on topic C5 [PEN.018.0824] at 0826: this appears to repeat the Collective Statement, but has been presented by Professor Gibson as her own evidence

<sup>174</sup> Ibid [PEN.018.0824] at 0827: this also appears to be an adoption of the Collective Statement

<sup>175</sup> Ibid [PEN.018.0824] at 0826



### The evidence of clinicians: testing and communication of test results

**34.126** In her statement Dr Gibson said that the testing for HCV in children with haemophilia took place in the same timeframe as the testing of adults, once antibody tests became routine in 1991. In the period from 1990 to 1995, blood samples were taken from all patients who had received blood products. She added that patients and their parents were routinely told that HCV testing was being carried out. Verbal consent was considered to be enough for hepatitis monitoring as it was considered to be a routine test.<sup>176</sup>

**34.127** If a patient proved to be HCV-positive, they and their parents were informed at their next scheduled clinic appointment, or at their next visit to the department. This gave patients and parents the opportunity to ask questions and discuss the significance of the test results. There was felt to be no immediate or urgent need to inform patients that they had tested positive.<sup>177</sup> The child's liver function test would be carefully monitored in future and they would be referred to a liver specialist for possible future treatment.<sup>178</sup>

**34.128** Patients were also given information leaflets about HCV from the Haemophilia Society and the British Liver Trust. Professor Gibson could not recall the Haematology Unit in Yorkhill having any of their own written guidelines or policies on communicating HCV test results to patients and parents. Where possible they adopted the UKHCCO guidelines.<sup>179</sup>

### *Ninewells Hospital, Dundee*

#### The evidence of a patient treated in Dundee

**34.129** 'Colin' received treatment for Haemophilia B on about six occasions prior to 1994, at Ninewells Hospital, Dundee. In 1995 Colin and his two brothers (who also suffer from haemophilia) were asked to attend Ninewells Hospital.<sup>180</sup> When they attended in August 1995 they were told that they should be tested for Hepatitis C. Colin's brothers were told in January 1996 that their blood test results were positive for this virus. As Colin had not heard the result of his own test he telephoned the hospital and was told in a short telephone call that if his brothers were positive for Hepatitis C, he would have it too. Colin and his wife then attended an appointment with Professor Cachia at which Hepatitis C and the implications of it were more fully discussed with him.<sup>181</sup>

The evidence of clinicians: the use of blood products and information about the risk of infection with NANB Hepatitis/Hepatitis C

**34.130** Professor Philip Cachia was a Consultant Haematologist at Ninewells Hospital, Dundee, from 1992. He had trained with Professor Arthur Bloom at the University Hospital of Wales in Cardiff.<sup>182</sup> He provided a written witness statement to the Inquiry and gave oral evidence about the dissemination of information about NANB Hepatitis/HCV at Ninewells Hospital.<sup>183</sup>

---

<sup>176</sup> Ibid [PEN.018.0824] at 0829-0830

<sup>177</sup> Ibid [PEN.018.0824] at 0830

<sup>178</sup> Ibid [PEN.018.0824] at 0831

<sup>179</sup> Ibid [PEN.018.0824] at 0831

<sup>180</sup> See Chapter 6, *An Examination of the Effects of Infection with Hepatitis C on the Patients and their Families, Including Treatment*, at paragraph 6.131

<sup>181</sup> Ibid paragraph 6.133

<sup>182</sup> Professor Cachia – Day 83, pages 8–11

<sup>183</sup> Witness statement of Professor Cachia [PEN.018.0853]; Day 83

**34.131** Professor Cachia explained that local practice in haemophilia care at Ninewells Hospital developed in three distinct phases:

- Before his appointment in 1992 there was no planned or managed process for discussing treatment or delivering ongoing care to patients with haemophilia. If counselling occurred it was on an essentially opportunistic, unstructured basis when patients were attending the hospital for other reasons.<sup>184</sup>
- From 1992 Professor Cachia was in post and in about 1993/1994 he took on the role of lead clinician for haemophilia care. He started to see patients and began to build relationships with them and deliver the required standards of care, although this still tended to be delivered on a somewhat opportunistic basis as he developed protocols and procedures over time.<sup>185</sup>
- A specialist nurse, June Ward, was appointed in January 1995 and helped to develop a formal appointment process. It was also around this time that a dedicated space for haemophilia care was found. Until that time a spare room in the day unit was used for interviews and delivering test results.<sup>186</sup>

#### The evidence of clinicians: testing

**34.132** When Professor Cachia arrived at Ninewells Hospital in 1992, he discovered during his initial assessment that HCV tests had been carried out by the virology laboratory on stored frozen blood samples and that there were around 25 haemophilia patients (of around 30 tested) who were HCV-positive.<sup>187</sup> Professor Cachia's predecessor in haematology had a list from the virology laboratory of the names of those patients who had tested positive for HCV.<sup>188</sup> It was not immediately clear to Professor Cachia if patient consent had been obtained for the tests to be conducted. The patients who tested positive had not been told of the results.<sup>189</sup>

**34.133** Professor Cachia discussed the matter with a consultant virologist at Ninewells who told him that the tests were performed on stored blood samples taken at previous appointments and that the tests had been performed 'more or less out of interest' when testing first became available, 'because they had the new assay'.<sup>190</sup> The consultant virologist was unable to tell Professor Cachia what patients had been told about why their samples were being taken and stored but was quite clear that, as far as he knew, consent had not been obtained prior to testing.<sup>191</sup>

**34.134** Professor Cachia said that he was 'horrified' to discover this. In the first instance, he said that he would not personally have sanctioned such testing without prior consent. Additionally, he was concerned that his first meetings with patients would require him to explain that they had been tested without their knowledge or consent, with some testing positive for HCV, and that this would be a poor start to the doctor-patient relationship. It was not something that he felt he could continue to withhold, however, and while telling patients what had happened would not necessarily be the very first thing he would say at their next review, 'clearly it would be a vital piece of information that I wouldn't withhold

---

<sup>184</sup> Witness statement of Professor Cachia [PEN.018.0853] at 0855

<sup>185</sup> Ibid [PEN.018.0853] at 0857

<sup>186</sup> Professor Cachia – Day 83, pages 44–45

<sup>187</sup> Witness statement of Professor Cachia [PEN.018.0853] at 0856

<sup>188</sup> Professor Cachia – Day 83, Page 25

<sup>189</sup> Witness statement of Professor Cachia [PEN.018.0853] at 0856

<sup>190</sup> Professor Cachia – Day 83, Page 26

<sup>191</sup> Ibid, page 26

from them'.<sup>192</sup> He therefore told patients that stored samples had been tested without their consent and asked for a fresh blood sample for further testing, after counselling the patients and obtaining their informed consent.<sup>193</sup>

**34.135** Shortly before moving to Ninewells, Professor Cachia had been involved in MRC research as part of his post-doctoral studies which had included obtaining 'informed consent' for participation in research projects. Asked what he took 'informed consent' to mean at that time around (1991–92) and in that context, he explained:

[T]he crucial issue is that the patient has a clear understanding, in language and terms that he or she can understand, of, in this case, the reason for undertaking research, the potential benefits to them and to future generations of doing that research, any potentially negative consequences of participating in the research and that they have control of that agenda and can get the information that they require and can then make a decision on a personal basis as to whether or not they wish to participate in that research.<sup>194</sup>

**34.136** Obtaining informed consent had to allow for variations in the understanding and comprehension of different patients:

[A] great deal of variation, and I think to really be able to obtain informed consent in that way, you need to firstly get to know and understand the patient. You need to develop trust as a mutual basis for the relationship, and once you have developed trust and know what their personal value systems are, what their intellectual capacity is, what their belief systems are, you can then have a real discussion that allows them to understand and, as I say, have control of the decisions that need to be made.<sup>195</sup>

**34.137** It appears from his subsequent evidence that this earlier experience in obtaining informed consent in a research setting had a significant bearing on, and informed, his practice when he became responsible for clinical haemophilia care at Ninewells Hospital.

**34.138** Professor Cachia told the Inquiry that the setting up of the Haemophilia Centre in Ninewells included establishing local protocols and guidelines for treatment and management of patients. He explained that the difference between a protocol and a guideline lay in the level of detail in each type of document and the purposes to which they would be put. A 'guideline' would be a regularly used document, perhaps printed, laminated and left in a ward for frequent consultation. A 'protocol' would be a more detailed document, not only setting out procedures to be followed but also providing a rationale for the advice, along with references to support it.<sup>196</sup>

**34.139** Professor Cachia was shown two documents and asked to comment on them in terms of this difference. The first,<sup>197</sup> although headed 'Protocol for monitoring patients with bleeding disorders and Hepatitis C infection', Professor Cachia described as a 'guideline' in terms of the distinction given above: it was a single sheet which could be kept on the ward as a 'helpful aide-memoire' for use in a busy clinic environment, a reminder as

---

<sup>192</sup> Ibid, page 27

<sup>193</sup> Ibid, page 29

<sup>194</sup> Ibid, pages 12–13

<sup>195</sup> Ibid, page 14

<sup>196</sup> Ibid, page 43

<sup>197</sup> Protocol for monitoring patients with bleeding disorders and Hepatitis C infection, December 2005 [PEN.018.0930] provided to the Inquiry by Haemophilia Nurse Specialist June Ward with her statement [PEN.018.1225]

to whether a patient should have a particular test conducted based on their particular circumstances.<sup>198</sup> By contrast, a protocol would have a more educational purpose. It would not necessarily be for day-to-day use due to its level of detail, but could be consulted as a reference document.<sup>199</sup>

**34.140** The second document was Clinical Guidelines, dated 2008 and entitled 'Tayside Hepatitis C virus (HCV) managed clinical network'.<sup>200</sup> The document was not produced by the Haemophilia Centre at Ninewells. Professor Cachia described it as an NHS Tayside regional approach to providing care for individuals infected with HCV. Until the production of this document, which was focused on the treatment options, if clinicians wanted to offer Interferon therapy to a patient an individual case had to be made to the medical director through a hepatologist. This document was an attempt to standardise Hepatitis C treatment across all patient groups in Tayside on the basis of a protocol.<sup>201</sup>

**34.141** He did not develop a haemophilia patient protocol specifically for HCV testing. He worked on this area with Dr John Dillon, who was the principal source of expert advice around Hepatitis B and C, and utilised his patient treatment protocols for people with haemophilia.<sup>202</sup>

**34.142** From the point at which he took up his post in Dundee, Professor Cachia started to see haemophilia patients on a regular basis, including those who were not severely affected and might previously have attended the Centre only infrequently. As part of haemophilia care, he would monitor patients' general well-being, including the condition of their joints and their dental health, for example, but would also discuss health risks associated with treatment: the hepatitis viruses and HIV. His practice was to ascertain at an early stage what his patients knew about NANB Hepatitis/HCV and to build on that knowledge towards obtaining their informed consent for participation in ongoing reviews and assessments of their liver function and HCV status.<sup>203</sup>

**34.143** He said that he would take care to ensure that patients took in the information they were given. He would take time to assess his new patients and try to determine their level of understanding at the outset of discussion. Some patients would be well informed because of their membership of the Haemophilia Society, through other patients or through informal contact with medical and nursing staff.<sup>204</sup> If the patient had no prior understanding he would start from the beginning and explain the risks of viral hepatitis as a consequence of treatment with blood products and the importance of testing.<sup>205</sup> Whatever a patient's level of background knowledge, he would explain what was known of HCV and about the test and then ask the patient to tell him what they had understood of the discussion. If they could not give an accurate account he would know he had not succeeded in getting the message across.<sup>206</sup> Patients were not simply told that a test would be carried out: after discussion, a patient would have the opportunity to decline to be tested and those who had their blood tested would all have given their informed consent.<sup>207</sup>

<sup>198</sup> Professor Cachia – Day 83, page 44

<sup>199</sup> Ibid, Page 44

<sup>200</sup> Tayside Hepatitis C Virus (HCV) Managed Clinical Network – Clinical Guidelines – July 2008 [PEN.018.0932] provided to the Inquiry by Haemophilia Nurse Specialist June Ward with her statement [PEN.018.1225]

<sup>201</sup> Professor Cachia – Day 83, page 43

<sup>202</sup> Ibid, page 44

<sup>203</sup> Ibid, page 46

<sup>204</sup> Ibid, pages 37–38

<sup>205</sup> Ibid, page 38

<sup>206</sup> Ibid, page 48

<sup>207</sup> Ibid, page 38 and Witness statement of Professor Cachia [PEN.018.0853] at 0861

**34.144** He went on to explain what ‘obtaining consent’ in this context would have involved:

[I]t would have to be individualised and based on what they already knew. I would then take the conversation forwards and explain the latest information we had about Hepatitis C, about the Hepatitis C test, if they had or hadn’t been tested for it, and explain the potential benefits of that test.<sup>208</sup>

**34.145** In retrospect, Professor Cachia felt that perhaps he had given too much information to his patients at their initial appointments. Conscious that ‘there are limits to the amount we can assimilate, remember and truly understand’ he now feels that, in retrospect, ‘if I were doing it all over again, I might spread the load of information over two or three visits’.<sup>209</sup>

### The evidence of clinicians: communicating test results

**34.146** Professor Cachia was asked to describe practice at Ninewells in relation to communicating the results of a positive anti-HCV test, including whether patients were immediately told of their results. In relation to the early appointments (for patients previously tested without their knowledge or consent) described above, he said:

So for all of the patients, including those in whom we had been given the results from virology ... we took a fresh blood sample to confirm the test, and our aim was, in seeing a lot of these patients for the first time, to give them a follow-up appointment fairly rapidly, within a month or so, to discuss again the gamut of tests that we had undertaken. And if their HCV status was positive, we would take a second blood sample for a confirmatory test.<sup>210</sup>

**34.147** Professor Cachia explained that he would discuss the implications of a positive diagnosis with a patient, even before he had conducted the confirmatory test:

[P]articularly if, you know, if there was other supporting evidence. If it was a patient who had had extensive treatment, then they almost certainly were HCV-positive. If they had evidence of abnormal liver function tests or clinical evidence of chronic liver disease, then I wouldn’t necessarily wait for the confirmatory test.<sup>211</sup>

**34.148** He would tell patients about the implications of their diagnosis, which would depend in each case on the clinical context:

[I]f they very clearly had evidence of chronic liver disease, you would have to be honest and say that, you know, ‘There is evidence of progressive liver disease, so you may be in the group of patients who are going to go on and develop cirrhosis.’ If somebody had no evidence and over a period had relatively normal liver function tests, you would tell them that they might be in the better prognosis group but that there was no guarantee of this ... So you would try and stratify the risk according to all of the evidence in front of you and give them an idea of progression over time. So over successive clinic visits you would either try to reassure them or to be honest with them about the risk of progression.<sup>212</sup>

---

<sup>208</sup> Professor Cachia – Day 83, page 47

<sup>209</sup> Ibid, page 47

<sup>210</sup> Ibid, page 51

<sup>211</sup> Ibid, page 52

<sup>212</sup> Ibid, pages 52–53

**34.149** What patients were told about the disease changed between 1992 and 1995 as knowledge of HCV increased. In common with other witnesses, Professor Cachia said it was becoming clearer that the condition was not necessarily as benign as previously considered, for at least some patients.<sup>213</sup> He would advise patients that there was a recognised risk of progression to cirrhosis, but in oral testimony was unclear whether the possibility of liver cancer was discussed at this time, as it was not until later fully identified as a risk. Once the link was established it became part of the discussion with patients as it became increasingly important to closely monitor HCV-positive patients.<sup>214</sup> This was also the time when early treatment for HCV first became available; this, too, entered into the discussions he had with his patients and this part of the discussion itself changed considerably over time as treatment options expanded.

**34.150** Professor Cachia summarised the changing position at the time:

Knowledge of the complications and therapeutic options for HCV were continuously changing over the period from 1992. The approach taken ... was to have an open and frank discussion using non-technical terms to explain the nature of the infection and its origin, risks of spread including sexual intercourse (but not through normal social contact), the importance of monitoring clinical signs and blood tests, the potential benefits and risks of liver biopsy and treatment options as they evolved including Interferon, dual Interferon and Ribavirin and pegylated Interferon. Our aim was to enable patients to make informed decisions in relation to requesting approval for anti-viral therapy.<sup>215</sup>

**34.151** With regard to a patient's lifestyle, he would advise on alcohol intake as it can adversely impact on liver disease. They would also review prescription medication for potentially hepatotoxic effects (those adversely affecting the liver) and discuss over-the-counter medication.<sup>216</sup> He would remind patients of the risk of transmission to third parties and the precautions to be taken to minimise that risk. As evidence emerged of low incidences of sexual transmission, advice would be given on the use of barrier contraception and partners were offered HCV tests.

**34.152** Professor Cachia said that he did not approach the SNBTS around this time (mid-1990s) seeking advice on counselling patients with HCV.<sup>217</sup> He explained that the set-up in Dundee was unusual in that there was a regional transfusion service in the city that provided hospital blood banking. His team would have had a lot of contact with them with regard to blood for transfusion, and in relation to storage of factor concentrate, but not with regard to their working relationships with donors.<sup>218</sup>

### The evidence of Nurse June Ward

**34.153** When Professor Cachia became the Haemophilia Consultant at Ninewells in Dundee in 1992 he saw his patients alone. He did not have a dedicated haemophilia nurse until June Ward was recruited.<sup>219</sup> She was subsequently involved in counselling

---

<sup>213</sup> Ibid, page 49

<sup>214</sup> Ibid, page 49

<sup>215</sup> Witness statement of Professor Cachia [PEN.018.0853] at 0862

<sup>216</sup> Professor Cachia – Day 83, page 55

<sup>217</sup> Screening for HCV was introduced for blood donors on 1 September 1991

<sup>218</sup> Professor Cachia – Day 83, page 57

<sup>219</sup> Ibid, page 36

haemophilia patients and assisting with testing, having received training from Professor Cachia. He said that they both believed in 'patient centred care' and had similar views about how the service for haemophilia patients should be developed.<sup>220</sup>

**34.154** Nurse Ward was employed as haemophilia nurse at Ninewells Hospital from January 1995. She provided the Inquiry with a short statement in response to two questions put to her about providing information on HCV, and communicating test results regarding HCV, to patients in the haemophilia ward from when she started in 1995.<sup>221</sup>

**34.155** She stated that there was a list of patients who had been identified as having a bleeding disorder and were HCV antibody positive. Those patients were prioritised and invited to attend the clinics at the haematology day area. They were offered further confirmatory testing, monitoring and treatment for HCV.<sup>222</sup> One of her roles from the beginning was to assist in the identification of patients who had been exposed to pooled plasma products and were at risk of HCV but had not yet been tested.

**34.156** There were no local (or indeed national) HCV guidelines or protocols in 1995. Nurse Ward told the Inquiry that the Haemophilia Centre at Ninewells followed the guidance provided by the *NHS Scotland Management Executive, Provision of Haemophilia treatment and care, MEL (1994) 29*, 23 December 1994. Over the next few years, the haemophilia service developed specific HCV protocols and Nurse Ward and Professor Cachia were involved in drawing up NHS Tayside HCV protocols, which have been reviewed and developed over the years to keep up with current knowledge.<sup>223</sup>

**34.157** Patients were invited to attend for review in relation to their bleeding disorder and, as part of their review, their HCV status was checked and discussed. In most cases Professor Cachia would take the lead at the consultation with Nurse Ward in attendance, but in his absence she would see patients by herself and advise them along similar lines. In this manner they ensured that all haemophilia patients were seen by an experienced and familiar member of staff. For patients not previously tested for HCV they would discuss with the patient the value of being tested and give them enough detail to enable them to make an informed choice. The patients identified as HCV-positive were offered a PCR test to confirm their illness.<sup>224</sup>

**34.158** She added in her statement that patients would be offered a combination of patient information booklets from the Liver Trust and the Haemophilia Society to back up the advice that they had been given verbally.<sup>225</sup> Test results were provided to the patient at an organised clinic within the haematology day area.

**34.159** In 1995 only Interferon was available for the treatment of HCV and none of their patients chose to take it up. Often patients' partners or family members attended these clinics and testing was offered where appropriate.<sup>226</sup>

---

<sup>220</sup> Ibid, page 37

<sup>221</sup> Statement of Haemophilia Specialist Nurse June Ward [PEN.018.1225]

<sup>222</sup> Ibid [PEN.018.1225] at 1225

<sup>223</sup> Ibid [PEN.018.1225] at 1226

<sup>224</sup> Ibid [PEN.018.1225] at 1226

<sup>225</sup> Ibid [PEN.018.1225] at 1226

<sup>226</sup> Ibid [PEN.018.1225] at 1226

***The evidence of patients or relatives of patients infected with Hepatitis C from blood transfusions or blood products***

**34.160** 'Bridie's' mother, Molly, was infected with Hepatitis C from a blood transfusion.<sup>227</sup> Molly received the blood transfusion due to very severe complications during the birth of her fourth child at a maternity hospital in 1974. In 1994 Molly was found to have cirrhosis of the liver during an unrelated surgical procedure. The circumstances surrounding her diagnosis with Hepatitis C are set out at paragraphs 6.77–6.82 of Chapter 6. Despite investigation of the cause of her cirrhosis by a consultant physician, it was not until Molly's GP tested her for Hepatitis C at the same time as he tested her liver function that she was diagnosed with the virus. That was in 1996. Molly's GP then wrote to Molly to inform her that she had tested positive for Hepatitis C. Molly's reaction to this news was that she had AIDS and was dying. Molly's GP referred her to a consultant physician who monitored her condition. She was referred to a consultant gastroenterologist in 1997. Molly's medical records show that she saw a nurse at this appointment who gave her written information about the virus and support groups.

**34.161** 'Gordon' acquired Hepatitis C from a blood transfusion after emergency and life-saving surgery in 1975. During the follow-up to this surgery Gordon was found to have abnormal liver function test results and in about 1978 he was told by the consultant physician reviewing him that NANB Hepatitis was the most likely cause of these results. Gordon continued to attend the hospital for monitoring until 1982. He moved to England in 1985. He was diagnosed with Hepatitis C in 1995 after being admitted to hospital for investigation of weight loss and exhaustion.

**34.162** 'Christine', who gave evidence mainly about her son John's infection with HIV, also gave evidence about her own infection with Hepatitis C from blood products. As detailed in paragraph 6.363 of Chapter 6, Christine was transfused with infected Factor VIII when she underwent elective surgery in 1981. She did not feel that she needed this treatment and asked for it to be stopped as soon as she became aware that she was receiving it. Christine found out from the SNBTS in 1991 that she had Hepatitis C. She donated blood and a couple of weeks after doing so received a letter from the SNBTS asking her to attend a meeting at their office. At that meeting she was asked if she had ever taken drugs, before it was suggested to her that she had been infected by the Factor VIII infusion. She did not recall receiving much information about the virus at that meeting. She was in shock. Afterwards she attended her GP who referred her to a liver specialist for treatment.

**Product inserts**

**34.163** Documents issued with SNBTS products contained information on risks associated with their use. These have been discussed generally in Chapter 33, *An Investigation into the Systems in Place for Informing the Patients about the Risks – HIV/AIDS*, paragraphs 33.75–33.92. The documents were described by Dr Robert Perry in an SNBTS document entitled 'Hepatitis Risk Warnings'.<sup>228</sup> Questions for Dr Perry were drafted by Messrs Thompsons. Dr Perry provided a witness statement responding to a list of eight questions.<sup>229</sup>

---

<sup>227</sup> Chapter 6, *The Effects of Infection with Hepatitis C, Including the effects of Treatment, on Patients and their Families*, paragraph 6.72

<sup>228</sup> *Hepatitis Risk Warnings*, SNBTS [PEN.012.0286]

<sup>229</sup> Dr Perry's statement in response to questions on SNBTS package inserts [PEN.018.0543]



**34.164** The fourth question posed for Dr Perry was: ‘Why was it considered appropriate to include a reference to the risk of hepatitis transmission in the PFC factor concentrate inserts’ over the period 1982 to 1985?

**34.165** Dr Perry said that the wording used in statements relating to the risk of transmission of hepatitis in PFC product leaflets was prescribed by the British Pharmacopoeia and approved by the UK licensing authority further to the PFC licence application in March 1978. Between 1978 and 1985 the description used in leaflets accompanying Factor VIII and Factor IX products which had not been heat-treated included reference to screening of donated blood for Hepatitis B surface antigen by specified tests, but continued: ‘Nevertheless none of these tests are of sufficient sensitivity to eliminate the possibility of transmitting hepatitis’. Similar warnings were given on vial labels, stating: ‘This preparation is of human origin and cannot be assumed to be free of hepatitis virus’.<sup>230</sup>

**34.166** Following the introduction of heat treatment of Factor VIII and Factor IX in 1985 the ‘warning statements’ in products’ leaflets changed. The package insert for Factor VIII now stated that the product could not be assumed to be non-infective. Factor IX was heat-treated differently, at a higher temperature, and its product leaflet stated: ‘The effect of this heat treatment on Hepatitis B and Hepatitis, non-A non-B has still to be elucidated and therefore, this product cannot be assumed to be non-infective with regard to the hepatitis viruses.’<sup>231</sup>

**34.167** Dr Perry said that prior to and during the period 1982–85, hepatitis transmission by coagulation factor concentrates was widely recognised and documented. Accordingly, all manufacturers were required by regulatory authorities to include hepatitis warning statements with their product packaging and information leaflets.<sup>232</sup>

**34.168** Dr Perry said that, as information leaflets were contained in the packaging of products supplied to patients for self-administration, patients on home treatment would have sight of such leaflets although they were not the primary intended recipients of the information prior to 1994. The information contained in package inserts at that time was detailed, technical and used specialist language.<sup>233</sup> They were designed for expert and experienced prescribers, in most cases haemophilia doctors. He did not think that such package inserts could be considered as providing relevant and material information for patients about the risk of transmission of viral hepatitis, including those patients on home treatment who might have had incidental sight of the information provided by the manufacturer.<sup>234</sup> Any discussion about treatment options and the risks involved was, he said, the responsibility of the doctor administering the treatment.

**34.169** For present purposes, therefore, the provision of information in the terms employed on SNBTS package inserts is irrelevant to the knowledge patients may have had about transfusion-associated transmission risk for the same reasons as are set out in Chapter 33, *An Investigation into the Systems in Place for Informing the Patients about the Risks – HIV/AIDS*. If the SNBTS had an obligation to inform patients using concentrates directly of the nature and extent of the risk of acquiring hepatitis infection, the package inserts and information leaflets would not have been sufficient for that purpose. However,

<sup>230</sup> Dr Perry's statement on package inserts and NANB Hepatitis [PEN.018.0556] at 0556

<sup>231</sup> Ibid [PEN.018.0556] at 0557

<sup>232</sup> Dr Perry's statement in response to questions on SNBTS package inserts [PEN.018.0543] at 0547

<sup>233</sup> Ibid [PEN.018.0543] at 0544

<sup>234</sup> Dr Perry's statement on package inserts and NANB Hepatitis [PEN.018.0556] at 0557

as the terms of the principal documents – the product licence applications – make clear, the procedure was regulated under the relevant Medicines Acts in force from time to time. In particular, the product constituents and specification had to be in accordance with the information contained in or supplied with the licence application. Hepatitis risk was identified as an aspect of the description of plasma. Until the regime changed in 1994 the SNBTS was not obliged to provide additional information to that prescribed.

### **The fallibility of memory**

**34.170** Before drawing conclusions – in particular on the practice in individual centres – it is appropriate to note evidence relating to the reliability of patients' recollections. It has been a common theme among the experts that patients often deny that they have received information or counselling and various reasons have been offered for that. It is understandable that stressful situations may affect the patient's ability to absorb information, and there may indeed be a reluctance to accept information about their condition and prognosis.

**34.171** The issue was focused in the evidence of the patient given the pseudonym 'Alex', and his father.<sup>235</sup> By the time of his first treatment for haemophilia in 1986, the potential seriousness of NANB Hepatitis was becoming known. Alex's parents found his first admission a traumatic experience. They had no experience of haemophilia. His mother was with him during this admission and she was provided with further information about haemophilia and was introduced to other parents of older children with the condition. The diagnosis caused his parents considerable and continuing stress, as was no doubt the case for many families in a similar position.

**34.172** These are not circumstances in which one could reasonably expect a clear and comprehensive account of what happened soon after the event. Twenty-five years later all of the factors apply that undermine the reliability of the evidence of those involved in or observing stressful events. Some positive elements will remain, but evidence of what did not happen or may not have happened is inherently less reliable. These are precisely the circumstances in which agreed and rigorously applied protocols are required to ensure that the patient is informed and that advice is also provided in written form that can be taken away and read and re-read as understanding of the condition grows. For treating clinicians, it is important that these events are recorded in patient case records at the time, to inform others co-operating in the patient's management both then and subsequently.

**34.173** However, there is no basis for assuming, or concluding on the evidence, that medical practitioners themselves generally have perfect recall. In relying on the fallibility of the patient's recollection of what happened, there is a danger that the doctor may be seen as simply serving his or her own interests in suppressing a similar failure of recollection. Comparison between statements in the Collective Response of what 'would have been' common practice in Scotland and the evidence of the clinicians who gave written and oral evidence to the Inquiry of their own approaches, is sufficient in itself to dispel any view that the recollection among medical practitioners was infallible. The position is relatively clear where the patient's medical records note that information or advice was given. Where that evidence is not available, a general assertion of what the witness recollects of common practice is not necessarily reliable. In such circumstances a practice protocol can provide not only guidance but can generate a document of record of what happened. That approach to record keeping was not adopted.

---

<sup>235</sup> See paragraphs 34.107–34.108 above

## Discussion and conclusions

### *Provision of information to patients*

**34.174** The evidence of practice from both patients and clinicians in the 1970s was that very little would have been said by haemophilia clinicians to their patients about the risk of infection with NANB Hepatitis. Dr Hay's evidence to that effect is accepted. The practice at the time was understandable against the background, firstly, of the widespread belief that NHS blood products (in particular Factor VIII concentrates) were less likely than imported commercial products to transmit viral hepatitis and, secondly, the understanding that NANB Hepatitis was a mild condition.

**34.175** As the 1970s progressed, and into the early 1980s, most patients had liver function tests. That raises a question as to whether a change in the approach to providing information and advice about NANB Hepatitis was appropriate. Dr Hay thought that from the late 1970s most patients having liver function tests would have been told that they had NANB Hepatitis. From 1978 at the latest, there was published information that there was at least the risk of transmission of NANB Hepatitis from the use of factor concentrates. Mr Watters' evidence about the discussion in Haemophilia Society Newsletters from 1978 illustrates that.

**34.176** It seems highly unlikely that asymptomatic patients would have been routinely advised of a relationship between the results of their liver function tests and the emerging risk of NANB Hepatitis, as long as overt clinical indications of hepatitis was a criterion for diagnosis.<sup>236</sup> The MRC definition of 'hepatitis', which included this criterion, was followed by most clinicians until at least the end of 1983 (when the article by Fletcher and others was published in the *BMJ*)<sup>237</sup> and by others until an anti-HCV assay was developed in 1989.

**34.177** The second factor of importance mentioned in paragraph 34.174 above (the understanding until late 1985 that NANB Hepatitis was a mild condition) meant that the risk of the virus was not thought to be serious enough to weigh in the balance against the need for treatment of coagulation disorders. When product selection first became a significant issue, it was in relation to the emerging knowledge of AIDS and the risk of transmission of an agent causing AIDS and AIDS-related diseases.

**34.178** In the circumstances, a uniform, invariable approach to the provision of information about NANB Hepatitis was not likely to be adopted by individual clinicians in the absence of authoritative advice from regulatory or advisory bodies or from the NHS. There was no advice until the late 1980s and none that was specific enough or relevant to HCV until the early 1990s.

**34.179** With the benefit of hindsight, it is clear that it would have been in the patients' interests for protocols to have been developed and applied in the 1980s, rather in the manner that Professor Cachia and the Tayside Health Board approached practice at Dundee in and after 1992. However, Professor Lowe was probably right in saying that it would have been impractical to prepare a protocol if one had to envisage a document that anticipated every individual patient's needs. Something rather less ambitious might

---

<sup>236</sup> The 1974 report of the UK Medical Research Council Working Party included in its definition of 'hepatitis' a finding of enzyme elevation in association with other clinical indications of hepatitis, typically jaundice.

<sup>237</sup> Fletcher et al, 'Non-A non-B hepatitis after transfusion of factor VIII in infrequently treated patients', *British Medical Journal*, 1983; 287:1754-57 [LIT.001.0239]

have sufficed if agreement could have been reached, however. It might have been practicable for the Scottish Haemophilia Directors to have promulgated a protocol that prescribed, for example, that what was known about NANB Hepatitis should be discussed from time to time with patients at risk, and as significant developments in knowledge occurred but without specifying the precise contents of the discussion or restricting the individual clinician's independence of judgement as to what was significant. No attempt to formulate a common approach was drawn to the attention of the Inquiry, however, and it is necessary to note individual practitioners' approaches and make such comment as seems appropriate.

**34.180** Patients receiving coagulation therapy using PFC products were exposed to the risks of transmission of NANB Hepatitis, up to October 1985 in the case of Factor IX, and April 1987 in the case of Factor VIII. For the vast majority of patients receiving concentrate therapy up to those dates, advice on the real risk associated with NANB Hepatitis came too late: almost all had been exposed to the virus. Depending on their individual genetic characteristics, patients in treatment had not been infected, had been infected but had cleared the virus spontaneously, were carriers of the virus but remained and were likely to remain asymptomatic, or were at some stage in the progression towards serious liver disease. In view of the long natural history of HCV, some people in the final group would not survive (dying of unrelated causes) to develop symptomatic disease.

**34.181** Whether a diagnosis of NANB Hepatitis would have been made depended on the position adopted by the clinician. Certainly until the end of 1983, those clinicians who applied the MRC definition of 'hepatitis' would have required clinical manifestations in addition to a finding of enzyme elevation. In the case of the Royal Infirmary of Edinburgh, Professor Peter Hayes' view was that few diagnoses of NANB Hepatitis would have been made. In their letter to *The Lancet* dated June 1987, Dr Dow and others commented that they had found reports in the west of Scotland of only 23 NANB Hepatitis cases in the previous eight years.<sup>238</sup>

**34.182** In Professor Hayes' experience of working in a large liver clinic, before HCV was discovered patients who presented with abnormal liver function test results were not usually diagnosed as suffering from NANB Hepatitis. There were many non-viral causes of abnormal liver tests. He said:

So a diagnosis of non-A non-B wasn't really considered in patients where an alternative explanation could be found and it tended to be triggered – or it's likely that it would have been triggered if somebody had had a blood transfusion and then had abnormal liver tests .... So if somebody just had abnormal liver function tests, it's relatively unlikely that a putative viral diagnosis would be made, but on the other hand, if somebody had had abnormal liver function tests following a blood transfusion, then that's more likely. But my understanding is it was not a very common diagnosis.<sup>239</sup>

**34.183** Until September 1983 the information that a haemophilia clinician would have been expected to give to patients about the risks of hepatitis infection associated with factor concentrates would have been that NHS products were safer and that, so far as there was a risk of infection, the disease was probably benign. In contrast, haemophilia

---

<sup>238</sup> Dow, Mitchell, Follett, 'Non-A, non-B Hepatitis surrogate testing of blood donations', *The Lancet*, 13 June 1987; 1366 [LIT.001.0346]

<sup>239</sup> Professor Hayes – Day 78, pages 46–47

was in fact associated with the risk of progression to serious and debilitating illness and possible death from haemorrhage. From September 1983, the NHS product would not have been thought less likely to transmit infection, but the perceived 'benign' prognosis for NANB Hepatitis would have remained the same until 1986 or 1987.

**34.184** It appears that from about 1980 at the latest there was widespread knowledge amongst patients and their parents that the use of factor concentrates was associated with the risk of developing hepatitis. Up to 1983 some patients in Scotland were expressly advised that the use of factor concentrates carried a fairly high risk of contracting viral hepatitis. Although some patients may not have been expressly so advised, it appears very likely that by 1983 all adult patients and parents of patients would have come to know, directly or indirectly, about the risk as understood at the time. What is less clear is whether, even by 1983, patients were being told explicitly of the risk of NANB Hepatitis as distinct from Hepatitis B.

**34.185** While in general terms the likely risks of 'hepatitis' from factor concentrate treatment were probably appreciated to a greater or lesser extent by most patients, what these risks truly were must have been less understood. Until 1985, no practitioner could have discussed the natural history of NANB Hepatitis infection in a fully informed way: the information was not available, and only began to be developed thereafter. No discussion of the risk of long-term progression to serious liver disease was likely to have taken place because no such risk was recognised. Any advice would have reflected the current understanding and that would not have reflected the reality of risk.

**34.186** It is questionable whether, apart from previously untreated patients and those who had previously received very little treatment, discussion would have been of practical assistance to patients. The critical time frame for advice relates to the point at which the diagnosis of a coagulation disorder was made and an initial decision on treatment had to be taken. Once the patient was on an established course of concentrate therapy, the risk of transmission of NANB Hepatitis/HCV crystallised and, at least until new information of relevance to the treatment regime or some other material change of circumstances emerged, the opportunity to give relevant and meaningful information about treatment (as distinct from the consequences of infection) was likely to have passed.

**34.187** In any event, even if some doctors, like Dr Willoughby, did not expressly advise their patients or patients' parents of the risk because at that stage they perceived that the risk of serious liver disease was negligible, Dr Nathanson's evidence was that she would not be critical of them on the basis of contemporaneous standards. In the 1970s and early 1980s medicine was more paternalistic and it was not unusual for doctors effectively to take decisions for their patients without discussing the balance of risks and benefits with them.

### Edinburgh

**34.188** Professor Ludlam's evidence that patients were informed about the risk of transmission of viral hepatitis from time to time as knowledge increased, is accepted on the basis that he described. It was done as circumstances required in the exercise of his professional judgement rather than as a matter of routine followed with all patients. There is reliable evidence that he did give explanations to some patients and those explanations appear to have been adequate, given the information in the public domain and available to clinicians at the time. Professor Ludlam's evidence was consistent with the evidence given by the patient witnesses in this respect.

**34.189** Professor Ludlam's practice throughout this period reflected his view that as far as possible his patients should be treated exclusively with NHS products. The slips issued to those travelling away from Edinburgh and the explanations given to patients would have left no room for doubt that his advice was that they should avoid commercial products because they carried a risk of transmission of viral hepatitis.

**34.190** That was one example of the application of his view that much information provision to people with chronic disorders who are being seen very frequently is done on a 'need to know basis' as it arises in their clinical care. Another example was discussion of the cause of jaundice, when it occurred in one of his patients that called for an explanation of how it could have arisen. On the other hand, he did not inform patients generally or systematically of the risk of transmission of NANB Hepatitis. He said that he would not have raised with his patients the topic of the different kinds of treatment that they could receive in the context of the emerging risk of NANB Hepatitis.

**34.191** Those of his patients who attended the local Haemophilia Society patients' group would have benefited from talks, by Professor Ludlam among others. Professor Ludlam provided leaflets and other Haemophilia Society publications. While it would not be appropriate for a clinician to rely on these as a substitute for giving information and advice directly, the general level of knowledge gathered from such sources, and from other casual sources such as media comment, would be matters to which a clinician would have regard. In particular it was appropriate to rely generally on the Haemophilia Society publications to supplement direct information and advice.

**34.192** Without adequate records generally, it is not possible to form a firm view that patients were fully informed of the risks associated with the therapy that they received. Having regard to the expert evidence of Professor Nathanson and Dr Hay about patients' abilities to absorb information, and thereafter to remember what they have been told, there was at all times a risk that information was not effectively communicated to or retained by patients. Whether from fear of confronting the implications of infection, or from an over-optimistic view of risk, built up over years of reassurance, or from a well-founded assessment of relative risk of bleeding and slowly progressing hepatitis, patients may not have understood the reality of their position. Practice now would be different, as Professor Ludlam accepted, but it is clear that from the earliest period patients accepted, and were expected to accept, that 'doctor knows best' and that was reflected in clinicians' practice in giving information and advice. Until the late 1980s, however, by which time viral inactivation had eradicated the risk of transmission of the putative NANB Hepatitis virus or viruses, there was no commonly accepted ethical principle or rule that would have been infringed by Professor Ludlam's treatment practice.

### **Glasgow Royal Infirmary**

**34.193** Professor Lowe's evidence is accepted that, throughout his period at the GRI, clinicians discussed 'hepatitis' with patients. Having regard to Professor Lowe's evidence, many patients attending the GRI throughout this period were informed of the risks of transmission of viral hepatitis associated with factor concentrate therapy, so far as it was understood. Review clinic practice appears to have been well adapted to provide opportunities for discussion and the provision of relevant information.

**34.194** The position with regard to providing information to patients about the specific risk of NANB Hepatitis is less clear. While Professor Lowe gave evidence of patients being advised prior to 1985 that NANB Hepatitis was a concern, and thereafter of the risk of developing serious liver disease, David recalled being warned only about the risk of Hepatitis A before being diagnosed with Hepatitis C in 1991. David was found to have abnormal liver function test results in 1983 and it was noted in his medical records that the likely cause of these was NANB Hepatitis. David did not recall being told of these results. There may be a number of explanations for this difference between the evidence of Professor Lowe and of David and, having not explored the matter in detail in evidence; it would be conjecture for the Inquiry to choose one. Whatever the explanation, David's evidence casts some doubt on the view that the risk of infection with NANB Hepatitis and the implications of the virus were consistently conveyed to all patients in the manner and detail stated by Professor Lowe.

**34.195** Practice varied across Scotland, not only as among haemophilia clinics, but within any particular clinic as among patients. Although general information about hepatitis was produced by bodies such as the Haemophilia Society, it could not be found that there were well-established and generally accepted procedural protocols (either written or understood and shared by practitioners) for communicating information to each individual patient about the risks associated with the use of therapeutic products, the relative risks of avoiding therapy, and the nature of the choice that the patient had to make about their own condition and treatment for it. Indeed, for much of this period the choice as to treatment was made for most patients in Glasgow, the same way it was made in Edinburgh.

### Yorkhill

**34.196** Christine's evidence of her experience at Yorkhill is consistent with the impression given by Dr Willoughby of practice during his period at Yorkhill. According to his written evidence he did not discuss the risk of transmission of viral hepatitis with children's parents. It appears that all major developments in the treatment regime applicable to Christine's son took place before 1983, when ethical practice would not have required discussion of such risks of transmission of NANB Hepatitis as were known to exist.

**34.197** Practice changed when Professor Hann succeeded Dr Willoughby in 1983. Professor Hann's evidence was instructive. New to Yorkhill, and entering a new specialist practice at a critical time, he faced the uncertainty of the aetiology of AIDS and its association with therapeutic blood products, yet had to communicate his position to parents of young children concerned about risk. He was also on course to change radically the regime of his predecessor and give up the use of commercial concentrates. He had a particular need to formulate his views. He had a clear preference for cryoprecipitate and otherwise preferred SNBTS concentrates. Of importance is his evidence of advising new patients' parents: the advice focused on the need for treatment, warning of side effects, but ultimately the choice was between cryoprecipitate and SNBTS Factor VIII. Not treating the child was not an option.

**34.198** Why Alex's parents may have been given insufficient information about the tests he underwent and about Hepatitis C generally can only, at this distance in time, be speculated upon. Equally, with whom responsibility for any such deficits lies can no longer be reliably ascertained. What can be said is that they found their experience in this respect to be unsatisfactory which underlines, should any underlining be required, the necessity for information to be provided to patients or, in the case of children, their parents.

**34.199** There is insufficient evidence in relation to the practice at Yorkhill to establish that, during the period in question, there was any breach of any principle or rule of ethical practice in force at the material time.

### Dundee

**34.200** In general, there is no evidence that haemophilia patients in Dundee had been told about the risk of NANB Hepatitis before Professor Cachia was appointed. Professor Cachia's evidence about the provision of information to patients was understandably limited by the fact that he did not start working at Ninewells Hospital until 1992. Professor Cachia's evidence was that until 1992 there was no planned or managed process for discussing treatment with or delivering ongoing care to haemophilia patients. Equally, counselling was then delivered on an opportunistic, unstructured basis. He sought to change and improve those practices including by discussing any health risks associated with treatment and devoting time to ensure that his patients understood any information provided by him. From the evidence available to the Inquiry, it appears that he and his colleagues succeeded in making significant improvements to the service in Tayside.

### *Testing and communication of test results*

**34.201** Routine blood tests in the course of management of coagulation disorder patients as described in this chapter do not raise any issue of ethical practice. Questions arise only where particular practices may have gone beyond the limits of implied consent and fallen into a category requiring specific or express consent from the patient.

### Edinburgh

**34.202** In one respect, there is a question whether practice at the Edinburgh centre fell short of what was acceptable. Professor Ludlam instructed testing for anti-HCV of stored samples from 61 patients in 1989 and the study was reported in a letter to *The Lancet* in September 1989. The patients were unaware that their blood samples were being tested in this way. The testing and the published material were anonymous: no reader could have identified the patients. Forty-one patients tested positive for anti-HCV. In 1991 samples from 85 patients were tested and these tests were confirmed by further testing in Dr Simmond's laboratory. The 1989 tests must have been carried out using first generation assays. Patients were not informed of the results of any tests until 1992 when fresh samples were sought for confirmatory testing. Many patients were unhappy that data about themselves had been published when they were unaware even that they had been subject to the tests.

**34.203** In 1988 the BMA guidance *Philosophy and Practice of Medical Ethics* had published the view that a patient should give consent before any investigation and treatment proposed by the doctor. (See Chapter 32, *An Investigation into the Systems in Place for Informing Patients about the Risks – Ethical Context*, paragraphs 32.43–33.44.) The publication of the results of the tests is not relevant: the data were anonymous. There are, however, issues as to whether testing the patients without informing them and obtaining consent to the study was contrary to the BMA guidance and whether there was an unacceptable delay in communicating the results. Dr Hay explained that at that time many practitioners did carry out testing on stored samples without consent. In addition, both he and Professor Nathanson explained that, in the context of patients who have already given consent to monitoring of liver function tests (LFTs), an anti-HCV test could be seen as an extension of that process.



**34.204** It was Professor Ludlam's stated view that he had explained to his patients that there was a risk of contracting NANB Hepatitis from the use of concentrates and that his patients had given consent to have their LFTs monitored for signs of that disease. It was probably implicit in that consent that new biometric tests for NANB Hepatitis viruses would be employed as they became available. Testing was routine over a long period and it was clear from the evidence of the witness Mark that he was frequently offered information about the test data recovered in his case. However, HCV was a newly discovered virus and was unknown when consent to monitoring LFTs had been obtained. It might be suggested that, by 1989, it was for the patients to decide whether the deficiencies in the accuracy of the test were acceptable before their samples were subjected to it and that specific consent should have been obtained. However, expert opinion did not support such criticism, particularly as the samples were anonymised before they were tested and no patient-specific results were therefore available.

**34.205** In relation to the second exercise in testing, which formed the basis of the 1991 paper, it is evident that this was conducted on named samples and therefore yielded results which could have been communicated to patients. It appears that the approach to communication of these results was not proactive: patients were instead offered a further test, with the appropriate explanation and consent, and then given the result of that at their next clinic visit. Inevitably, that meant there was a delay between the obtaining of the result for an individual patient in the course of the study, and the communication to that patient of the result of the further test.

**34.206** In these circumstances, while it is inappropriate to be critical of Professor Ludlam's approach to testing stored samples in 1989 and 1991 without permission, once the results became available they should have been communicated to patients within a reasonable time. The information belonged to the patients and should not have been withheld. For any one individual, it will be a question of whether the time taken for them to learn their HCV positive status was reasonable.

**34.207** With regard to the witness Elaine and her belief that her husband was not told of his diagnosis with HCV, as stated in paragraph 5.235 of Chapter 5, this may be explained by the fact that Brian's Hepatitis C positive test result was reported only a month before his death. If he was not told this diagnosis, any failure on the part of the doctors to disclose this diagnosis may be mitigated by the short interval between Brian's diagnosis with HCV and his death. Understandably, Elaine suffered some anxiety when she discovered that her husband had this virus. She was concerned that he could have passed the virus to her and that she could have had it for a number of years without knowing and without receiving treatment. As stated in paragraph 32.207 of Chapter 32, family members of competent adult patients had no right to know a diagnosis and so, while the failure to inform her caused her distress and anxiety, there was no duty on the part of those treating Brian to inform Elaine of his diagnosis.

## Glasgow

**34.208** There is no evidence of anti-HCV testing of stored samples without consent in the GRI or Yorkhill.

**34.209** David's recollection that he was not told much about the virus when he was diagnosed with it in 1991 is consistent with Professor Lowe's evidence that, in the early 1990s there were several deficiencies in knowledge about the virus.<sup>240</sup>

---

<sup>240</sup> See paragraph 34.103 above

**34.210** According to Christine, her son, John, was unaware when he died in March 1995 that he had Hepatitis C. His medical treatment was transferred to the GRI from Yorkhill, in 1991 when he was 16 years old.<sup>241</sup> The referral letter recorded that John was positive for the antibody to Hepatitis C. Further tests will undoubtedly have been carried out at the GRI to confirm this diagnosis. There is perhaps a very remote possibility that John was aware of this diagnosis or even that he was told it, but due to the ongoing monitoring and treatment for AIDS, it did not register with him or even sufficiently for him to tell his parents about it. Against this possibility is Christine's evidence that John would have told her or her husband had he known. A further explanation is that the medical staff at the GRI assumed that John had been told he was positive to the antibody to the virus while still a patient at Yorkhill, and so did not discuss it further with him. These explanations can only be conjecture and no conclusion can be reached about what John was or was not told about his diagnosis with Hepatitis C. Whatever happened, the manner in which Christine found out that her son had the virus was insensitive, to say the least, and can only have added to her suffering.

### Dundee

**34.211**, There is no evidence that haemophilia patients in Dundee had given their consent to have their LFTs monitored or had consented to having samples stored prior to Professor Cachia's appointment. The available evidence from Professor Cachia suggests the contrary.

**34.212** In relation to testing stored samples for anti-HCV, the timing in Dundee was substantially the same as in Edinburgh. Stored samples of sera were tested with the new HCV test when it became available in about 1989 and results were not communicated to patients until about 1992. That delay was inappropriate.

**34.213** It appears that the system for communicating test results to patients broke down in relation to Colin who was told his diagnosis with Hepatitis C by telephone and in an insensitive manner. The system for informing patients of their test results, which Professor Cachia sought to implement, failed in Colin's case as systems sometimes do. The reason for this is unknown.

### Stephen

**34.214** As noted in paragraph 34.3 above, practices at Edinburgh, Glasgow and Dundee have been explored in detail in this chapter as practitioners from these areas gave evidence to the Inquiry. A discrepancy arose in the evidence of Stephen, who was treated in Aberdeen, surrounding his diagnosis with Hepatitis C.<sup>242</sup> In summary, despite Stephen's medical records recording that Stephen had been found to have antibodies to Hepatitis C in 1992 and that he discussed his diagnosis with doctors in 1995, Stephen thought that he became aware that he had Hepatitis only in the late 1990s or early 2000s. No clinicians involved with Stephen's care gave evidence to the Inquiry and so this issue was not explored in detail at the public hearings. For this reason it is inappropriate for the Inquiry to form a view about when Stephen was told of his diagnosis with Hepatitis C. That said, this discrepancy may be an illustration of a point already made in this chapter which is pertinent to the issues in this series of chapters, namely that just because a diagnosis was conveyed by a doctor did not necessarily mean that it was heard by the patient.

---

<sup>241</sup> See paragraph 34.106 above

<sup>242</sup> Paragraphs 6.18–6.23 of Chapter 6

### Patients who received HCV from blood transfusions

**34.215** The fact that it took almost two years, from 1994, for the cause of Molly's cirrhosis to be identified as Hepatitis C, is indicative of the lack of knowledge about the virus amongst more general clinicians (as opposed to haematologists) in the early days of the virus being discovered. The manner in which Molly was informed of her diagnosis was unfortunate, and is very likely to have contributed to her reaction to the diagnosis. Without specific guidance about conveying blood test results to patients, clinicians including GPs will have adopted their own approach to doing so. Many will have had little knowledge of the virus. As a result of this the manner in which blood transfusion patients, like Molly, were told of their diagnosis with Hepatitis C varied considerably.

**34.216** This is borne out by the other witness statements obtained by the Inquiry. The extent of the information patients, like Molly, were given about the virus will have depended on the knowledge of the person diagnosing them. In the early days of the virus many clinicians, through no fault of their own, will have had little information to pass on to patients and so patients will have been diagnosed with a virus but given very little information about it. This is likely to have added to their distress and anxiety on receiving such an uncertain diagnosis.

**34.217** Despite being diagnosed with NANB Hepatitis in about 1978, Gordon was not diagnosed with Hepatitis C until 1995 when he was admitted to hospital for investigation of his symptoms of the virus. It is unfortunate that his diagnosis with NANB Hepatitis did not trigger a test for Hepatitis C earlier, but by the time the test became available Gordon had moved to England. The procedure for testing patients with NANB Hepatitis for Hepatitis C in England is not within the remit of this Inquiry.

**34.218** Anne was diagnosed with Hepatitis C in late 1995 by her GP after being identified in the UK look-back exercise as a recipient of infected blood. After agreeing to counsel and test Anne, Anne's GP was provided by the SNBTS with written guidelines entitled 'Transfusion-transmitted Hepatitis C: Guidelines for counselling patients April 1995' which ran to 25 paragraphs over five pages. These guidelines included an introduction and sections on background, implications of a positive test – prognosis, epidemiology, modes of transmission, avoiding infecting others, further assessment and follow up and notes about management at specialist centres. Despite these guidelines, when he diagnosed her with Hepatitis C, Anne's GP gave her the impression the virus was nothing to worry about. He gave her very little information about the virus or the implications of it. It is unclear why Anne's GP did not convey to Anne the information he had been given but the outcome for Anne was that she was worried and concerned for her future. She sought further information herself from her local hospital.

**34.219** Christine's evidence is disturbing.<sup>243</sup> She did not want to receive Factor VIII in connection with surgery. She found that despite her wishes medical staff transfused her with Factor VIII, relying on a general waiver contained in her consent form to the surgery.

**34.220** It is very unfortunate that she was treated with what transpired to be infected Factor VIII when she did not believe that she required such treatment. Those who treated Christine did so on the basis of her consent to the surgery and this was indicative of the paternalistic nature of medical practice at the time.

---

<sup>243</sup> Christine – Day 28, pages 26-27

**34.221** It is understandable that Christine was shocked when she was diagnosed with Hepatitis C at a meeting with a representative of the SNBTS in 1991. After all her son, she and her family had been through this must have been particularly difficult information to hear. Her reaction to this is unlikely to have been helped by the questioning she received about drug-taking.

### **Final comment**

**34.222** The ethical principles and rules governing clinicians' relationships with their patients in the period covered by this chapter were not settled. The transition from 'doctor knows best' to the current (and still evolving) principle of patient-centred care was prompted by experience of managing and treating patients exposed to the risk of HIV/AIDS infection and to the associated risks of social exclusion and financial difficulties that arose with it. The course of events has been traced in Chapter 32. For present purposes it should be noted that it was in 1988 that the General Medical Council published its guide *HIV Infection and AIDS: The Ethical Considerations*. AIDS had become 'dramatically apparent' in about 1982–83. But the medical profession took time to understand the implications for clinical practice and the need to adapt to the challenges presented by this new and emerging infection.

**34.223** The risks of serious morbidity and of death associated with NANBH, later HCV, infection began to be generally understood late in 1985, in the middle of the AIDS period. The lessons from dealing with HIV/AIDS had not been fully understood and assimilated into general ethical practice by that time. The conclusions in Chapter 32 include that no criticism can be made of clinicians relating to their management and treatment of patients generally over the critical period down to the late 1980s. It would be the early 1990s before the position in relation to NANBH/HCV became clear and there was a basis in generally accepted principles and rules against which to measure the care of patients.

**34.224** The conclusions reached in Chapter 32 address issues of ethical practice. Developments in the principles and practice of medical ethics now in general application should ensure that patients receive the information they need to reach informed conclusions on their illness and on treatment.

**34.225** However, the complaints of patients and their families discussed in this chapter – very similar to those made in relation to the HIV virus – of inadequacies in the information provided to them about the Hepatitis C virus, in the manner in which their diagnoses were communicated to them, and about testing for infection without counselling and consent, serve to underline an important message for medical practitioners. Patients infected with a potentially fatal virus such as HIV, or infected with HCV and at risk of developing the serious complications of cirrhosis, possibly hepatocellular cancer, and other fatal complications, are entitled to this information and should not have to wait while the medical profession deliberates on general ethical issues. At a basic human level help is needed in real time as it becomes clear that the patient has acquired a serious infection or other illness.

**34.226** The examples discussed in this chapter, and in Chapter 33, reflect the anger and dismay of individuals discovering that their medical advisers had information about them, or intended to investigate their condition, without involving the patient in discussion about his or her health and the clinician's response to it. The examples of blood disorder patients are particularly telling. They and their clinicians had been confronted in the first half of the 1980s with the unprecedented, extreme and worrying circumstances surrounding AIDS

and, when it was established as the cause of the profound immune deficiencies leading to AIDS, the HIV virus. In the second half of the decade they were confronted by the reality that what had been seen, and represented to them, as a life-changing treatment which both extended life expectancy and promised an unprecedented quality of life experience, carried an additional risk, of developing serious and potentially fatal complications of a disease previously thought to be relatively benign. The result has been distress, anger and distrust of clinicians, clearly demonstrated by the evidence of witnesses at the public hearings and from witness statements received by the Inquiry.



## CHAPTER 35

### AN INVESTIGATION INTO THE STEPS TAKEN TO IDENTIFY THE INDIVIDUALS WHO WERE INFECTED (LOOK-BACK)

#### Introduction

**35.1** Previous chapters have discussed the information available to doctors about HIV and Hepatitis C virus (HCV) infection as knowledge of the diseases and their treatment developed, the provision of relevant information to patients, and the introduction of HCV screening in September 1991. This chapter deals with the methods available to identify patients put at risk of HCV transmission by treatment with blood or blood products, and with the steps taken in that regard.

**35.2** The methods of investigation available to regional directors included 'look-back'. Look-back seeks to connect information about patients, blood components or products thought to be transmitting infection and the donors who provided the blood. In practice, two types of look-back were developed, called in the UK 'targeted' and 'reverse' look-back.

**35.3** In 'targeted look-back' the process begins when a blood donor is found to be infected when tested for a specific pathogen such as HIV or HCV. The donation history of the infected individual is then investigated with a view to tracing possible recipients of blood, blood components or products prepared from previous donations by that person to ascertain whether such recipients may have contracted the virus harboured by the donor. Any blood, blood components or products derived from an infected donor still in stock can be identified; blood banks and peripheral hospitals can be advised and material they hold quarantined.

**35.4** In 'reverse look-back' (in North America often called 'trace-back') the process begins when a patient presents to a clinician with relevant signs and symptoms of a disease. In the case of HCV the clinician would often be a hepatologist and the signs and symptoms would be of liver disease. If investigations disclose HCV infection and there is a history of previous transfusion with blood, blood components or products, the clinician informs the relevant blood bank which then endeavours to trace the donor or donors who may have donated infected blood. Withdrawing blood, blood components or products is generally not possible as a result of reverse look-back, at least initially and often generally; the starting point is not the infective donor but the infected recipient and, quite often, the transfusion that transmitted infection will have taken place many years previously so that it would be almost certain that all of the blood, components or products derived from the implicated donation would have been used or gone out of date by the time of the investigation.<sup>1</sup> In contrast to targeted look-back, reverse look-back is not dependent on the availability of a screening test for the virus or its antibodies.

**35.5** This chapter is concerned primarily with look-back as it relates to HCV. However, the approach to HCV look-back was influenced by previous experience of exercises related to HIV and it is appropriate to comment on that experience in the first place.

---

<sup>1</sup> Components are allocated a limited shelf-life, or 'use-by' date.

## Early experience with look-back in the United Kingdom

**35.6** As discussed in Chapter 10, *Knowledge of the Geographical Spread and Prevalence of HIV/AIDS 2*, growing awareness of cases of AIDS among haemophilia patients, particularly those with Haemophilia A, in 1984–85 spurred attempts to estimate the prevalence of HIV infection in the UK. In Scotland, the infection of ‘the Edinburgh Cohort’ was discovered and disclosed at the end of 1984.<sup>2</sup> It was initially thought that one specific batch of Scottish National Blood Transfusion Service (SNBTS) Factor VIII concentrate had probably caused the infection but, at the time, a definitive investigation would have to await a reliable test for infectivity. All but one of the 16 patients with Haemophilia A who had developed anti-HTLV-III had received the so-called ‘implicated batch’ between March and May 1984.<sup>3</sup> At about the same time it was discovered that a number of west of Scotland patients had also been infected. Details were disclosed in May 1985.<sup>4</sup> These discoveries presented the initial data for a reverse look-back exercise, which concentrated on following up data from the Edinburgh and south east Scotland region.

**35.7** In this respect, the exercise was an illustration of the SNBTS’ ability to undertake reverse look-back procedure for investigating the histories of recipients of blood or blood products who had been found to be infected. It was a means, in at least some cases, of ascertaining information on transmission of infection, however difficult and limited in the circumstances, independent of the targeted look-back studies discussed in this chapter.

**35.8** The SNBTS recording system allowed the tracing of donations which had made up an ‘implicated batch’. Regional Transfusion Centres (RTCs) kept records of donations sufficient to identify the specific donors who had contributed to a batch of blood products thought to have transmitted infection.<sup>5</sup> It was then possible to follow up those donors who returned to later donation sessions and were screened.<sup>6</sup> As noted below, and discussed more fully in Chapter 28, *Donor Selection – AIDS*, at the same time as the SNBTS was attempting to identify ‘implicated donors’ there was a well-publicised, and effective, campaign to discourage ‘high-risk donors’ from donating blood.

**35.9** Subsequently, the SNBTS considered undertaking a look-back exercise aimed at tracing and testing the donors of all 4000 donations potentially associated with the transmission of HIV infection to the Edinburgh Cohort. These would have been all of the individuals who had donated blood which had contributed to the implicated batch, not just those who might have been captured as return donors. However, blood samples were available for only 50% of these donors and the view was taken that it would therefore be impossible to trace the course of donations by this method.<sup>7</sup>

**35.10** In one respect at least, the work done on HIV look-back was to have a lasting significance. In September 1984, Dr John Gillon was appointed as a Senior Registrar in the South East Scotland Blood Transfusion Service (SEBTS). He became a Consultant Physician in that service in April 1985. His responsibilities included the selection and medical care of donors.<sup>8</sup> On 20 November 1984 he was asked to visit transfusion centres and discuss

---

<sup>2</sup> The ‘Edinburgh Cohort’ was a group of haemophilia patients in Edinburgh who were discovered in October 1984 to have been infected through treatment with Scottish Factor VIII concentrates. See Chapter 10, paragraphs 10.16–10.26

<sup>3</sup> Chapter 10, *Knowledge of the Geographical Spread and Prevalence of HIV/AIDS 2*, paragraph 10.60

<sup>4</sup> Ibid paragraph 10.62

<sup>5</sup> Ibid paragraph 10.135

<sup>6</sup> Ibid paragraph 10.136

<sup>7</sup> Ibid paragraph 10.137

<sup>8</sup> Dr Gillon’s statement on HCV look-back [PEN.018.0410]



the care and selection of donors and to prepare a memorandum on the subject for consideration by the SNBTS Directors.<sup>9</sup>

**35.11** Around the time Dr Gillon took up his post, and following the introduction of an HIV test in late 1984, it was agreed across the UK that donor testing for HIV would be accompanied by targeted look-back, when donors tested positive on screening, from the outset. Dr Gillon assumed responsibility for this in his area, the south east Scotland region, and inherited files on the one or two historical look-back studies arising from instances where clinicians had identified an HIV-infected donor and carried out a targeted look-back.<sup>10</sup>

**35.12** By way of preparation, Dr Gillon and Dr Jan Davidson, one of the sessional medical doctors in his centre, had each spent one or two weeks at St Mary's Hospital in London with Dr Tony Pinching, who at that time had the largest cohort of HIV-positive patients in the country. Dr Pinching provided a counselling course on HIV testing at St Mary's, which Dr Davidson attended. Dr Gillon also visited the genito-urinary medicine (GUM) clinic and had discussions with microbiologists.<sup>11</sup>

**35.13** Dr Gillon and Dr Davidson shared the work of counselling blood donors found to be HIV-positive on screening. Dr Gillon took responsibility for counselling the patients who came to attention through the look-back exercise that followed identification of an HIV-positive blood donor, because the number of affected individuals was small. Dr Gillon explained that, through this work, he and Dr Davidson gained valuable experience of the sort of issues that would crop up when dealing with donors who either tested positive after donating blood or who were found to be infected through look-back.<sup>12</sup>

**35.14** Dr Gillon was later to play a significant role in the development of a local HCV look-back programme. He explained the procedure involved in reverse look-back in more detail, with reference to non-A, non-B Hepatitis (NANB Hepatitis).

**35.15** On receiving a report of NANB Hepatitis infection in the recipient of blood, blood components or products, the SNBTS would seek details of the relevant transfusion episode(s), including all of the units that were transfused, and would then identify the donors associated with the implicated blood, blood components or products and carry out investigations to see if they could find the donor(s) who had transmitted infection. This could clearly be an onerous task as all of the relevant donors would have to be recalled: sometimes there could be hundreds of donors although more often it would be a smaller number.<sup>13</sup>

**35.16** Having identified the donors possibly implicated in transmitting infection, those individuals would be called in, told there had been a problem with a patient who had received their blood (usually along with other donations) and that there was a need to investigate the source of infection. Each donor would have a full medical history taken with a view to identifying any possible risk factors and also have a liver function test performed. Before effective screening for HCV was introduced in the UK in 1991, the end result was often inconclusive, with the result that often both the donors and the SNBTS, as Dr Gillon remarked, were left 'in limbo to some extent'.<sup>14</sup>

---

<sup>9</sup> Minutes of a meeting of the SNBTS Co-ordinating Group held on 20 November 1984 [SNB.003.8945] at 8951

<sup>10</sup> Dr Gillon – Day 86, pages 7–8

<sup>11</sup> Ibid pages 9–10

<sup>12</sup> Ibid pages 8–10

<sup>13</sup> Ibid pages 1–3

<sup>14</sup> Ibid page 3

## Experience of HIV look-back in the United States

**35.17** The history of HIV look-back studies in the USA was discussed in an article by MP Busch (University of California) in the journal *Transfusion*.<sup>15</sup> The first initiative calling for notification of HIV infection had arisen from the case of the infection of the 'San Francisco child' (discussed in Chapter 11, *HIV/AIDS Aetiology*, paragraphs 11.24–11.25). The US Centers for Disease Control (CDC) sponsored and funded investigations of all reported AIDS cases in an attempt to identify infected donors and thereby trace, enrol and follow recipients of their blood. However, only a few US blood centres participated in the programme until 1985, when routine donor screening was introduced. The term 'look-back' was adopted at that point to describe the process of tracing transfusion recipients of donations triggered by screening. The procedure was expanded by some blood banks to include other methods of investigation and, according to Busch, became slow and possibly inherently inadequate. The CDC recommended that physicians should consider testing recipients of multiple units of blood or components ('general look-back').

**35.18** When antibody screening for HTLV-III (later HIV) was introduced in the USA in 1985, targeted look-back was implemented without much discussion. Busch set out to test the effectiveness of the HIV look-back programmes with specific reference to the San Francisco Bay area. He reported that it was found that the implementation of early high-risk donor education coincided with a dramatic reduction in the frequency of infected donations and, consequently, in the risk to recipients. It was estimated that approximately 90% of infected, high-risk donors self-deferred or were deferred prior to the availability of specific anti-HIV screening. A second study reported that standard targeted look-back was only minimally effective. The conclusion was that:

[T]hese studies show that the overall yield and efficacy of HIV look-back programs were poor. Standard, targeted look-back was limited, ironically, by the effectiveness of early self-exclusion measures, in that almost all of those responsible for HIV infections had stopped donating before they could be identified by anti-HIV screening.<sup>16</sup>

Additional limitations included the high death rate of recipients of infected blood together with the delay in, and logistics of, manual record searching and individual recipient tracing and notification through hospitals and private physicians.<sup>17</sup>

**35.19** Busch predicted that standard targeted HCV look-back would be enormously cumbersome and expensive and would also be ineffective for the same reason as the HIV look-back programme: the vast majority of infected former donors would already have been deferred or excluded from donation by the 'surrogate' measures in force long before the anti-HCV test became available. Those individuals would be 'invisible' to targeted look-back. Busch noted that the US Public Health Service had recently decided not to recommend anti-HCV testing of previous transfusion recipients. The reasons given were that, first, HCV was endemic in the general population, unlike HIV which was an epidemically spreading fatal infection clustered in specific regions, with transfusion of blood, blood components or blood products a major route of transmission. Secondly, sexual transmission of HIV was well documented; in contrast modes of community spread

---

<sup>15</sup> Busch, 'Let's look at human immunodeficiency virus look-back before leaping into hepatitis C virus look-back', *Transfusion* 1991; 31:655–661 [PEN.017.2307]

<sup>16</sup> *Ibid* [PEN.017.2307] at 2311

<sup>17</sup> *Ibid* [PEN.017.2307] at 2311

of HCV were much less well understood. Thirdly, therapy for HCV infection was of limited effectiveness. Fourthly, the relative risk of HCV transmission in transfusion recipients was much lower in relation to the background risk of the illness than had been the case with HIV. Lastly, there were public health financial considerations that were peculiar to the USA.

**35.20** Busch stated:

So what do we do?

....

I am convinced that the appropriate response to this situation is an aggressive education campaign for both physicians and the lay public about the risks and benefits, both in the past and the present, of transfusions.<sup>18</sup>

**35.21** He advocated a well orchestrated, long-term education campaign, targeting past and future transfusion recipients and donors, and felt that the long-term gains from committing necessarily limited resources to this would 'far outweigh' the 'minimal short-term yield of any specific HCV look-back effort'.<sup>19</sup>

**35.22** Busch's paper was published in 1991. An anti-HCV test, first available in 1989, was introduced into routine screening in the UK in September 1991.<sup>20</sup> As the article indicates, in the USA 'trace-back' followed on from well-documented cases of post-transfusion NANB Hepatitis before the isolation of HCV allowed for specific testing, using 'surrogate testing' methods. Surrogate testing by the methods adopted in the USA was not adopted in the UK, as discussed in Chapter 27, *Surrogate Testing of Donated Blood for non-A, non-B Hepatitis*. The SNBTS Directors recommended in March 1987 that surrogate testing should be introduced in 1988 (or at least considered that its introduction was inevitable).<sup>21</sup> Others in the transfusion services in Scotland and England did not support the introduction of such testing. Nor did the government health departments in Scotland or England. Irrespective of the merits of the arguments about surrogate testing, it appears to be important to note that Busch's argument against 'trace-back' relied heavily on a factor that did not apply in this country.

### The institutional arrangements

**35.23** Difficulties with the administrative control of, and responsibility for, policy in Scotland in relation to transfusion generally have been discussed in Chapter 17, *Blood and Blood Products Management*. The events discussed in this chapter provide an illustration of some of the practical problems that arose from the lack of well defined boundaries between bodies with an interest in providing advice on, and in the implementation of, look-back. It is appropriate in the first instance to note the formal position.

**35.24** There were two national (UK) advisory committees with an interest in the topic of look-back during the material time. The Advisory Committee for Virological Safety of Blood, later renamed the Advisory Committee on Microbiological Safety of Blood or Microbiological Safety of Blood and Tissue, advised Ministers of all four territorial departments of the UK. To avoid confusion, this committee will be referred to in this

---

<sup>18</sup> Ibid [PEN.017.2307] at 2313

<sup>19</sup> Ibid

<sup>20</sup> Chapter 31, *The Introduction of Screening of Donated Blood for Hepatitis C*, paragraph 31.1

<sup>21</sup> See Chapter 27, *Surrogate Testing of Donated Blood for non-A, non-B Hepatitis*, paragraph 27.160

chapter as the ACVSB/MSBT. The Advisory Committee on Transfusion Transmitted Diseases, otherwise known as the Advisory Committee on Transfusion Transmitted Infections, gave advice to the ACVSB/MSBT on transfusion-transmitted infections but did not advise Ministers directly. This committee will be referred to as the ACTTD/I.

**35.25** Nominally, statutory responsibility for the provision of blood and blood products in Scotland was devolved to the Common Services Agency (CSA). Evidence before the Inquiry, however, would suggest that for most practical purposes the SNBTS operated independently of the CSA in technical and scientific matters, in direct contact with the Scottish Home and Health Department (SHHD). An additional advisory committee, the Medical and Scientific Committee (MSC) of the SNBTS, was established in August 1990 and had its first meeting for regular business on 6 November 1990.<sup>22</sup> The MSC advised the SNBTS Board and became closely involved in the topic of look-back.

**35.26** Mr David McIntosh was Chairman and General Manager of the SNBTS from 1990 until 1996 and was responsible for the overall performance of the service at the time anti-HCV screening was introduced and the issue of look-back was under active consideration. In 1996, by mutual agreement between himself and his employers, his contract was not renewed.

**35.27** He said that, when he joined the SNBTS in 1990, it was run by the Regional Directors. They were members of a national organisation but mainly ran their own transfusion services in the major cities in Scotland independently of centrally imposed policies. All of the Directors were medically or scientifically qualified. The commonly accepted assertion of professional clinical independence meant that, within their regions, Directors could run things and make their own decisions almost as they wished, provided it conformed to the overall ethos of the SNBTS.<sup>23</sup> He found that 'none of the normal management common sense you can take for granted in most organisations outwith the public sector applied'.<sup>24</sup> Mr McIntosh described the difficulties he faced in attempting to introduce modern management practice to the SNBTS and, in particular, the resistance he encountered from the medically and scientifically qualified Directors with whom he had to deal.<sup>25</sup>

**35.28** He was asked about his role in establishing, and subsequent involvement with, the MSC. After three months with the SNBTS he recommended they set up a Medical and Scientific Committee as an advisory scientific sub-committee of the SNBTS Board in order to make a clear distinction between the medical and scientific side of the SNBTS and the managerial wing that he, as general manager, was responsible for.<sup>26</sup> His role in relation to the committee, he felt, was to help professional colleagues to come to clear conclusions on appropriate recommendations, intervening in detailed debate if asked to do so and ensuring that an appropriate, practical plan of action was prepared, authorised and implemented when decisions were reached. He assisted the members in achieving their goals by, as he put it, 'cajoling and persuading and coaching', but attended MSC meetings only occasionally.<sup>27</sup> Mr McIntosh commented that the role of the committee 'should have been to produce lucid recommendations'.<sup>28</sup> He went on to point out that

---

<sup>22</sup> Minutes of the first meeting of the SNBTS Medical and Scientific Committee on 6 November 1990 [SNB.009.5513]

<sup>23</sup> Mr McIntosh – Day 84, pages 76–78

<sup>24</sup> Ibid pages 74–75

<sup>25</sup> Ibid page 74

<sup>26</sup> Ibid pages 77–78 and 'Management of the SNBTS in the '90s – Part 1 – The Skeletal Structure' [SNB.002.4674]

<sup>27</sup> Mr McIntosh – Day 84, pages 91–92

<sup>28</sup> Ibid page 79

a public health exercise like look-back was not just about the SNBTS testing blood: it would involve the cooperation of haemophilia directors, hepatologists, GPs and hospital administrators.<sup>29</sup>

**35.29** The impression Mr McIntosh gave of his early experience was of frustrated impotence in the face of an organisation that had been in existence for 50 years, staffed by highly qualified professionals (20% of whom had PhD degrees) without ever having any expert management.<sup>30</sup> He felt that the MSC came to be 'the government in exile of the SNBTS', with precedence over 'silly little administrative people called "managers"'.<sup>31</sup> Professor Cash did not consider that Mr McIntosh's assessment of the managerial competence of the SNBTS was accurate, observing that many of the tools of modern management were already in place throughout the SNBTS when Mr McIntosh took over. He pointed out that prior to the arrival of the General Manager the service had developed successful Research and Development programmes which were internationally recognised. The size and complexity of these Service and Research Developments were of such a magnitude that their success was inevitably dependant on at least some aspects of sound modern management practice.

**35.30** Dr Mitchell and Professor Urbaniak also did not accept Mr McIntosh's suggestion that prior to his arrival there had been an absence of expert management. Professor Urbaniak noted that in about 1986 the General Manager of the CSA introduced a number of seminars and courses on management principles for all the senior officers of the CSA. The SNBTS Directors, whose responsibilities within their respective regions included budgeting and staff, attended those events. Professor Cash did not accept that Mr McIntosh had been met with collective resistance to managerial change. Dr McClelland considered that the history and managerial structure of the organisation might have resulted in certain tensions arising at a higher management level. Neither Dr Brookes nor Professor Urbaniak accepted Mr McIntosh's description of his relationship with the Regional Directors, the latter suggesting that assistance given to Mr McIntosh by the Directors due to his unfamiliarity with the public sector might have been misinterpreted by him as resistance.

**35.31** Dr Perry, whilst aware of Mr McIntosh's concerns and frustrations in connection with perceived resistance from SNBTS Directors, considered that he and the General Manager had enjoyed a productive and mutually supportive relationship which resulted in many positive developments and outcomes. Whether Mr McIntosh's assessment of the position was correct or fair is, perhaps, of less significance than the fact that he clearly believed that his management was resented and that he had little managerial authority over the affairs of the SNBTS. What is clear is that regional autonomy gave Directors the scope to adopt their own policies and that became important in the context of HCV screening generally and HCV look-back in particular.

## **Donor screening for HCV**

### *Early screening in Scotland*

**35.32** On 21 June 1990, Professor Cash wrote to Dr Gillon in anticipation of the commencement of full anti-HCV donation screening, inviting him to chair a working party to draft operational guidelines, for consideration by the SNBTS Directors, on

---

<sup>29</sup> Ibid page 81

<sup>30</sup> Ibid pages 77-78

<sup>31</sup> Ibid page 79

counselling<sup>32</sup> donors confirmed to be anti-HCV positive.<sup>33</sup> As there was a wish to see as much harmonisation north and south of the border as possible, he asked Dr Gillon to keep Dr Harold Gunson, adviser on blood transfusion to the DHSS, informed.

**35.33** As a result of the HIV exercise, the south east region of the SNBTS (the SEBTS) and other regions held extensive archives of samples of blood donations. The first archive of blood samples started in the SEBTS in the middle of 1984 and Dr Gillon said that by early 1986 all of the Scottish centres were laying down a sample of every donation. That has continued to this day and all of those samples, very many millions, are still retained, apart from those that have been used up in retrospective testing.<sup>34</sup>

**35.34** Dr Gillon's previous experience indicated that, though the numbers of donors found positive for HIV were not huge, there were some regular donors among them. The working group was aware of the experience of researchers in San Francisco, reported by Dr Busch, and knew that look-back was not an easy process.<sup>35</sup> They also knew from their own experience with HIV that HCV look-back would be difficult.<sup>36</sup> Dr Gillon said that, with a new HCV test, it was likely that within the first six months of testing a large proportion of regular donors would be processed and that there would be a 'hump' in the curve of infections found following the introduction of a new test. Dr Gillon's working party came to a unanimous decision that there should be a look-back following identification of donors found to be HCV-positive. This was recommended in its report which went to the Directors of the SNBTS for discussion.<sup>37</sup>

**35.35** The availability in 1990 of first-generation HCV tests in Scotland for validation studies, gave some indication of the number of individuals likely to be involved. Dr Eddie Follett and Dr Brian Dow (West of Scotland Blood Transfusion Service) had first-generation kits to examine and had looked at some archived samples and, Dr Gillon thought, probably some fresh donor samples as well. The numbers were daunting and gave rise to the anticipation of considerable logistical and resource issues. Dr Gillon explained that initially it looked as though 0.5–0.6% of Scottish donors would test positive for antibodies to HCV. Based on assumptions about the daily rate of donations given on weekdays, this indicated that about 10 samples a day in Scotland would test positive for HCV and it was clear that a look-back exercise based on those numbers would require extra resources. He explained that the likely requirement for extra resources was one of the reasons why he felt that the working party made an early recommendation to commence look-back by saying 'in principle we think this needs to be done'.<sup>38</sup>

**35.36** The recommendation was inconsistent with discussions that had been progressing at national (UK) level and it is appropriate to note these before returning in more detail to the output from Dr Gillon's working group.

---

<sup>32</sup> 'Counselling' in this context refers to discussions with individuals unexpectedly found on donor screening possibly to be harbouring the HCV. It has to be distinguished from the 'counselling' of NHS patients in the course of investigation or treatment discussed in Chapter 32, *An Investigation into the Systems in Place for Informing Patients about the Risks – Ethical Context*, before a blood test is taken and relating to what would follow if the result of the test were positive.

<sup>33</sup> Letter from Professor Cash to Dr Gillon dated 21 June 1990 [SNB.005.5023]

<sup>34</sup> Dr Gillon – Day 86, page 10

<sup>35</sup> See paragraphs 35.17–35.22

<sup>36</sup> Dr Gillon – Day 86, pages 14–15

<sup>37</sup> *Report for the National Medical Director – Donor Counselling: HCV*, Draft No. 4, dated February 1991 [SNB.001.8803]; Dr Gillon – Day 86, page 8

<sup>38</sup> Dr Gillon – Day 86, pages 16–17

*Discussions at the United Kingdom level*

**35.37** On 1 May 1990, Professor Cash wrote a letter to Dr Gunson headed 'HCV: Look Back'.<sup>39</sup> In the letter, Professor Cash suggested that, in advance of anticipated universal HCV testing of donations, the tests then available should be used in cases of post-transfusion NANB Hepatitis 'so that we can more readily locate "the offending donor" with a view to taking him/her off the panel'. From its terms, the letter, and Dr Gunson's reply (referred to below), related to reverse look-back as defined by Dr Gillon. Dr Gillon thought that this correspondence between Professor Cash and Dr Gunson related to reverse look-back. Professor Cash confirmed in evidence that he was not referring to targeted look-back at this stage.<sup>40</sup>

**35.38** As reflected in his evidence, Professor Cash's recollection of the background to the correspondence was poor. He said that he could not remember what specific discussions he had held with Dr Gunson at about this time. In general terms, however, he said that Dr Gunson was 'pretty unenthusiastic for a very long period of time, at the whole notion of look-back because ... for England and Wales, the nature of their structure of their transfusion services made it ... a giant of a task'.<sup>41</sup> In what appears to have been his reply to Professor Cash, Dr Gunson wrote on 21 May 1990 commenting that he was unsure whether RTCs in England and Wales would have access to anti-HCV test material and suggesting that it might be worthwhile carrying out 'the usual investigations' when a transfusion-associated NANB Hepatitis case was reported and to ensure that a library sample of serum was retained from each donor seen.<sup>42</sup> At that time, the 'usual investigations' referred to reverse look-back. The letter referred to an intended meeting on 27 June but in his oral testimony Professor Cash could not recall if the topic of look-back was, in fact, discussed when they met.<sup>43</sup> The Inquiry was left with Professor Cash's general impressions of the developing position.

**35.39** Professor Cash said that his initial response to Dr Gunson's position was to accept his reservations, at least for a while, describing his attitude as: 'Okay, we will buy it so far, Harold'. Subsequently, however, he said that he 'took this matter further'. Professor Cash was asked why he thought it was an important factor in making a decision about look-back that he had to discuss the topic with Dr Gunson and then report to the SNBTS. It was suggested to him that it should, perhaps, have been the other way round, that he should have first discussed the matter with the SNBTS Directors and then held discussions with Dr Gunson. In response, Professor Cash said that, as could be seen from contemporaneous correspondence, he did, in fact, discuss it with the SNBTS Directors and had said to them that he would start liaising with his counterparts in England and Wales: 'So it had been discussed, as I understand it, before July 1990'.<sup>44</sup>

**35.40** Professor Cash was, however, unable to recall in detail the relevant facts and circumstances that would have clarified his position on look-back at this period. He acknowledged that at this point the SNBTS did not have a general policy, saying: 'we were fishing around to explore are we really going to push this or not ...'. As noted, the SNBTS had instituted a look-back procedure for HIV and Professor Cash considered that the SNBTS ought to have at least been thinking about something similar in relation to HCV.<sup>45</sup>

<sup>39</sup> Professor Cash's letter to Dr Gunson dated 1 May 1990 [SNB.005.3102]

<sup>40</sup> Professor Cash – Day 85, page 9

<sup>41</sup> Ibid pages 9–10

<sup>42</sup> Dr Gunson's letter to Professor Cash dated 21 May 1990 [SNB.004.5010]

<sup>43</sup> Professor Cash – Day 85, pages 10–11

<sup>44</sup> Ibid page 15

<sup>45</sup> Ibid pages 11–12

**35.41** Dr Gillon provided some background information on what was happening in Scotland at the time.<sup>46</sup> As noted above, in 1990 some limited reverse look-back was being done by SNBTS doctors. However, it was on an informal and less than systematic basis. SNBTS doctors knew that Dr Follett could test 'implicated' donor samples and they would ask him to do that and follow up the results. Dr Gillon said that 'it would have been crazy not to'.<sup>47</sup> However, targeted look-back could only begin once routine donor screening was introduced across the donor population. The impression given by Dr Gillon's evidence was that practice on the ground was more varied, and in some respects and in some regions more developed, than was implicit in the correspondence between the medical directors.<sup>48</sup>

**35.42** Professor Cash's letter of 1 May 1990 to Dr Gunson was copied to the Scottish Directors, including Dr Ruthven Mitchell who was a member of the ACVSB/MSBT. In a letter dated 14 May, Dr Mitchell defined the problem from a UK perspective: whether or not the UK blood transfusion services generally (the SNBTS and the NBTS) should have a policy of identifying donors who may have transmitted disease when there had been a report of NANB Hepatitis transmission.<sup>49</sup> He noted that he had raised the issue at a recent meeting of the ACVSB/MSBT, and reported:

I have advised Bob Crawford at the present time that we have no look-back policy, although you will understand that in doing so, the Service could be considered to be negligent in not advising about potential future use of donor blood.

At this stage, therefore, look-back was not supported by blood transfusion service policy.

**35.43** Professor Cash suggested that Dr Mitchell was also signalling in this letter that, if the SNBTS did think about a look-back programme that would include the west of Scotland (where Dr Mitchell was Director), it was going to be 'a big, difficult problem'.<sup>50</sup>

**35.44** The UK policy position appears to have become further refined by early July. On 9 July 1990 Professor Cash wrote to Drs Whitrow, Urbaniak, Brookes, McClelland, Mitchell and Perry, copying the letter to Dr Gunson and Mr McIntosh.<sup>51</sup> He stated:

[I] have discussed this topic with Harold Gunson.

We both agreed the following:

(a) It would not, after we start anti-HCV donation screening, be appropriate to introduce a systematic look-back programme on previous recipients – as was done for HIV-1.

(b) It would be appropriate, in the period before routine anti-HCV donation screening commences, to examine the anti-HCV status of donors who have been implicated in a case of reported PTH [post-transfusion hepatitis].<sup>52</sup>

---

<sup>46</sup> Dr Gillon – Day 86, pages 3–5

<sup>47</sup> Ibid page 4

<sup>48</sup> Ibid pages 5–7

<sup>49</sup> Dr Mitchell's letter to Professor Cash dated 14 May 1990 [SNB.004.5009]

<sup>50</sup> Professor Cash – Day 85, pages 11–12

<sup>51</sup> Letter from Professor Cash to SNBTS Directors dated 9 July 1990 [SNB.005.3586]

<sup>52</sup> Ibid [SNB.005.3586] at 3586. Emphasis in the original.



**35.45** Professor Cash's letter to Dr Gillon dated 21 June 1990 inviting him to chair the drafting of operational guidelines was therefore written against a background of continuing debate about look-back exercises generally. By the time Dr Gillon submitted his working group's proposals, a preliminary decision had been reached at the UK level not to begin a programme of targeted look-back when donor testing for HCV commenced.

### **Draft guidelines**

#### *First draft*

**35.46** Against the background of these exchanges between the medical directors, Dr Gillon's group proceeded to prepare a draft guidelines document on donor counselling as requested in Professor Cash's letter of 21 June.<sup>53</sup> A copy of a draft was sent to Professor Cash on 20 September 1990.<sup>54</sup> The document took the form of a report to Professor Cash as National Medical Director of the SNBTS.<sup>55</sup> As indicated in the letter, an earlier draft of the guidelines had been sent to Dr Gunson for comment but by 20 September comments had not been received. Dr Gillon anticipated that the MSC would debate the guidelines.

**35.47** The draft guidelines reflected the group's view that it was important for careful consideration to be given to the provision of information to all blood donors. The draft contained detailed proposals for counselling donors found positive for anti-HCV on screening. The working group had received information that there had been practical difficulties in donor counselling in the north region and commented:

The Group therefore agreed that the extent of counselling and investigation undertaken must be at the discretion of any RTD, depending on local circumstances. It is our view that our duty is to inform the donor personally, ie at an interview with a member of SNBTS medical staff or another doctor recruited for that purpose.<sup>56</sup>

**35.48** Follow-up investigations would involve the donor's GP or a local specialist. The report also formally introduced the notion of HCV look-back:

The Group discussed the question of lookback. Donors may well ask about the outcome of their previous donations, and a clear policy on lookback is essential. We note the logistical difficulties, which have been taken as justification by the AABB [American Association of Blood Banks] for not recommending a lookback, but our view was that this position is untenable in view of the desirability of informing recipients so that they can protect others, and also receive treatment with Interferon if the benefits of this form of therapy are confirmed.<sup>57</sup>

**35.49** The final part of the report contained advice on 'informing the donor'.<sup>58</sup> Dr Gillon said that it was an attempt to be very practical. The working group was trying to describe in very clear terms what needed to be done to make the look-back work so that doctors who did not have much experience of look-back would be able to do it with little additional training. It was not envisaged that this section would be given to the patient. Rather, it

---

<sup>53</sup> Letter from Professor Cash to Dr Gillon dated 21 June 1990 [SNB.005.5023]

<sup>54</sup> Letter from Dr Gillon to Professor Cash dated 20 September 1990 [SNB.004.5074]

<sup>55</sup> Draft report for National Medical Director, *Donor Counselling: HCV*, dated 20 September 1990 [SNB.005.3647]

<sup>56</sup> *Ibid* [SNB.005.3647] at 3649

<sup>57</sup> *Ibid* [SNB.005.3647] at 3650

<sup>58</sup> *Ibid* [SNB.005.3647] at 3654

would be used by the doctor to impart information and was framed as a set of potential questions and suggested answers.<sup>59</sup>

**35.50** One of the questions a donor found to be infected might ask of a consultant, Dr Gillon noted, was 'what about my previous donations?'. The guidelines provided possible answers to this question together with general advice:

The recipients of previous donations will be traced and their Consultants or GPs informed. We hope to obtain results of any tests carried out. However, it may cause distress to the donor to discuss this matter in any detail. A general comment suggesting that we are going to check to see that the recipients are alright, that they get any treatment they may require, should be sufficient.<sup>60</sup>

**35.51** Dr Gillon said that this was a reference to targeted look-back.<sup>61</sup> As indicated above, this proposal was at variance with the policy position agreed between Professor Cash and Dr Gunson.

***First draft: reception and reaction***

**35.52** Professor Cash said that he realised when he read the draft guidelines that Dr Gillon was advocating a look-back policy. He did not accept that it was an expression of SNBTS policy. Rather, it was a proposal from Dr Gillon's working group which was delivering the view that the SNBTS needed to do a look-back. He considered that it was an issue that the SNBTS needed to think about carefully.<sup>62</sup>

**35.53** Professor Cash circulated the report prepared by Dr Gillon's group to Dr Perry and the Regional Directors, Dr Brookes, Dr McClelland, Dr Mitchell, Dr Urbaniak and Dr Whitrow, on 4 October 1990 with a copy to Mr McIntosh for information.<sup>63</sup> The letter asked the Directors to review the report before the MSC meeting on 6 November 1990.

**35.54** Dr Gillon was not a member of the MSC, but attended part of the meeting on 6 November to present his guidelines document. As the minutes of the meeting make clear, the report was discussed before he joined the meeting.<sup>64</sup> Dr Mitchell is reported to have advised that 'Dr Gunson was anxious to take this Gillon document to the National Advisory Committee in the near future'.<sup>65</sup> Dr Gillon then joined the meeting and gave a brief summary of the report, following which there was lengthy discussion. Dr Gillon did not have a clear memory of the discussion about the guidelines. He drew attention to paragraph 10 of the minute, headed 'HCV Look-Back', which recorded that:

After discussion it was agreed that Professor Cash should write to the Chairman of the DoH Advisory Committee on the Virus Safety of Blood, asking that careful consideration be given to the matter of HCV look back of recipients of previous donations.<sup>66</sup>

---

<sup>59</sup> Dr Gillon – Day 86, pages 20–21

<sup>60</sup> Draft report for National Medical Director, *Donor Counselling: HCV*, dated 20 September 1990 [SNB.005.3647] at 3656

<sup>61</sup> Dr Gillon – Day 86, page 21

<sup>62</sup> Professor Cash – Day 85, pages 23–24

<sup>63</sup> Letter from Professor Cash's PA to SNBTS Directors dated 4 October 1990 [SNB.005.3646]

<sup>64</sup> Minutes of the first meeting of the SNBTS Medical and Scientific Committee on 6 November 1990 [SNB.009.5513] at 5516–17

<sup>65</sup> *Ibid* [SNB.009.5513] at 5516

<sup>66</sup> *Ibid* [SNB.009.5513] at 5519

**35.55** Dr Gillon said that decision was a reference to targeted look-back. His recollection was that the MSC at this stage had a generally positive attitude to targeted look-back. However, he thought that there were some people who had reservations, particularly in the west of Scotland, where, as Professor Cash had noted, the size of the region and number of people involved could pose logistical problems. He recalled that even Dr Crawford, who was a member of the working party which had put forward the recommendations, was 'very leery' of look-back because of the amount of work it would create. Dr Gillon felt that the answer to that was to provide more resources: he and his colleagues would need secretarial help. He did not consider that they were talking about a vast amount of money but they knew that they would need extra funds to carry out the work.<sup>67</sup>

**35.56** It was agreed by the Committee that Dr Gillon should re-draft the document:

- (i) In a format which was that of professional/operational guidelines.
- (ii) That counselling information which all HCV confirmed positive donors would be advised was clearly delineated.
- (iii) That thereafter a series of supplementary questions/answers were made available.
- (iv) That consideration be given to including information on the treatment of HCV hepatitis and the issue of safe sex.<sup>68</sup>

**35.57** Dr Gillon agreed to prepare a draft Standard Operating Procedure based on the report by 30 November 1990 for submission to the members of the MSC for their consideration.<sup>69</sup>

**35.58** Dr Gillon recalled that Professor Cash wrote to him and said that the guidelines were 'very well received' and that the Scottish Directors had accepted them and that he would be sharing them with colleagues in England and discussing it with them.<sup>70</sup>

**35.59** In his oral evidence, Professor Cash was initially unable to recall what his own attitude was to look-back at that point although he thought that he was 'enthusiastic', though not without reservation.<sup>71</sup> He went on to say that he was a 'strong supporter of look-back' but that his reservations related to the absence of treatment for HCV at the time: 'I was very warmly in favour [of the idea of look-back], but I wasn't prepared to push it until I had some good evidence ... that there was a treatment option'. He thought this was 'a very interesting philosophical issue' and that his attitude probably reflected attitudes common at the time: 'I had been brought up in a different era, in which doctors should do their best, as part of their caring, to filter in some way stuff that really they didn't feel the patient needed to know'.<sup>72</sup> As discussed in Chapter 32, *An Investigation into the Systems in Place for Informing Patients about the Risks – Ethical Context*, the approach of the medical profession to patients up to at least the mid-1980s was generally 'paternalistic' in nature, and only progressively less so in the early 1990s. As presented in evidence, Professor Cash's reservations may reflect that stance when he said: 'if you haven't got some good news for the patient, i.e., "We have got some treatment here that can be of serious benefit to you," ... loading a lot of innocent people with bad news,

---

<sup>67</sup> Day 86, pages 22–25

<sup>68</sup> Minutes of the first meeting of the SNBTS Medical and Scientific Committee on 6 November 1990 [SNB.009.5513] at 5517–18

<sup>69</sup> Ibid [SNB.009.5513] at 5517

<sup>70</sup> Dr Gillon – Day 86, page 22

<sup>71</sup> Professor Cash – Day 85, page 26

<sup>72</sup> Ibid

unnecessarily, is not a good thing to do'.<sup>73</sup> However, as Dr Gillon pointed out, the lack of treatment for HIV was not considered sufficient reason for not introducing targeted HIV look-back in the mid-80s.<sup>74</sup>

### **Perceptions at the United Kingdom level**

**35.60** Following the MSC meeting of 6 November 1990, Professor Cash wrote to Dr Jeremy Metters, Deputy Chief Medical Officer at the Department of Health (DoH) and Chairman of the ACVSB/MSBT. The letter, headed 'HCV: Donation Testing: Look back',<sup>75</sup> said that the SNBTS Directors had asked Professor Cash to write requesting that the ACVSB/MSBT consider a policy of look-back in anticipation of the commencement of testing blood donations for HCV throughout the UK. In oral evidence, Professor Cash said that he had come to the conclusion that look-back was something about which the SNBTS ought to 'touch base' with the advisory committee, although he was not sure whether he had come to this conclusion because of discussions with Dr Gunson or SNBTS colleagues. He explained that it was important to him that Dr Archibald McIntyre, SHHD, Dr Mitchell and Dr Perry received a copy of the letter because they sat on the ACVSB/MSBT. They had been briefed and knew that the Scottish Directors were very keen that look-back should be discussed.<sup>76</sup> In its terms, the letter appears to follow the decision of the MSC of 6 November, though with less specification of the interest of the members of the committee.

**35.61** Professor Cash explained that the reason he wanted the ACVSB/MSBT to consider the question of look-back was because he was of the view that initiating look-back would require the Chief Medical Officer (CMO) to instruct the Regional Health Authorities in England and Wales and the Health Boards in Scotland and because it would require the active collaboration of clinicians and peripheral laboratories. He stated that 'the only route we had at that time, that I am aware of, to get into ministerial approval was the Metters committee'.<sup>77</sup>

**35.62** At this stage, it is important to note that the precise sequence of events is less than clear. The ACTTD/I met on 8 January 1991.<sup>78</sup> There was extensive discussion of the procedures to be put in place for anti-HCV screening. Dr Gillon's paper was discussed, as was a paper by Dr Contreras. Dr Gillon agreed that he would amend his paper in the light of written comments he was to receive from Dr Contreras and others. It was noted that arrangements should be made for counselling donors reported to be positive by recombinant immunoblot assay (RIBA) and subsequently confirmed as positive by a polymerase chain reaction (PCR) test. In further discussion, it was agreed that:

[T]here may be an ethical obligation to inform patients who may have received transfusions in the past from anti-HCV positive donations. This will involve considerable additional work including testing of library samples and will have to be funded. Extension of this to epidemiological investigations should be the subject of separate research studies.<sup>79</sup>

---

<sup>73</sup> Ibid

<sup>74</sup> Dr Gillon – Day 86, page 98

<sup>75</sup> Professor Cash's letter to Dr Metters dated 22 November 1990 [SNB.004.4388]

<sup>76</sup> Professor Cash – Day 85, pages 25–26

<sup>77</sup> Ibid pages 29–30

<sup>78</sup> Minutes of meeting of UK Advisory Committee on Transfusion Transmitted Diseases on 8 January 1991 [SNB.001.8770]

<sup>79</sup> Ibid [SNB.001.8770] at 8773

**35.63** After its meeting on 6 November 1990, the MSC next met on 19 February 1991. In relation to donor counselling, the minutes of the meeting state:

The Committee examined Dr Gillon's final draft document, which had been previously circulated and agreed it was excellent. The Committee proposed and agreed that the latter pages be used as Guidelines in leaflet form for use by the RTCs.

In the light of national events, it was agreed no "Look Back" should be introduced at present.<sup>80</sup>

From the terms of the minutes it appears that intelligence was available that there had been a decision at the UK level that HCV look-back should not be implemented. The ACVSB/MSBT had last met on 21 November 1990. It would next meet on 25 February 1991.<sup>81</sup> It could not have been involved, as a committee, in articulating objections to screening on grounds of 'national events'. The Inquiry has not uncovered any record of 'national events' leading to an agreement that look-back should not be introduced at that stage.

**35.64** Professor Cash was unable to recall what the 'national events' referred to were. He said it was possible that 'signals' had been made through Dr Gunson to him indicating that the ACVSB/MSBT was minded to reject look-back at their next meeting, as discussed below, and that he had reported this to his colleagues.<sup>82</sup> He later suggested that he may have spoken with Dr Gunson directly in advance of the MSC meeting and become aware that 'look-back was not a runner at the moment'.<sup>83</sup>

**35.65** Professor Cash also said that he could not recall whether there had been much discussion about the advisability of proceeding with look-back at the MSC meeting, beyond what is recorded in the minutes. He did not accept that he would have gone to the meeting and simply explained that, because it appeared that look-back was not going to proceed in England and Wales, he did not think it would be possible to do look-back in Scotland. He thought it more likely that he thought that it would be necessary to 'get more ammunition' to press the case for action in Scotland.<sup>84</sup>

**35.66** The ACVSB/MSBT held its ninth meeting on 25 February 1991.<sup>85</sup> The events leading up to that meeting are discussed in detail in Chapter 31, *The Introduction of Screening of Donated Blood for Hepatitis C*. On 21 November 1990 the ACVSB/MSBT had sufficient information about the test kits then available, manufactured by Ortho and Abbott, to conclude, on Dr Gunson's advice, that the kits could be 'deemed' to be satisfactory for routine use.<sup>86</sup> The committee concluded that a combination of RIBA and PCR tests would provide a confirmatory service and agreed that it was important to start screening as soon as possible.<sup>87</sup> A full submission was sent by the DoH to Ministers on 21 December 1990.<sup>88</sup> Discussion of the delay that then occurred in processing Ministerial consideration of the issue need not be repeated here. What is relevant is that, as time passed, the emphasis shifted to the need for 'proper' evaluation of the second-generation Abbott and

---

<sup>80</sup> Minutes of meeting of the SNBTS Medical and Scientific Committee on 19 February 1991 [SNB.009.5668] at 5671

<sup>81</sup> Minutes of meeting of the Advisory Committee on the Virological Safety of Blood on 25 February 1991 [SNB.001.8934]

<sup>82</sup> Professor Cash – Day 85, page 33

<sup>83</sup> Ibid page 41

<sup>84</sup> Ibid pages 34–35

<sup>85</sup> Minutes of meeting of the Advisory Committee on the Virological Safety of Blood on 25 February 1991 [SNB.001.8934]

<sup>86</sup> Minutes of meeting of the Advisory Committee on the Virological Safety of Blood on 21 November 1990 [SNF.001.1777] at 1778

<sup>87</sup> Ibid [SNF.001.1777] at 1780

<sup>88</sup> Submission dated 21 December 1990 [SGH.002.7893]

Ortho kits that were expected to become available in July 1991.<sup>89</sup> Abbott had launched their second-generation test on 8 April 1991.<sup>90</sup> More widely, financing the introduction of screening had increasingly become recognised as a problem for health authorities in England and Wales. The start date for screening of 1 September 1991 was adopted against that background.

**35.67** On 25 February 1991 the ACVSB/MSBT understood that licensing of the second-generation kits by the US Food and Drug Administration (FDA) had not been completed, that issues over patent rights had not been resolved and that further tests might identify new markers of infection.<sup>91</sup> There was an air of uncertainty about the screening kits that might be selected. All 10,000 of the archived samples already tested were to be re-tested by second-generation kits.<sup>92</sup> Funds for continued testing were to be sought by RTCs through normal channels.

**35.68** At the meeting, Dr Mitchell reported orally on the discussions at the recent meeting of the ACTTD/I, and in particular on the procedures for anti-HCV testing.<sup>93</sup> In relation to look-back, paragraph 14 of the minutes of the ACVSB/MSBT meeting states:

The Committee discussed the problems of look-back and recommended that it should not be undertaken as a service, leaving the option for those carrying out research. However, all cases of post-transfusion hepatitis should continue to be investigated.<sup>94</sup>

The reasons for this recommendation were not minuted. The second sentence appears to support reverse look-back, leaving it unclear whether the first sentence relates to all forms of look-back.

**35.69** Professor Cash explained that the phrase 'not undertaken as a service' meant that look-back would not be a routine part of the Blood Transfusion Service delivery. Asked if this applied to all blood transfusion services throughout the UK, Professor Cash replied that it was his understanding that the Ministers who were being advised by this committee included Scottish Ministers, although that did not necessarily prevent Scotland 'doing their own thing'.<sup>95</sup>

### *The position of the Scottish Home and Health Department*

**35.70** There was no direct evidence available to the Inquiry of the position adopted by the SHHD at this stage. Dr Aileen Keel, Acting Chief Medical Officer for Scotland at the time of this Report, was appointed a Senior Medical Officer in the SHHD in March 1992 and was, therefore, not in office at the material time in 1990 and 1991 when targeted look-back was first discussed. She commented on the documentary evidence available from the earlier period and from her personal experience from 1992 onwards.

---

<sup>89</sup> See Chapter 31, *The Introduction of Screening of Donated Blood for Hepatitis C*, paragraph 31.511

<sup>90</sup> Preliminary Report, paragraph 9.263 narrates Abbott's launch of their second-generation anti-HCV ELISA on 8 April 1991. See also Dr Gillon – Day 86, pages 41–42

<sup>91</sup> Minutes of meeting of the ACVSB on 25 February 1991 [SNB.001.8934] at 8936–37

<sup>92</sup> *Ibid* [SNB.001.8934] at 8938

<sup>93</sup> *Ibid*

<sup>94</sup> *Ibid* [SNB.001.8934] at 8939

<sup>95</sup> Professor Cash – Day 85, pages 31–32

**35.71** Dr Keel was referred to the minutes of the meeting of the ACVSB/MSBT held on 25 February 1991.<sup>96</sup> Dr McIntyre, who was the Principal Medical Officer with responsibility for laboratories and blood transfusion when Dr Keel joined the department, was an observer at that meeting. When Dr Keel was appointed she took over responsibility for those areas and she thought that Dr McIntyre would probably have briefed her about previous meetings.<sup>97</sup> As noted above, the minutes of this meeting of the ACVSB/MSBT recorded the decision not to proceed with look-back.<sup>98</sup>

**35.72** Dr Keel agreed that the effect of the decision was that the advice to Ministers was that look-back should not be pursued. She was referred to an SHHD minute from Dr McIntyre to Mr Panton dated 10 July 1991.<sup>99</sup> Mr Panton was one of her policy colleagues who reported to Mr George Tucker, Assistant Principal, and was a key policy colleague in relation to look-back. The minute referred to a copy of recommendations for counselling HCV-positive donors, presumably Dr Gillon's working group document. Dr McIntyre was concerned with the comment in the minute that look-back would be initiated 'in accordance with SNBTS policy'. He queried whether look-back would be a good idea, because at that stage it was not clear whether those testing positive would have been infectious. He also commented: 'In certain circumstances it could also give rise to litigation and it may be that you would wish to discuss this particular point with our Solicitors before this policy is put into effect'. Although Dr Keel acknowledged that, from this memo, it appeared that Dr McIntyre was concerned that look-back might give rise to litigation, she could not remember this being an issue that was particularly stressed in discussions about HCV look-back at that time. The main memory that she had was that look-back 'wasn't considered feasible, that logistically it would be too difficult to undertake, rather than any major concerns around litigation'.<sup>100</sup>

**35.73** Professor Cash said he had no memory of concern within the Scottish Office at the time that look-back could give rise to litigation and did not consider that this was a factor that was taken into account when deciding about implementing look-back at this time.<sup>101</sup>

**35.74** So far as the evidence available to the Inquiry discloses, the SHHD position around mid-1991 was that targeted look-back had been advised against by the ACVSB/MSBT. There was no evidence that it was a 'live issue' for administrators in advising Ministers.

### **Reaction in the south east Scotland region to the Medical and Scientific Committee's decision of 19 February 1991**

**35.75** Professor Cash wrote to Dr Gillon on 12 March 1991 informing him that the MSC had agreed to the proposal that the latter pages of the draft guidance (those containing guidance on practice at RTCs) should be used nationally as guidelines in leaflet form within the RTCs.<sup>102</sup> However, he commented that 'in the light of national events' (a phrase repeated from the MSC meeting minutes of 19 February), the section answering the question, 'What about my previous donations' and implying that look-back would be implemented, 'should be omitted from the final document'. Professor Cash agreed that that comment was made because of the stated attitude of the ACVSB/MSBT.<sup>103</sup>

---

<sup>96</sup> Minutes of meeting of the ACVSB on 25 February 1991 [SNB.001.8934]

<sup>97</sup> Dr Keel – Day 86, page 109

<sup>98</sup> Minutes of meeting of the ACVSB on 25 February 1991 [SNB.001.8934] at 8939

<sup>99</sup> Minute from Dr McIntyre to Mr Panton dated 10 July 1991 [SGF.001.2163]

<sup>100</sup> Dr Keel – Day 86, pages 110–112

<sup>101</sup> Professor Cash – Day 85, pages 46–47

<sup>102</sup> Professor Cash's letter to Dr Gillon dated 12 March 1991 [SNB.005.1689]

<sup>103</sup> Professor Cash – Day 85, pages 40–41

**35.76** Dr Gillon said that, at the time, he had no idea what the phrase ‘in light of national events’ meant. He thought that he must have understood that there was disagreement in England about doing look-back. He did not recall ever being given an explanation by Professor Cash as to why the section relating to look-back had been omitted from the final draft. He thought that he would have understood it to be largely a resource issue but he knew that there were also some people in London who disagreed with look-back for ethical reasons: some clinicians had doubts about going ahead with look-back when affected patients could not be offered anything in the way of specific treatment. Despite an emerging body of evidence at this time about possible treatment with Interferon, his own 1990 guidelines having referred to it, Dr Gillon recalled that, if there was an ethical objection to look-back, it was ‘usually couched in terms of no treatment being available’.<sup>104</sup>

**35.77** Dr Gillon noted that by March 1991 second-generation tests were becoming available which were both more specific (that is, had a low false positive rate) and more sensitive (that is, had a low false negative rate) and would pick up more true instances of HCV infection. Initial evaluation exercises suggested that the number of people affected might reduce tenfold. He also noted that, around the turn of the year 1990–91, a confirmatory test for HCV (a PCR test) was in the later stages of development and that it was available for use by September 1991, when routine screening for HCV in blood donation began. Thanks to the innovative work of Professor Peter Simmonds, Scotland was one of the very few countries, and possibly the only country, that had PCR testing as part of their confirmatory process right from the start.<sup>105</sup>

**35.78** Dr Gillon said that when he received the letter from Professor Cash in March 1991 he was ‘pretty appalled’.<sup>106</sup> He believed that the MSC had agreed, at least in principle, to implement look-back. He was confident that, from an ethical point of view, it was right to proceed with look-back and he felt strongly that the health service should be doing look-back from the point when donor screening for HCV commenced, as had been the case when HIV screening was introduced. He felt that, even if there was difficulty in coping with the number of people involved or the reliability of test kits, the attempt should at least be made. If more resources were required, these should have been sought. He said that he was willing to debate the question with anybody. He did not have an opportunity to debate it with Professor Cash other than being at meetings such as the MSC where it had seemed to him to have been accepted that look-back should be implemented. He explained that it came as a bit of a surprise that Scotland was not going to be doing look-back.<sup>107</sup>

### **Screening technology: England and Wales and Scotland compared**

**35.79** Dr Graeme Alexander was asked by the Inquiry to comment on the introduction of the test for HCV antibodies in England and Wales and, later, the eventual introduction of the UK-wide HCV look-back programme in 1995. Dr Alexander was involved in the UK-wide look-back exercise as Chairman of the Hepatitis C Virus Steering Group, a body set up to ensure that the look-back strategy was managed ‘efficiently and effectively and in line with ethical standards’. A database was developed over time for research purposes, for those involved directly with the steering group and other people in the UK

---

<sup>104</sup> Dr Gillon – Day 86, pages 29–30

<sup>105</sup> Ibid pages 34–35

<sup>106</sup> Ibid page 31

<sup>107</sup> Ibid pages 31–32



with an interest in this area of research.<sup>108</sup> It is important to bear in mind that, although he became closely involved in the implementation of look-back in the UK as a whole, Dr Alexander's evidence of the background to the exercise reflected the experience of an English practitioner and was, in some respects, in marked contrast to Dr Gillon's evidence.

**35.80** Dr Alexander said that, when screening for HCV was introduced in England in September 1991, it was performed with a 'first generation' enzyme-linked immunosorbent assay (ELISA) kit. This assay proved to be both insensitive and non-specific (that is, gave rise to a large number of both false negative and false positive results) and a great deal of skill was required to ensure that the tests were interpreted appropriately. In particular, the false positive rate was between 50% and 70% when a low-risk population, such as blood donors, was screened.<sup>109</sup> So far, experience was similar to that described by Dr Gillon above; in Scotland also, the first-generation kits produced a very high rate of false positive results.

**35.81** Dr Alexander continued:

Within 18 months or so these tests were replaced by second generation ELISAs. At this point ... it was agreed generally that a second RIBA test ... should be performed before telling patients that they were positive for HCV.<sup>110</sup>

**35.82** The RIBA was often described as a 'confirmatory test' but Dr Alexander noted in oral evidence that the RIBA was really the same test as the ELISA, using the same proteins but performed using a different method. Nevertheless, it made practitioners more confident they had the correct test result for their patients.<sup>111</sup>

**35.83** Despite their obvious deficiencies, Dr Alexander thought that the early anti-HCV tests were a major breakthrough for clinicians in the management of HCV infection. Even the early kits with poor specificity and sensitivity were of considerable use in monitoring higher-risk groups (such as haemophilia patients, transplant patients and post-transfusion patients). In his evidence, he observed: 'if a patient was likely to be at risk of catching Hepatitis C, then the test was probably more valuable than in a patient who was picked randomly from the street who wasn't at risk'.<sup>112</sup> In his statement he noted: 'The correct approach to using the first generation tests was circumspection and careful review'.<sup>113</sup>

**35.84** Dr Alexander told the Inquiry what would happen to a donor who tested positive for HCV with the early assays:

If after 1991 a donor was found to be positive for HCV the donor was informed by the transfusion service and a recommendation was made to the general practitioner that the patient should be followed up by a hepatologist or a gastroenterologist with an interest in hepatology; for almost all transfusion centres in the UK at that time there was a list of named hepatologists who could be contacted.<sup>114</sup>

---

<sup>108</sup> Dr Alexander's statement on HCV testing [PEN.018.1360] at 1364

<sup>109</sup> Ibid [PEN.018.1360]

<sup>110</sup> Ibid [PEN.018.1360]

<sup>111</sup> Dr Alexander – Day 85, pages 117–118

<sup>112</sup> Ibid page 116

<sup>113</sup> Dr Alexander's statement on HCV testing [PEN.018.1360] at 1360

<sup>114</sup> Ibid [PEN.018.1360] at 1362

**35.85** Blood donors were tested prospectively. HCV-positive donors were only picked up if they returned to donate blood after the introduction of testing. At the same time people were discouraged from donating blood if they belonged to a 'high-risk group' (such as those who had a history, no matter how remote, of injecting drug use and practising homosexuals) for the safety of potential recipients, particularly following the AIDS period. As Busch had discovered in his review of HIV look-back in San Francisco, high-risk donor education programmes could lead to a dramatic reduction of infected donations as donors in high-risk groups self-deferred. Donors who had given blood in the past and were HCV positive and who did not attend after the introduction of screening in September 1991 (perhaps, high risk donors who had self-deferred) were not identified and neither were any of their corresponding recipients.<sup>115</sup>

**35.86** Dr Alexander's practice was to follow up donors with equivocal anti-HCV test results until third generation tests were introduced, at which point he explained that almost all of the patients in the group who had been followed up (nearly 200 at one stage) were found to be unequivocally negative for HCV and were no longer followed up.<sup>116</sup>

**35.87** Dr Alexander's account of the timetable of introduction of the successive stages of testing was challenged by Dr Gillon, who did not accept the section of Dr Alexander's report dealing with the use of first-generation tests in donor screening in September 1991. Dr Gillon said that he did not think that this was correct; he did not think that in any part of the UK a first-generation test was used at that stage.<sup>117</sup>

**35.88** As discussed more fully in Chapter 31, *The Introduction of Screening of Donated Blood for Hepatitis C*, a full test of second-generation kits was in operation in Scotland in the summer of 1991. Finance for the introduction of routine screening in English and Welsh regions was problematical. While on one view one can understand Dr Gillon's reservations, the position appears to be that some regions in England and Wales probably had not taken any steps to introduce screening at all, even on a research basis, prior to September 1991. Dr Alexander spoke from personal experience of the position in England and Wales and his evidence is accepted that, given the variation among regions in that part of the UK, first-generation ELISA tests were in use, at least in some regions, for up to 18 months after September 1991, notwithstanding that the second-generation test had become available in April 1991.<sup>118</sup>

**35.89** Scotland's position was privileged, not only in comparison with England and Wales, but internationally. In 1991 the USA was still screening with first-generation kits which had a high false positive rate.

**35.90** Dr Gillon noted that the screening and follow-up of the 200 individuals mentioned by Dr Alexander was carried out with an ELISA test and RIBA 'confirmatory' test, but without the benefit of PCR testing, which was developed in Scotland by Professor Simmonds. He explained that the RIBA confirmatory test could be very difficult to interpret; there was a category of results which was referred to in Scotland as 'indeterminate' where there might be limited evidence of positivity. The SEBTS did a lot of work with Professor Simmonds and some of these intermediate positives were shown to have a true positivity by PCR testing.

---

<sup>115</sup> Ibid [PEN.018.1360] at 1362 and Day 85, page 125

<sup>116</sup> Ibid [PEN.018.1360] at 1360

<sup>117</sup> Dr Alexander – Day 86, page 39

<sup>118</sup> Referred to in the chronology set out in the minutes of the meeting of the ACTTD ad hoc group on HCV antibody testing of blood donations held on 13 September 1991 [SNB.001.8919] at 8920. See also Day 86, pages 41–42

In Scotland, Dr Gillon's colleagues were able to 'drill' into the indeterminates using PCR. In England and Wales they would have simply remained equivocal. Dr Gillon agreed that, with the help of Professor Simmonds, his group was in a privileged position because they had access to PCR testing from 1991, in marked contrast to the position described by Dr Alexander.<sup>119</sup> Dr Alexander noted:

Around 1993 and 1994 the majority of centres with a particular interest in HCV infection had introduced PCR testing, often in house, to identify the presence of HCV RNA in blood and tissue. These were of variable quality and not available to all.<sup>120</sup>

**35.91** Taking the evidence of Dr Alexander and Dr Gillon together, it appears that Scotland had significant advantages over at least parts of England and Wales in September 1991 that would have been relevant to commencing look-back following the introduction of donor screening:

- All Scottish RTCs had access to second-generation ELISAs and RIBA confirmatory tests. In contrast, for up to 18 months after September 1991 some regions in England and Wales continued to be dependent on first-generation ELISAs and RIBA confirmatory tests.
- Highly effective PCR testing was available in south east Scotland in particular from the beginning of routine donor screening in September 1991 but PCR tests of variable quality only reached the majority of those centres in England and Wales that had a particular interest in HCV infection around 1993 and 1994.

**35.92** In using second-generation tests with ready availability of PCR testing, the SEBTS had exceptional technology, possibly unique in the UK, available to undertake look-back from the outset of donor testing in September 1991.

### **Scotland's ability to take unilateral action on look-back**

**35.93** Given the wide differences in the ability to implement look-back as described in the discussion so far, there was inevitably a question for the Inquiry as to whether Scotland could, and should, have proceeded to implement look-back at its own pace, irrespective of the difficulties English and Welsh colleagues might have experienced in following suit. As discussed below at paragraph 35.178, the legal position was resolved in December 1994 when Lord Fraser of Carmyllie, Minister of State at the Scottish Office covering home and health affairs, informed the Parliamentary Under Secretary of State at the DoH that, in the light of the medical and legal advice, he had little choice but to carry forward general look-back. His decision related to Scotland alone.<sup>121</sup>

**35.94** Lord Fraser of Carmyllie was Lord Advocate in 1991. He was succeeded by Lord Rodger of Earlsferry in 1992. It is extremely unlikely that, while the circumstantial context may have changed in the interval, the general principles on which legal advice available to Scottish Ministers was based would have changed between 1991 and 1994.

---

<sup>119</sup> Dr Gillon – Day 86, pages 39–41

<sup>120</sup> Dr Alexander's statement on HCV testing [PEN.018.1360]

<sup>121</sup> Lord Fraser's letter to Mr Tom Sackville MP dated 22 December 1994 [SNB.008.4848]

**35.95** Professor Cash stated that he was never prepared to accept ‘the notion that England can’t do it and therefore we can’t do it’.<sup>122</sup> He saw great advantages in ‘doing all sorts of things together’ when possible but said that ultimately it was up to Scottish Ministers to make the decision for Scotland, although he accepted that the decision of the Scottish Ministers would be based on advice from the SNBTS. He also accepted that at this point the SNBTS policy was not to institute a look-back programme.<sup>123</sup>

**35.96** There is a wider context that may have had a bearing on events. As discussed in Chapter 31, *The Introduction of Screening of Donated Blood for Hepatitis C*, at paragraphs 31.265–31.266, the demands for blood expected to arise from the first Gulf War had persuaded Professor Cash that anti-HCV testing could not begin until the Gulf conflict had ended or SNBTS personnel had shown that they could cope with the demands of the military and testing at the same time. Dr Gillon was a member of the committee working on preparations for the war. The SHHD had commandeered a hangar at Edinburgh Airport and his RTC was filling it with blood and making preparations for receiving wounded soldiers. He agreed that the opaque expression ‘national events’ might have been a reference to the preparations for the war.<sup>124</sup> The Gulf conflict, however, ended on 28 February 1991. At most it would have had an indirect, and reducing, impact on the capacity of the SNBTS to handle testing or look-back thereafter. Dr Gillon’s alternative explanation, that the expression in Professor Cash’s letter related to English reluctance to embark upon the programme in consequence of their resource difficulties, is more cogent.<sup>125</sup>

**35.97** There is no question as to whether Scotland *could* have proceeded unilaterally to implement Dr Gillon’s proposals, accepting that there was a compelling ethical obligation to inform patients who might have received infected transfusions. The critical question, whether the service *should* have proceeded with look-back before it did so, is considerably more complex. In the end, the advice Lord Fraser received relied on medical as well as legal factors. Dr Keel confirmed that Lord Fraser was given advice by policy colleagues, medical experts and legal advisors. This was the advice upon which he based his observation that look-back was no longer simply a matter of policy but of ‘legal liability’, and that it should begin as soon as possible in Scotland. The ability to treat patients became one factor among others. The decisions taken were clearly influenced by the actions Dr Gillon and his colleagues took following rejection of the proposal for general look-back. It is appropriate to discuss those actions first.

### **The south east initiative**

**35.98** The rejection of the proposal for a targeted look-back programme in parallel with the introduction of screening for anti-HCV was not welcomed by the transfusion service in the SEBTS and Dr Gillon in particular, as indicated by the evidence already noted.

**35.99** Dr Gillon could not remember precisely what discussions he had with Dr Brian McClelland, Director of the SEBTS, but he remembered saying to him, some time between March 1991 and the introduction of routine HCV testing in September 1991, ‘Right, I am going to be doing this [look-back] and I hope you will support it’, and that Dr McClelland

---

<sup>122</sup> Professor Cash – Day 85, page 35; Compare Professor Cash’s evidence on the introduction of HCV screening set out in Chapter 31, *The Introduction of Screening of Donated Blood for Hepatitis C*.

<sup>123</sup> Professor Cash – Day 85, pages 35–37

<sup>124</sup> Dr Gillon – Day 86, page 43

<sup>125</sup> *Ibid* page 29

said he would support it.<sup>126</sup> Dr Gillon could not recall whether this was formally fed back to Professor Cash and he had no record of either he, or Dr McClelland, having written to the Medical Director, although he did think that they would at least have had a conversation about their intentions. He could not recall any specific discussions with other SNBTS members about his plans but recalled that the matter was discussed at a meeting of the SNBTS Donor Consultants' Group.<sup>127</sup> He did not feel that he was 'hiding' the fact that he was intending to begin look-back in the SEBTS area.<sup>128</sup>

**35.100** Dr Gillon accepted that the whole idea of HCV look-back was a contentious issue at the time. He said that, before the start of screening in September 1991, look-back was an issue which was being debated by people in the blood transfusion community in the UK and internationally. He and his colleagues went to international meetings every year and the topic was frequently discussed. Other than a 'few relatively small countries', including the Netherlands, most countries appeared to be against the idea. Dr Gillon suggested that the reluctance on the part of the USA to introduce HCV targeted look-back was probably influential in this regard.<sup>129</sup>

**35.101** Between March 1991 and a symposium in Edinburgh on HCV in October 1993 (discussed below), the debate about targeted look-back was ongoing in the blood transfusion community. Dr Gillon thought that the debate probably took a back seat to some extent because the introduction of universal HCV testing of blood donations was a major preoccupation: the work of getting it in place, developing confirmatory procedures, dealing with false positives and counselling the patients who had tested positive would have kept people 'pretty busy'.<sup>130</sup>

**35.102** Dr Gillon confirmed that he took the decision to proceed with look-back in the knowledge that he would not be using a first-generation test.<sup>131</sup> Using second-generation tests alongside confirmatory PCR testing, it became apparent that the original estimate of 0.5–0.6% of donors who would require to be followed up was reduced to less than 0.1%.<sup>132</sup> There was confidence that, by that stage, if a virologist using PCR stated that a donor was HCV-positive it was likely that the diagnosis was correct. A paper published by Dr Gillon's group following the first six months' experience in south east Scotland reported 20 HCV-positive donors, a number considerably smaller than the less reliable first-generation tests would have produced.<sup>133</sup>

#### *Implementation of the south east initiative: donor call-up and counselling*

**35.103** Dr Gillon said that in September 1991 he simply went ahead with targeted look-back in his region, south east Scotland, an area encompassing Lothian, the Borders and Fife.<sup>134</sup> The procedure was much as described above for targeted look-back generally. Donors who had been identified as positive on screening were sent a standard letter. The wording was bland but it encouraged the donor to come to see Dr Gillon's group because they wished to get a second sample to confirm the initial test result.<sup>135</sup>

<sup>126</sup> Ibid page 32

<sup>127</sup> Ibid pages 32–33

<sup>128</sup> Ibid page 47

<sup>129</sup> Ibid page 33

<sup>130</sup> Ibid page 42

<sup>131</sup> Ibid pages 38–39

<sup>132</sup> Ibid pages 35–36

<sup>133</sup> Ayob et al, 1994 [LIT.001.3802] and Day 86, pages 43–44

<sup>134</sup> Dr Gillon – Day 86, page 43

<sup>135</sup> Ibid pages 55–56

**35.104** The initial testing was exactly the same as was being introduced throughout Scotland at the time. Every blood donation in Scotland was subjected to a (second-generation) ELISA test – a fully automated, rapid screening test. A sample of material from donations which were reactive in the screening test was sent to the Microbiology Reference Unit for further extended testing, including an ELISA test from a different manufacturer and a more sophisticated supplementary RIBA-2 test. The PCR test was also available, which looked directly for the genetic material of the virus and could resolve indeterminate cases with a very high degree of accuracy.<sup>136</sup>

**35.105** In the case of donors confirmed to be HCV positive who had previously donated before the introduction of screening, the look-back followed the available SNBTS data on previous donations. The first step was to identify what had happened to each of those previous donations: what components were made from them, where they were sent and what was known about their fate. Some of them would have been time-expired without being transfused, some would have been used for quality control purposes but most would have been sent to hospitals for clinical use.<sup>137</sup> Dr Gillon was assisted in this part of the exercise by Dr Yasmin Ayob. Seconded to the south east Scotland RTC from the blood centre in Malaysia, Dr Ayob was a haematologist moving into a career in transfusion medicine. She provided assistance in looking at medical records, identifying the date(s) of transfusions and identifying the consultant(s) to be written to.<sup>138</sup> She also helped Dr Gillon draft the preliminary report on the exercise around the end of 1992 and was the lead author of an article published in the journal *Transfusion* describing the SEBTS look-back exercise ('the Ayob paper').<sup>139</sup>

**35.106** Dr Gillon explained that for the purposes of 'recipient identification', the SEBTS had direct access to the majority of the relevant medical records because they were located in the Royal Infirmary of Edinburgh (RIE). The blood bank was under SNBTS control and Dr Gillon could obtain any patient's medical records within about 24 hours. This increased their workload in cases dealt with at the RIE. They were doing that part of the look-back exercise which, in other circumstances, would have been done by an outside hospital holding the blood bank. In cases where outside hospitals were involved, the hospitals were contacted through formal routes, informed of the facts and asked for details of the fate of the individual components: whether the component was still in stock or was time-expired and had been disposed of, or whether a patient had received it and, if so, whether the recipient patient could be identified. Dr Gillon's team would then receive a report back. Although, as noted, the arrangement in the south east region increased the workload for Dr Gillon and his team, having access to the majority of relevant medical records undoubtedly speeded up the process because certain vital information about the fate of the component and the recipient could be established from the hospital records in most cases.<sup>140</sup>

### ***Knowledge of the south east initiative***

**35.107** Professor Cash was unable to recall when he first found out that Dr Gillon was pursuing look-back independently in the south east region. He thought that it was probably at some point between 1992 and mid-1993 but speculated that it might have been even earlier than that.<sup>141</sup> Dr Gillon thought that he had informed Professor Cash of the look-back

---

<sup>136</sup> Ibid pages 54–55

<sup>137</sup> Ibid pages 75–76

<sup>138</sup> Ibid page 44

<sup>139</sup> Ibid page 51

<sup>140</sup> Ibid pages 56–58

<sup>141</sup> Professor Cash – Day 85, page 57

exercise at some point between March 1991 and September 1991.<sup>142</sup> Professor Cash could not remember if the SEBTS had started the look-back programme without reference to him or the MSC, but said that there came a point when the Directors of the SNBTS became generally aware of Dr Gillon's work. He was certain that he had become aware of the project, at the latest, by the date that the Ayob paper on the early experience in carrying out look-back was accepted for publication in November 1993. He recalled that it had been mentioned at an MSC meeting and that Dr Gillon was asked for a pre-publication copy.<sup>143</sup> However, Professor Cash made it clear that he would defer to either Dr Brian McClelland's or Dr Gillon's recollections on the question of when he was informed.<sup>144</sup>

**35.108** Although Professor Cash said that the study was not 'secret', he recalled that it was his suggestion, when it became known, that it should be called a 'pilot' or 'feasibility' study so as not to 'ruffle any feathers'.<sup>145</sup> He accepted that, in point of fact, when Dr Gillon's study started it was not a pilot scheme but his reaction when he first heard about Dr Gillon's work was that he was 'a little nervous' because he knew that there was opposition to the whole idea of look-back in some quarters, stating that there were 'vast amounts of sensitivity lurking around in government circles' about look-back. He thought that, if the SNBTS wanted to roll out what had been going on in Edinburgh to other parts of Scotland, they would need the support of Ministers and CMOs. It seemed to him that the best approach to describing what had been going on in Edinburgh was to label it a 'pilot scheme'.<sup>146</sup>

**35.109** Dr Gillon thought that the scheme was first labelled as a 'pilot scheme' either by himself and Dr McClelland together or by Professor Cash, with or without input from the pair of them. However, he noted that Professor Cash would not have so labelled the scheme unless they knew this was to happen. Dr Gillon was not unhappy to call it a 'pilot study'. He recalled, however, that at a meeting he referred to it as the 'SNBTS pilot study' and was sharply reprimanded by Professor Cash who said it was not to be regarded as the 'SNBTS' pilot study. Dr Gillon considered that Professor Cash had said that, either because he did not want to be personally associated with the exercise or because he felt that it had the potential to damage the reputation of the SNBTS. Dr Gillon was happy to go along with that as well and refer to it as the 'South East Scotland pilot study'.<sup>147</sup> He noted that on instituting look-back he had expected that he might get into trouble with Professor Cash, and that he had not anticipated that it would all go 'swimmingly'.<sup>148</sup>

**35.110** Mr McIntosh introduced his involvement with the look-back exercise by explaining that he took a 'relatively backseat' position at the time. He went on to say that this was mainly because he considered it:

[O]ne thing that my Medical and Scientific Committee could simply absolutely be trusted to take responsibility for. So my involvement with it was very much ... I was overseeing it ... it happened on my watch. I was responsible for doing certain things to make sure that it went smoothly.<sup>149</sup>

<sup>142</sup> Dr Gillon – Day 86, page 33

<sup>143</sup> Professor Cash – Day 85, pages 53–54

<sup>144</sup> Ibid page 61

<sup>145</sup> Ibid page 54

<sup>146</sup> Ibid pages 58–60

<sup>147</sup> Dr Gillon – Day 86, pages 51–52

<sup>148</sup> Ibid pages 47–48

<sup>149</sup> Mr McIntosh – Day 84, page 75

**35.111** So far as the SEBTS initiative is concerned, it appears to be clear from Mr McIntosh's evidence that he had little idea of what was going on at the time. At some stage he came to understand that it was described as a 'pilot study'. Shown Dr Gillon's evidence on the establishment of his working group and the way look-back was initiated in September 1991, he realised that he had misunderstood the nature of the exercise. It had not, as he had understood at the time, begun as a pilot study and later 'became a reality'.<sup>150</sup> In any event, if his evidence as a whole were to be accepted, it would not be possible to find that he did understand the background to Dr Gillon's actions in 1991 or the true nature of the look-back exercise when it was implemented. He speculated that in the light of what had happened when Newcastle began screening for Hepatitis C before the date agreed for the UK, the clinician responsible being 'practically hounded out of the profession' for it, Dr Gillon would have had good reason for his exercise having a low profile. Further, he would be concerned that the exercise should not be stopped, which Mr McIntosh thought might have been a possibility if its true nature had been disclosed.<sup>151</sup>

**35.112** Professor Cash could not recall what he told Mr McIntosh about Dr Gillon's programme but asserted that they did have regular briefing meetings, usually every week, and said that at the meetings anything 'that was on the go', would be discussed with Mr McIntosh. He felt that he must have told Mr McIntosh about Dr Gillon's work and was surprised to hear that, when Mr McIntosh gave evidence, he had said that he had not realised that it was not a pilot scheme at the time.<sup>152</sup>

**35.113** Unfortunately, there are no records available to cast any additional light on this matter. Given the sensitivity of the project, as adverted to by Professor Cash, it may be that his description of it, before it became known as a 'pilot study', was less clear than he subsequently remembered. Whatever the precise explanation for this difference in the evidence, Mr McIntosh's assertion that he did not know about the study until after it was described as a 'pilot study', and even then did not fully understand the nature of the exercise, is accepted.

### *Publication and reaction*

**35.114** The published report of the first period of study showed that screening took place between 1 September 1991 and 29 February 1992, when 42,697 donors were screened routinely.<sup>153</sup> Twenty donors were identified as HCV-positive, 15 of whom had given around 63 previous infected donations among them.

**35.115** Because some of the individuals who were identified had been donating for many years, the number of components was not inconsiderable – 83 in total from the 63 infected donations – but it was considered to be manageable. All of the recipients of infected components still alive, nine in total, were found to be HCV-positive. Dr Gillon said that it was a bit surprising that his group found so few recipients of infected blood or components who were alive, even at that stage of their investigations, having started look-back as rapidly as possible. Before starting the look-back they did not have any indication as to how many positive donors would turn up.<sup>154</sup>

---

<sup>150</sup> Ibid page 90

<sup>151</sup> Ibid pages 114–115

<sup>152</sup> Professor Cash – Day 85, pages 60–62

<sup>153</sup> Ayob et al, 1994 [LIT.001.3802]

<sup>154</sup> Dr Gillon – Day 86, page 53



**35.116** Dr Gillon thought that the paper helped to answer the question as to whether targeted look-back should be pursued nationally. He felt that it at least gave it 'a nudge' and that it must have been one of the factors that revived discussion about look-back at the various committees.<sup>155</sup> In the discussion section of the paper, it was estimated that around 3300 patients might be alive and infected with HCV as a result of transfusion in the UK. Dr Gillon explained that the extrapolation was based simply on what was known about the prevalence of Hepatitis C in the donor population from the first six months of testing. This gave a figure of roughly 300 for Scotland and 3000 for the rest of the UK.<sup>156</sup> The report concluded by saying: '[T]his problem should not be ignored on logistical grounds when, in each case, there is an overwhelming responsibility to the individual patient'.<sup>157</sup>

**35.117** Dr Gillon also referred to the finding that no recipient was alive and traceable more than five years after transfusion. Dr Gillon said that this very important finding confirmed that if one were to go back more than five years there would not be many patients at all who were still alive to be found. Broadly speaking, he considered that this would support the argument that look-back should be started as soon as possible: if there was a chance to do anything about it, it was necessary to identify the patients sooner rather than later.<sup>158</sup>

**35.118** The methodology adopted by the SEBTS would probably not have been feasible in the west of Scotland for logistical reasons.<sup>159</sup> The advantages that the SEBTS possessed, in comparison to other regions, were that the majority of the records they required to consult were housed in one location in the Royal Infirmary of Edinburgh; they had excellent IT available; and the blood bank was under their control. In addition, they had Dr Ayob's services. The practical difficulties in the west of Scotland region are discussed in greater detail below. However, the SEBTS experience clearly demonstrated the feasibility of targeted look-back in general terms.

### The workshop on HCV

**35.119** Until the early 1990s, there was no treatment for HCV infection that was thought to be effective. Until such treatment became available, there was an ethically sustainable argument that it was inappropriate to tell patients that they had been, or may have been, infected, given that there was nothing that could be done to deal with their infection. However, as Dr Gillon pointed out, by the stage at which he proposed look-back there was already a body of evidence that Interferon might give some beneficial results. It was noted in the fourth and, it appears, final draft of the guidelines that: 'Progressive chronic hepatitis C has been treated successfully with Interferon, and though this treatment is at present experimental, it holds out considerable promise for the future'.<sup>160</sup> There was also available a paper, from Makris and others in the north of England, about Interferon treatment.<sup>161</sup> Research into treatment was a continuing concern of the pharmaceutical industry.

<sup>155</sup> Ibid page 62

<sup>156</sup> Ibid page 64

<sup>157</sup> Ayob et al, 1994, [LIT.001.3802] at 3805

<sup>158</sup> Dr Gillon – Day 86, pages 66–67

<sup>159</sup> Ibid pages 58–61. With the exception of the RIE, Ninewells Hospital, Dundee, Aberdeen Royal Infirmary, Raigmore, Inverness, and Law Hospital, where there were SNBTS administered blood banks, blood banks were invariably located in hospitals' haematology departments and the SNBTS did not manage them. Tracing a component involved the consultant haematologist in charge of the blood bank and through that officer the clinician responsible for the patient's treatment. See more detailed discussion below at paragraph 35.129 onwards.

<sup>160</sup> Report for the National Medical Director – Donor Counselling: HCV, Draft No. 4, dated February 1991 [SNB.001.8803] at 8809

<sup>161</sup> Makris et al, 'A randomized controlled trial of recombinant interferon- $\alpha$  in chronic Hepatitis C in hemophiliacs', *Blood*, 1991; 78/7:1672–77 [PEN.018.1384]

**35.120** A workshop on HCV infection was held at the Royal College of Physicians of Edinburgh in October 1993. It had been arranged by Professor Cash. Among the speakers was Dr Geoff Dusheiko of the Royal Free Hospital, London, who gave a talk on the latest information about treatment for HCV. In retrospect, Dr Dusheiko was one of a small group of doctors claiming cure rates for Interferon which turned out later to be somewhat optimistic. However, the perception that there might be an effective cure was important in shaping opinion, and his views were relevant at the time. Asked whether he remembered, broadly, the contents of Dr Dusheiko's address, Professor Cash stated:

No, I don't but I have the memory, which may be purely spurious and something that is thought up for my convenience: I think he harangued us .... And I am almost certain in my mind – I don't have any records of this – he actually said "You should be look-backing".

Professor Cash was 'pretty sure' that he had spoken with Dr Dusheiko before the workshop and told him that, if better treatment for HCV was becoming available, he should 'plug' look-back.<sup>162</sup>

**35.121** Professor Cash's recollection was that Dr Dusheiko also strongly recommended instituting HCV look-back programmes. He said that it was at this point that, having been enthusiastic about look-back from the start, he now felt that the SNBTS 'could now really pursue this very hard'.<sup>163</sup>

**35.122** Dr Gillon also attended the workshop and presented a paper entitled 'Epidemiology of Hepatitis C'.<sup>164</sup> Although he was mainly concerned with broader epidemiological issues, setting out what was known about the patterns, causes and effects of HCV for a largely non-specialist audience, Dr Gillon said that a relatively small part of his talk was concerned with his experience of look-back in the south east of Scotland. The transcript of the proceedings noted that there was a discussion after Dr Gillon presented his paper but he said that nobody asked a question about the look-back exercise. Dr Gillon stated that Dr Dusheiko did not refer to look-back in his talk and that the question of look-back did not come up in the discussion after his presentation either. It was his view that after the topic had been aired it had interested Dr Dusheiko 'and maybe one or two others there'. He recalled that Dr Dusheiko was interested in the topic from a clinical standpoint, and asked 'why isn't this happening?'.<sup>165</sup>

**35.123** Initially, Professor Cash recalled that Dr Gunson had attended the Edinburgh HCV workshop and had stayed overnight at his home afterwards. He also recalled being in the lecture theatre with Dr Dusheiko, by the lectern, and shouting to Dr Gunson 'come over here'. He said that Dr Gunson was 'extremely anxious' about the position taken by Dr Dusheiko. Professor Cash regarded the workshop as a watershed moment in the development of his thinking about look-back and decided that, 'We [the SNBTS] are just going to press on ourselves and see where it takes us and I'll keep Harold informed but you are on your own, Harold'. He told Dr Gunson of his decision that evening. Professor Cash was somewhat reluctant to describe Dr Gunson's reaction but said that 'the body language wasn't happy ... I think he knew in his heart they [the NBTS] couldn't deliver'.<sup>166</sup>

---

<sup>162</sup> Professor Cash – Day 85, pages 68–71

<sup>163</sup> *Ibid* page 72

<sup>164</sup> Workshop programme, *Hepatitis C Virus Infection*, Royal College of Physicians of Edinburgh, 8 October 1993 [PEN.018.0553]; Gillon, 'Epidemiology of Hepatitis C', *Proceedings of the Royal College of Physicians of Edinburgh*, 1995; 25:583-859 [PEN.018.1420] at 1421

<sup>165</sup> Dr Gillon – Day 86, pages 70–72

<sup>166</sup> Professor Cash – Day 85, pages 85–86

**35.124** Professor Cash was referred to a letter he wrote to SNBTS Directors dated 15 October 1993 following the workshop. The letter stated:

One of the outcomes of the recent HCV Symposium ... was that there is a need to refer patients who have recently acquired HCV infection to specialists for consideration as to whether they should have early interferon therapy.

I do believe this places an obligation on the BTS to use its best endeavours to advise clinical colleagues accordingly when we have evidence that a recipient may have acquired HCV.<sup>167</sup>

It appears that the relevant 'outcome' relates to Dr Dusheiko's advocacy of Interferon therapy, strengthening the case for reverse look-back. But it does not help resolve the question whether Dr Dusheiko spoke in favour of targeted look-back in the course of his presentation (as Professor Cash maintained) or, as Dr Gillon suggested, only after the formal presentations and the discussions following thereon had finished.

**35.125** Dr Keel also attended the workshop. Unfortunately, she had little memory of the event. She said that she was aware of developing interest in emerging treatment using Interferon and the idea that clinicians might at some point be able to offer treatment to patients, although she noted that it was by no means universally accepted that it was an effective treatment, with experts such as Professor Zuckerman expressing doubts.<sup>168</sup> Dr Keel assumed that she had attended the morning session of the workshop and remembered Dr Dusheiko talking about treatment during the afternoon session, but could not remember the details of his presentation. She had no memory of Dr Gillon's talk and had no recollection of data from the pilot study being made available at the symposium. She was referred to the text of Dr Gillon's presentation and accepted that it was describing a look-back exercise but still had no recollection of it.<sup>169</sup> She had no clear recollection either of any details about the SEBTS look-back exercise nor of any renewed emphasis being given by Professor Cash and his colleagues to the need to institute look-back by October 1993.

### **A change of direction: Medical and Scientific Committee meeting on 9–10 November 1993**

**35.126** The MSC met on 9 and 10 November 1993.<sup>170</sup> Dr Mitchell, Dr McClelland, Dr Perry and Professor Cash were all present. Dr Keel was present for certain agenda items only, including item 4.6.4 headed 'Look-back HCV'. Professor Cash said that it was felt to be very important that Dr Keel was present at this meeting because, if the SNBTS wanted to take look-back forward effectively, they would have had to engage with the Scottish Office who would be advising Ministers.<sup>171</sup> He explained in oral evidence that putting look-back on the agenda was an attempt at 'upping the ante'. He considered that his new attitude to look-back had been affected by the positive response he got from colleagues at the SNBTS to his letter of 15 October.<sup>172</sup>

---

<sup>167</sup> Professor Cash's letter to SNBTS Directors dated 15 October 1993 [SNB.005.2107]

<sup>168</sup> Dr Keel – Day 86, page 116

<sup>169</sup> Ibid pages 118–120

<sup>170</sup> Minutes of meeting of the SNBTS Medical and Scientific Committee on 9 and 10 November 1993 [SNB.009.9176]

<sup>171</sup> Professor Cash – Day 85, page 74

<sup>172</sup> Ibid pages 75–76

**35.127** Professor Cash said that he could not remember the discussion at the meeting in detail. However, he was clear that he was arguing that the position on look-back had changed and that the SNBTS needed to begin to think about it more seriously. He was advocating look-back 'right across the board' rather than just the Edinburgh 'feasibility study'.<sup>173</sup> He thought that Dr Crawford had already determined that the SNBTS could not implement look-back<sup>174</sup> because he was extremely anxious at the size and the nature of the problem raised by such a programme.<sup>175</sup>

**35.128** Professor Cash said that he considered that this was the time to come up with 'a firm policy proposal' although after great discussion it was decided that it 'wasn't quite appropriate'.<sup>176</sup> The minute of the meeting noted:

After a full discussion in which the principles of lookback of HCV PCR positive donor archive samples and appropriate communication with recipient's GPs were agreed, it was felt that the position concerning PFC products required further consideration. The Committee felt it would be inappropriate to make a policy decision at this time and that further discussion was required.<sup>177</sup>

Among the documents recovered by the Inquiry was an action log following the meeting which indicated that Professor Cash was to ensure that 'look-back-HCV' received further discussion.<sup>178</sup>

**35.129** Although he could not recall why a policy decision was not made at that point, he speculated that it would be because other regions – Inverness, Aberdeen and Dundee but particularly the west of Scotland – would have had concerns about the difficulty of implementing look-back and would have been asking to see the 'nuts and bolts' of what had been going on in the south east region before agreeing. Professor Cash explained that Edinburgh was 'hugely well resourced'. They had a superb IT programme for the blood-bank and, in practical terms, Dr McClelland and Dr Gillon had control of over 70% of all of the clinical cross-matching in the south east of Scotland.<sup>179</sup> As in that region, in Dundee, Aberdeen and Inverness the RTCs dominated the 'clinical interface' with blood transfusion. This was not the position in the west of Scotland.

**35.130** Professor Cash said that Dr Mitchell, Director of the West of Scotland, 'didn't have a thing such as a blood bank' in the way other centres did.<sup>180</sup> In Glasgow, the Royal Infirmary, the Western General Hospital and Stobhill Hospital each had departments of haematology with their own blood banks. These blood banks were supplied with blood by Dr Mitchell from 'a chilled warehouse in the West of Scotland', but the blood was not attached to any patient at that stage. Requests for blood in Stobhill, the Royal Infirmary Ayrshire and Fort William, for example, came in from clinical units to the local blood bank and were dealt with locally.<sup>181</sup> Glasgow BTS had no blood banking IT system because they did not have overall responsibility for blood banking.

---

<sup>173</sup> Ibid page 77

<sup>174</sup> Ibid page 81

<sup>175</sup> Ibid page 87

<sup>176</sup> Ibid page 78

<sup>177</sup> Minutes of meeting of the SNBTS Medical and Scientific Committee on 9 and 10 November 1993 [SNB.009.9176] at 9185–86

<sup>178</sup> List of action points attached to agenda for meeting of SNBTS Medical and Scientific Committee on 18 May 1994 [SNB.009.9172] at 9173

<sup>179</sup> Professor Cash – Day 85, pages 78–80

<sup>180</sup> Ibid page 79. This was a slight exaggeration since Dr Mitchell had administrative control over Law Hospital's blood bank; but in practical terms it was true for the region taken as a whole.

<sup>181</sup> Professor Cash – Day 85, pages 81–82

**35.131** If HCV look-back were to be introduced in the west of Scotland region, Dr Mitchell would have had to rely on ‘first trigger information’ about possible transmission of infection generated from a very wide geographical area. Information about infective donations would have come from locations as far apart as Oban and Ayrshire and Fort William and central Glasgow, a widespread geographical area over which he had no effective overall control. This led to anxiety about ‘rushing to a policy’, particularly in the west. Despite the fact that screening had started in September 1991, in operational terms, if there was a look-back policy to implement, it was felt that things were going to have to be done suddenly.<sup>182</sup>

**35.132** Although not specifically minuted, Professor Cash stated that these concerns would have been ‘ventilated very effectively’ at the meeting in November 1993.<sup>183</sup> Despite the outcome, Professor Cash said that by the end of the meeting his attitude was to keep going with trying to implement look-back throughout Scotland. A note in the minutes stated that Dr McClelland was to circulate look-back information.<sup>184</sup> This was an early copy of the paper relating to the Edinburgh feasibility study and was to be provided to assist colleagues ‘to get a feel as to what was involved’.<sup>185</sup> Professor Cash explained that he wanted the Edinburgh document to be taken back to the west of Scotland BTS to be read and talked about in order to begin to put together a picture of how things might proceed there. He felt by that stage that ‘as night follows day,’ look-back would be implemented. Now that HCV treatment was available, the SNBTS was reaching a point where they had ‘a total moral obligation’ to implement look-back and the question now was how they were going to do it. At the back of his mind was that ‘the Edinburgh way might not be the best for the likes of the West of Scotland’.<sup>186</sup> In fact, Dr Ewa Brookes in Dundee had, since the inception of screening in 1991, also been attempting to follow up donations given by HCV positive donors who had donated prior to screening, in order to try and trace their recipients. Dr Keel recollected attending the meeting but said that although look-back was on the agenda, along with many other matters, she had no recollection of any emphasis being given by Professor Cash and his colleagues to the need to get on with look-back and was certain that no details of the SEBTS feasibility study had been revealed at that stage to her. She also did not recall getting any written information after the meeting from Brian McClelland and thought that its lack might explain why, when details of Dr Gillon’s exercise had subsequently been provided to her, it had been such a revelation.<sup>187</sup>

**35.133** Professor Cash was referred to a letter he had written to Dr Gunson on 18 November 1993.<sup>188</sup> The letter commented briefly on the Edinburgh symposium in terms suggesting that Professor Cash was providing information about the proceedings. Coupled with the fact that he did not refer to Dr Gunson having attended the symposium in the letter, Professor Cash came to doubt whether Dr Gunson actually had attended the symposium.<sup>189</sup> Leaving aside the doubt cast on Professor Cash’s recollection, the letter stated, with reference to the MSC meeting: ‘colleagues stepped back from introducing a look-back policy until such times as further (UK) deliberations had taken place’.

<sup>182</sup> Ibid pages 79–81

<sup>183</sup> Ibid page 83

<sup>184</sup> Minutes of meeting of the SNBTS Medical and Scientific Committee on 9 and 10 November 1993 [SNB.009.9176] at 9186

<sup>185</sup> Professor Cash – Day 85, page 83

<sup>186</sup> Ibid pages 84–85

<sup>187</sup> Dr Keel – Day 86, page 143–144

<sup>188</sup> Professor Cash’s letter to Dr Gunson dated 18 November 1993 [SNB.005.5560]

<sup>189</sup> Professor Cash – Day 85, pages 87–88

**35.134** The letter was copied to Dr Mitchell and Dr Perry who sat on the ACVSB/MSBT. It was also copied to Dr Keel. The letter stated: 'It occurred to me that it might be appropriate for the item to be researched for, and discussed by, MSBT. I would value your comments and support'. Professor Cash explained that his intention in writing the letter and copying it to these recipients was to speed things up by encouraging the ACVSB/MSBT to advise Ministers to proceed with look-back. He was not in a position to insist, without ACVSB/MSBT support, that look-back should proceed.<sup>190</sup> As noted above, Professor Cash thought that actually delivering look-back would have required the Chief Medical Officer (CMO) or the Department of Health or Ministers to instruct health board doctors to work closely with their local transfusion service to undertake look-back. He considered that it required that level of authority and that many people shared his view. He noted that there were some clinicians who were 'not very collaborative' and several claimed they 'were far too busy'. If people were not prepared to go and find records of transfusion practice because it was a lot of extra work, it 'required a CMO ... to say "I'm instructing, in the name of the minister, that you go and do it"'. Professor Cash considered that the easiest way for the SNBTS to have look-back implemented would be for the ACVSB/MSBT to say, 'We think the time has come [for look-back], let's go'. That would have been 'immediately flashed to the Scottish Office and something could have happened'. He considered that would have been a 'great comfort' to Dr Mitchell's team.<sup>191</sup> If the decision had been reached at Ministerial level, securing the extra resources to implement a programme would have been easier.

**35.135** The matter was also raised by Professor Cash at the meeting of the ACTTD/I on 18 January 1994.<sup>192</sup> He noted Dr Dusheiko's advocacy of look-back on the grounds of the potential benefits of Interferon treatment, especially if initiated early in the course of infection. The minutes noted support only for the concept of look-back and encouraged 'grant seeking for this potentially clinically beneficial undertaking'.<sup>193</sup> Various members of the committee were to look into the issue further and report back at the next meeting.

### Issues Meeting on 16 May 1994

**35.136** An 'Issues Meeting' attended by members of the SNBTS and the Scottish Office was held on 16 May 1994.<sup>194</sup> Dr Keel explained that Issues Meetings were set up with a view to providing a forum for discussion of issues of mutual concern. She commented that, in 1994, while Issues Meetings were more sporadic than they are today, they were not ad hoc meetings in response to specific events. They would take place when policy colleagues felt that there was enough on the agenda to make a meeting worthwhile.<sup>195</sup> Professor Cash agreed that Issues Meetings were very infrequent.<sup>196</sup> The SNBTS personnel in attendance on 16 May 1994 were David McIntosh, Dr Perry, Dr McClelland and, from the Scottish Office, Dr Keel, Dr Young and Mr Tucker. Dr Gillon was not present.

**35.137** Dr Keel said that, from the time she joined the SHHD up until the beginning of 1994, her sense of the general attitude at the SHHD to implementing look-back was that 'we shouldn't be proceeding with it because ... it wouldn't be feasible and ... there was

---

<sup>190</sup> Ibid pages 90–91

<sup>191</sup> Ibid pages 88–90

<sup>192</sup> Minutes of meeting of ACTTI held on 18 January 1994 [MIS.001.0061]

<sup>193</sup> Ibid [MIS.001.0061] at 0065

<sup>194</sup> Minutes of SNBTS Issues Meeting held on 16 May 1994 [SGH.004.0847]

<sup>195</sup> Dr Keel – Day 86, page 114

<sup>196</sup> Professor Cash – Day 85, page 94

no really evidence-based treatment which would be effective for individuals identified with the virus'. According to her evidence, the SHHD view was informed by the SNBTS' view but also more widely by the view which had been expressed by committees south of the border, in particular the ACVSB/MSBT, and by expert opinion across the UK and abroad.<sup>197</sup>

**35.138** Dr Keel said that prior to the Medical and Scientific Committee (MSC) meeting on 18 May 1994<sup>198</sup> she did not know that there had been a look-back exercise going on in Edinburgh and south east Scotland.<sup>199</sup>

**35.139** At paragraph 13 of the minute of the 16 May Issues Meeting, it is recorded that HCV look-back was discussed:

Mr McIntosh indicated that when HEP C testing of donations was introduced in 1991 it was not thought appropriate to look back over previous donations. Mr Panton confirmed that any claims for compensation following infection with Hepatitis C should be refuted. After discussion it was agreed that Mr McIntosh would send a draft policy statement about look back to the Department for clearance. This would be used in any newspaper/media enquiries received by SNBTS. (Following further developments after the meeting a meeting was arranged for Tuesday 24 May to discuss SNBTS look back proposals).<sup>200</sup>

**35.140** Dr Keel was referred to the comment that Mr McIntosh would send a draft policy statement about look-back to the department 'for clearance'.<sup>201</sup> She had no strong recollection of a discussion about look-back although clearly it was discussed. Her clearest recollection of Dr Gillon's work was at the meeting two days after this at the MSC. Despite Mr Panton's comments about refuting claims for compensation, she did not consider that it was a major element in the department's thinking about why look-back should not go ahead. Their attitude was then based on a lack of effective treatment, logistical difficulties and lack of feasibility. Directed to the passage about media interest, she said that she had no memory of any particular media interest in look-back at that stage and was not aware from where it might have come or what might have stimulated it. At the time Dr Keel left the meeting she did not think that look-back was a 'particularly hot issue'.<sup>202</sup> In his evidence Dr Gillon noted that in the 'early part of 1994' stories were beginning to appear about it in newspapers, and that the *Sunday Mail*, or one of the Scottish papers, made it 'into a bit of a crusade'.<sup>203</sup>

**35.141** In contrast to Dr Keel, Professor Cash said that he thought that the link between the look-back programme and compensation was 'chronically there'. The whole concept of liability and compensation 'lurked around in [his] memory' all the time.<sup>204</sup>

---

<sup>197</sup> Dr Keel – Day 86, pages 114–115

<sup>198</sup> Minutes of meeting of the SNBTS Medical and Scientific Committee on 18 May 1994 [SNB.009.9331]

<sup>199</sup> Dr Keel – Day 86, pages 115–116

<sup>200</sup> Minutes of SNBTS Issues Meeting held on 16 May 1994 [SGH.004.0847] at 0849

<sup>201</sup> Ibid [SGH.004.0847] at 0849

<sup>202</sup> Dr Keel – Day 86, pages 120–122

<sup>203</sup> Dr Gillon – Day 86, page 63

<sup>204</sup> Professor Cash – Day 85, pages 94–95.

### Medical and Scientific Committee meeting on 18 May 1994

**35.142** The MSC met on 18 May 1994.<sup>205</sup> The agenda for the meeting did not include the topic of look-back.<sup>206</sup> The action log, attached to the agenda, recorded that look-back HCV was then 'being discussed' by the ACTTI.<sup>207</sup> Both Dr Keel and Dr Gillon were present. Under Any Other Competent Business 1, sub-heading, 'HCV lookback', the minutes set out elements of the procedure to be followed on finding a 'known' (that is, return) donor who tested anti-HCV positive.<sup>208</sup> These related to re-testing archived samples and follow-up steps. It was agreed that the procedure would be based on an outline in the forthcoming publication in *Transfusion* of Dr Gillon's protocol (the Ayob paper) and Dr Gillon was to circulate a pre-publication copy.

**35.143** In terms of follow-up procedure, the minute stated:

v. From a SHHD perspective, [Dr Keel] expressed a view that the SHHD may not have a locus in this matter and that the SNBTS should make a decision on lookback for HCV that was based on their professional judgement. However, before SNBTS took any action [Dr Keel] asked to be given the opportunity to discuss the issues with SHHD colleagues to seek their views and asked that the SNBTS take no formal action until she had subsequently contacted [Professor Cash].

vi. Once [Dr Keel] had communicated the SHHD position to [Professor Cash] and provided SHHD were in agreement that the SNBTS should implement this policy, [Professor Cash] would write to [Mr McIntosh] to provide details of the SNBTS policy, thereby allowing a decision to be taken on a starting date for the process. [Professor Cash] also would formally advise NBA, NIBTS, SACTII and MSBT of the SNBTS policy.

vii. If SHHD agreed that SNBTS should develop and implement a lookback policy for HCV, [Dr Keel] subsequently would communicate this to DOH.<sup>209</sup>

**35.144** Professor Cash's recollection was that Dr Keel was invited along specifically for the look-back discussion.<sup>210</sup> Dr Keel disagreed: she said that it was normal for her to attend MSC meetings; she wouldn't necessarily always be there for the whole event but she would attend for part of the meeting depending on other diary commitments. She would look at the agenda in advance to decide which parts of the meeting to stay for. Generally, she tried to be there at the beginning and stay for as long as she could.<sup>211</sup>

**35.145** Notwithstanding the minutes, there were widely differing impressions of the proceedings at the meeting. Professor Cash considered that the Directors were saying 'we have had enough of procrastination, it's go for it time' and that this was 'game, set and match'. He felt it was a hugely important meeting because Dr Keel had expressed the view that the SHHD 'may not have a locus' with regard to look-back and that the SNBTS should make a decision on look-back for HCV based on their professional judgement. He

---

<sup>205</sup> Minutes of meeting of the SNBTS Medical and Scientific Committee on 18 May 1994 [SNB.009.9331]

<sup>206</sup> Agenda for meeting of the SNBTS Medical and Scientific Committee on 18 May 1994 [SNB.009.9166]

<sup>207</sup> List of action points attached to agenda for meeting of SNBTS Medical and Scientific Committee on 18 May 1994 [SNB.009.9172] at 9173

<sup>208</sup> Minutes of meeting of the SNBTS Medical and Scientific Committee on 18 May 1994 [SNB.009.9331] at 9335

<sup>209</sup> Ibid [SNB.009.9331] at 9336

<sup>210</sup> Professor Cash – Day 85, pages 95–96

<sup>211</sup> Dr Keel – Day 86, pages 122–123



explained that most of the SNBTS people ‘fell off our seats’ when they heard Dr Keel say that. They were unaccustomed to such language and, indeed, Professor Cash recalled that they had gone through a pretty painful process of instituting donation testing for HCV, when it was made ‘absolutely clear’ to them that the professionals could not decide themselves whether they would start testing and when they would start testing. He had assumed that the same was going to apply to HCV look-back and that it would be Ministers that would say to the Scottish transfusion service that they could ‘go ahead and do it now’. The SNBTS representatives were surprised that it might be left to them.<sup>212</sup> Dr Keel, the representative of the Scottish Office, now seemed to be saying, ‘that’s ok but ... before you do anything, let the department have just some consultation’ but that once the SNBTS’ ‘masters [that is, the Scottish Office] had spoken’ they could proceed to inform everybody what they had been told to do.<sup>213</sup> He agreed with the suggestion that the SNBTS ought to ‘touch base with the Scottish Office’ and believed that agreement on that had been reached at the meeting.<sup>214</sup> From his perspective, Professor Cash believed that by the end of the meeting the main issues to be resolved were the practicalities of introducing look-back in Scotland generally.

**35.146** Dr Keel thought that if Professor Cash had indicated to her before the meeting that the SNBTS now wanted to go ahead with the look-back exercise, she would have spoken to policy colleagues before she attended it as that would have constituted a considerable change in the SNBTS’ view on look-back. She explained the reasons why the Scottish Office (and the UK Government generally) did not want to proceed with look-back, and that was the policy which was in her mind before attending the meeting. If she had been given advance notice that the SNBTS was going to present her with evidence that suggested that it should be moving towards look-back, she thought it would have been obvious to her that she should have discussed it with policy colleagues in advance. No decision in government is ever taken unilaterally; decisions are corporate and advice is developed by a number of people before approaching Ministers. As far as she was concerned it would not have been the SNBTS’ decision to proceed unilaterally with look-back.<sup>215</sup>

**35.147** Dr Keel said that, at the meeting, Dr Gillon’s report had demonstrated that look-back was feasible. Although it was not minuted, she recalled that Dr Gillon gave a presentation at the meeting which, for the first time that she could remember, very explicitly laid out how he had gone about look-back in the south east region, how many people had been identified and how successful they had been in tracing recipients of blood and blood components derived from infected donors.<sup>216</sup> Her recollection was that Dr Gillon’s presentation provided convincing evidence of the feasibility of undertaking a look-back exercise and of tracing infected donations to recipients, and made a powerful impression on her.<sup>217</sup> She became conscious of what had been going on: as far as she was concerned, this was new evidence that she needed to discuss with her colleagues. She felt that it was really a clinical judgement as to whether to go ahead with look-back. Although the SNBTS would need help with organising look-back, in ‘purely professional terms’, they had identified that they could do it and they were already identifying recipients of blood

<sup>212</sup> Professor Cash – Day 85, pages 96–98

<sup>213</sup> Ibid pages 97 and 99

<sup>214</sup> Ibid pages 96–97

<sup>215</sup> Dr Keel – Day 86, pages 123–124

<sup>216</sup> Ibid page 126

<sup>217</sup> Ibid page 130. The Ayob paper was accepted for publication on 21 July 1994. It was clearly available to SNBTS Directors by November 1993 at the latest. It appears on her evidence that Dr Keel cannot have seen it by May 1994.

that was infected (in the south east region) and therefore had a duty of care to those individuals. She explained that that was why she said that the 'SHHD may not have a locus in this matter and that the SNBTS should make a decision on lookback for HCV that was based on their professional judgement'.<sup>218</sup> At the meeting the MSC suggested that look-back should be pursued. Despite what Dr Keel said at the meeting about the SHHD not having a locus, she accepted that the SHHD did in fact have a locus in the matter of look-back and that one of the reasons that she said what she did was because she was relatively new in her post.<sup>219</sup>

**35.148** She did not agree that the minutes were accurate in noting that Professor Cash would inform the ACVSB/MSBT of a change of SNBTS policy on look-back. She would have expected him to use the SHHD or one of the SNBTS members of the ACVSB/MSBT to convey the SNBTS change in view rather than doing it directly himself.<sup>220</sup> She had a recollection of someone from the SNBTS saying to her that Professor Cash was planning to phone Dr Gunson to pass on the views that she had expressed in the meeting and that the SNBTS would be going ahead with the look-back. At that point she thought she had better get back to St Andrew's House to discuss this with policy colleagues as a matter of urgency. She thought that Professor Cash was proposing to tell Dr Gunson that the SHHD had said that the SNBTS could go ahead with look-back and therefore look-back would be happening in Scotland.<sup>221</sup> Dr Keel felt that this was not correct, however, and that her view was reflected in the minutes which, indeed, noted that the SNBTS was to 'take no formal action' until Dr Keel had discussed the matter with her colleagues and spoken again with Professor Cash.<sup>222</sup> By the end of the May meeting, Dr Keel considered that it had been agreed that the SNBTS would wait until she had conferred with colleagues before confirming their policy on look-back.<sup>223</sup>

**35.149** It appears that Dr Gillon's presentation had made a great impression on Dr Keel. She explained that, when she left the meeting, she was convinced that it was now her job to convince policy colleagues that the right thing to do was to implement look-back. Dr Gillon's pilot had demonstrated its feasibility. She was also aware that treatment was now available for infected patients. She accepted, further, that the implication of the fact that look-back was feasible was that there might be some legal liability on grounds of duty of care.<sup>224</sup>

**35.150** Dr Keel had personally been persuaded. When she returned to St Andrew's House she discussed the question with Mr Panton. Her recollection is that both of them then went to speak to Mr Panton's senior, Mr George Tucker, and they then had a collective discussion.<sup>225</sup>

**35.151** At some time after this discussion, they sought legal advice on the issue of liability. The date on which they approached Scottish Office solicitors for advice is not known. Although the relevant files relating to that period were not available, her recollection was that Mr Panton organised obtaining the legal advice. Similarly, she did not know who provided the advice but Lord Fraser's letter (discussed below at paragraph 35.178)

---

<sup>218</sup> Minutes of meeting of the SNBTS Medical and Scientific Committee on 18 May 1994 [SNB.009.9331] at 9336; Day 86, pages 126–127

<sup>219</sup> Dr Keel – Day 86, pages 123–125

<sup>220</sup> Ibid pages 132–133

<sup>221</sup> Ibid page 134

<sup>222</sup> Ibid pages 132–135; Minutes of meeting of the SNBTS Medical and Scientific Committee on 18 May 1994 [SNB.009.9331] at 9336

<sup>223</sup> Dr Keel – Day 86, page 139

<sup>224</sup> Ibid pages 135–137

<sup>225</sup> Ibid page 135

referred to it and Dr Keel spoke about it at the ACVSB/MSBT Committee. It follows that at some time between May and September 1994 she had obtained legal advice which would have come to her from a Scottish Office solicitor. Her recollection was that the advice was that, having demonstrated the feasibility of look-back, Scottish Ministers would be vulnerable if the programme was not extended across the country.<sup>226</sup>

### **Start/Stall**

**35.152** As anticipated at the Issues Meeting on 16 May, (paragraph 35.139 above) there was emerging media interest. Dr Gillon noted that there were various media campaigns going on around the time that the decision was taken to start, and that the headlines that appeared were 'really quite toxic at times and damaging to the reputation of the Transfusion Service'. On 19 May 1994, Mrs Mairi Thornton, National Donor Services manager, sent an internal memo to the SNBTS board, the CSA and others. It stated:

As you may know there has been media interest in Hepatitis C. The following paper confirms our agreed position and the information is being made available to the Sunday Mail which is running an awareness campaign on Hepatitis.<sup>227</sup>

**35.153** The paper, dated 18 May 1994, included the following:

6) Until very recently there has been no treatment known to provide an effective cure [for Hepatitis C] and there was thought to be little benefit in the early identification of the virus in any particular individual. Therefore when routine anti Hepatitis C testing of blood donations was introduced in 1991, it was not judged medically appropriate to seek out those few patients who might have contracted the virus from a blood transfusion in the years before testing was introduced.

7) However, the BTS has kept this policy under review. Recent clinical trials now suggest that beneficial treatment for some patients with acute hepatitis C may be a possibility. The Service is, in consultation with medical colleagues, assessing if any benefits might be gained from a 'look-back' exercise.<sup>228</sup>

**35.154** David McIntosh sent Mr Panton a faxed letter dated 19 May 1994.<sup>229</sup> It stated that the MSC 'has now formally recommended to me that the Service should implement a look-back policy without delay'. He commented that he was satisfied that the medical and scientific reasons for this, combined with good ethical and legal arguments, as well as obvious public relations implications, gave him sufficient grounds for the immediate acceptance of the MSC's recommendations, and said: 'I would therefore intend to give colleagues in England, Wales and Northern Ireland prior warning of our intentions and to activate look-back with effect from 1 June 1994'.

**35.155** Dr Keel did not have a recollection of seeing the fax at the time but she considered that colleagues would have made her aware of it. She thought that she would have been surprised by the terms of the fax 'standing the discussions at the meeting' and her understanding of what had been agreed.<sup>230</sup>

---

<sup>226</sup> Ibid pages 137–139

<sup>227</sup> Mrs Thornton's memo dated 19 May 1994 [SNB.008.4777]

<sup>228</sup> *SNBTS Policy Position on HCV, Briefing Notes for Staff*, 19 May 1994 [SNB.008.4778] (emphasis in original)

<sup>229</sup> Faxed memo from Mr McIntosh to Mr Panton dated 19 May 1994 [SNB.008.4779]

<sup>230</sup> Dr Keel – Day 86, page 140

**35.156** Professor Cash also considered that this fax was premature on the basis that it had been agreed that the SNBTS would wait to be sure that the Scottish Office would go along with it.<sup>231</sup> As it turned out, the Scottish Office was unhappy about this and there was a meeting on 24 May 1994. In a fax from Mairi Thornton to the SNBTS Management Board dated 25 May, she wrote:

David ... asked me to let you know that he, John Cash, Brian McClelland, Jack Gillon and I attended a meeting at SOHHD yesterday where the SNBTS proposal for hepatitis C look-back got a sympathetic hearing.

SOHHD are to consult with the Department of Health in London before a final decision is reached, while the SNBTS is to investigate the operational aspects of introducing a look-back policy.<sup>232</sup>

**35.157** Professor Cash's best recollection of the 24 May meeting was that the Scottish Office officials had made it clear that the SNBTS should not go ahead until given the final instruction to do so.<sup>233</sup> Dr Keel did not remember the meeting on 24 May.<sup>234</sup>

**35.158** This was followed by a faxed letter from David McIntosh dated 30 May 1994 and addressed to SNBTS Regional Directors in which he said:

Following our meeting in the Scottish Office on 24th May this is to confirm that official moves are now afoot to follow up the recent MSC discussions with active consideration of the steps necessary to put an appropriate look back programme into effect.

No final decision has yet been taken ....<sup>235</sup>

**35.159** Mr Tucker was asked to comment on the minutes of the ACVSB/MSBT of 29 September 1994 where he was noted to have said that 'approaches to institute HCV look-back in Scotland had been resisted, and it was important that a UK wide approach was adopted'.<sup>236</sup> He thought it was an inaccurate report of what he had said. Mr Tucker drew attention to an internal note dated 5 October 1994 he had produced of the ACVSB/MSBT meeting where he noted he had told the meeting 'we [the SHHD] had reservations about a look-back unless it was on a UK basis and there were real benefits for patients in treatment'.<sup>237</sup> He added it would not be accurate to say that the SHHD was 'resisting' attempts to introduce HCV look-back.<sup>238</sup> Mr McIntosh considered that, in hindsight, the introduction of look-back in Scotland, as a whole, was delayed due to pressure from England and the natural tendency of Scottish civil servants to acquiesce to pressure from England.<sup>239</sup> He was of the view, shared by Dr Gillon, Dr Keel and Professor Cash, that introducing look-back into England, Wales and Northern Ireland would be a more difficult exercise.

---

<sup>231</sup> Professor Cash – Day 85, pages 100–101

<sup>232</sup> Faxed memo from Mrs Thornton to the SNBTS Management Board dated 25 May 1994 [SNB.008.4783]

<sup>233</sup> Professor Cash – Day 85, pages 101–102

<sup>234</sup> Dr Keel – Day 86, page 140

<sup>235</sup> Mr McIntosh's letter to SNBTS Directors dated 30 May 1994 [SNB.008.4784]

<sup>236</sup> Minutes of meeting of ACMSBT on 29 September 1994 [DOH.001.0021] at 0024

<sup>237</sup> Mr Tucker's note to Dr Keel and Mr Panton dated 5 October 1994 [SGH.008.7015] at 7016

<sup>238</sup> Mr Tucker's statement [PEN.018.0406] at 0408

<sup>239</sup> Mr McIntosh – Day 84, page 146

## Towards a decision

**35.160** Over the next few months the DoH appears to have sought advice from the ACTTD/I before making its recommendation. Professor Cash commented on the delay this created, saying 'we were just slightly scuppered there just for a short period of time'.<sup>240</sup> By letter dated 21 June 1994 to the SNBTS Directors, and copied to Dr Keel, Professor Cash advised that the ACTTD/I was to convene an extraordinary meeting to consider look-back and that it was important for the SNBTS to consult with senior hepatologists on look-back.<sup>241</sup> Professor Cash explained that Dr Gillon had come from a hepatology department and that would have made look-back easier for him in comparison, for example, to Dr Mitchell.<sup>242</sup> A meeting was held within the SHHD on 21 September 1994 to discuss SNBTS issues.<sup>243</sup> Dr Keel was present at the meeting along with Mr Tucker, Mr Panton and Mr Wildridge. The minutes record that she had attended a meeting of hepatologists and their view was that look-back was necessary as part of a general 'duty of care'. Dr Keel said that there was general agreement at this stage that look-back should go ahead. She could not remember if any discussions had taken place with DoH colleagues about look-back by this stage although the evidence that the SNBTS had demonstrated that look-back was feasible would have been distributed.<sup>244</sup>

**35.161** Dr Keel stated that it would be wrong to get the impression that look-back was starting to become less urgent. She explained that there was a desire that look-back should proceed on a UK basis. Scotland was slightly ahead of the game and there needed to be a lot of planning and advanced warning to the blood transfusion services in other parts of the UK before they could undertake look-back. She did not consider that the situation south of the border was holding up look-back being implemented in Scotland.<sup>245</sup>

**35.162** The ACVSB/MSBT met on 10 February 1994. The minutes of that meeting have not been recovered. But it is clear that look-back was referred to an advisory committee, the Standing Advisory Committee on Transfusion-Transmitted Infection to the MSBT (SACTTI). The SACTTI reported to the ACVSB/MSBT on 29 September 1994 when Dr Robinson presented their paper.<sup>246</sup> Members of the SACTTI included Professor Cash and Dr Gillon. The recommendation was that there was a serious case for considering a look-back policy for HCV. Dr Gillon's work was not relied on in the report which dealt with the position of the National Blood Service and noted that the facilities were available to undertake tracing, counselling and referral, with a potential case load of 3000 (the number estimated by Dr Gillon at an earlier stage). The outcome on 29 September was a further postponement of any decision, with members asked to submit written comments to be considered at the next meeting.<sup>247</sup>

**35.163** A further Issues Meeting took place on 14 October 1994 at St Andrew's House.<sup>248</sup> Those present were Mr Donald from the CSA, Mr McIntosh, Dr Perry and Mr Tucker, Mr Panton, Mr Wildridge and Dr Keel from the SHHD. It was noted that the ACVSB/MSBT were examining proposals for look-back and would return to the matter in December. It was

<sup>240</sup> Day 85, page 105

<sup>241</sup> Professor Cash's letter to SNBTS Directors dated 21 June 1994 [SNB.009.9571]

<sup>242</sup> Professor Cash – Day 82, pages 104–105

<sup>243</sup> Note of SNBTS General Issues Meeting held on 21 September 1994 [SGH.004.0840]

<sup>244</sup> Dr Keel – Day 86, page 142–143

<sup>245</sup> Day 86, pages 147–148

<sup>246</sup> Minutes of ACMSBT meeting held on 29 September 1994 [DOH.001.0021] at 0023

<sup>247</sup> Ibid [DOH.001.0021] at 0024

<sup>248</sup> Minutes of SNBTS General Issues meeting held on 14 October 1994 [SGH.004.0803]

reported that the effectiveness of Interferon therapy for HCV infection had been questioned at the meeting of the ACVSB/MSBT on 29 September 1994. Press interest was noted to be 'another potential problem'. Dr Keel and Dr Perry were noted as awaiting the decision but pointed out that 'MSBT had no real locus in this since it was not a matter of blood safety'.<sup>249</sup> Dr Keel thought the comment about the MSBT (ACVSB/MSBT) not having any real locus was a 'nitpicking point' and 'not terribly material to any of the discussions that were going on'. She did not feel that this represented an attempt to 'stall' look-back and did not consider that this represented a change of view within the SHHD, but acknowledged that it would have been undesirable from a Scottish perspective if the ACVSB/MSBT had stepped in and declined to implement the policy from its position as a UK-wide advisory committee.<sup>250</sup> In his evidence, Mr McIntosh said that there had been no need to take the decision back to a scientific committee at that stage. By then it was about practical matters such as logistics and computers, rather than the sorts of matters in which the committee specialised.<sup>251</sup>

**35.164** The MSC met on 10 November 1994.<sup>252</sup> At that meeting, Professor Cash provided an update and introduced discussion on HCV look-back under reference to a report of the recommendations of the SACTTI. The report referred to an ad hoc assembly of experts held on 5 August 1994, convened specifically to discuss the feasibility of look-back, along with others including Professor Tedder, Dr Gillon, Dr Mortimer, Dr Robinson and Dr Alexander.<sup>253</sup> The meeting noted, amongst other things, that, although not clinically apparent in most cases, HCV infection was not trivial, and might cause serious, progressive liver damage leading to cirrhosis and hepato-cellular carcinoma in the long term. It narrated that treatment offered early after diagnosis was mostly likely to be effective in arresting liver damage, while patients with established fibrosis and portal hypertension would not benefit. Early evidence from pilot studies showed that combination therapy with Interferon and Ribavirin might achieve virus clearance in up to 60% of patients. Interferon Alpha was not yet licensed for use in HCV infection. It was also noted that it was still not known whether therapy would affect the long-term natural history of the infection and prevent relapse after therapy was discontinued. Reference was made to the fact that when HCV screening was introduced in September 1991, look-back was not then introduced due to doubts about the long term effects of Hepatitis C, coupled with a lack of effective therapy. Furthermore, secondary transmission of HCV to sexual partners and offspring was then thought to rarely occur. The experts concluded that:

[T]here is a serious case for considering a look-back policy for HCV. To do otherwise, when a look-back programme for HIV already exists, suggests double standards. The wider implications of such a policy will need further consideration and the SACTTI recommends that the Hepatitis Advisory Group and the MSBT consider the matter further as soon as possible.<sup>254</sup>

**35.165** The ACVSB/MSBT met on 15 December 1994. Dr Keel was present as an observer.<sup>255</sup> A report of the SACTTI recommendations on HCV look-back was presented by Dr Robinson. Discussion at that meeting was extensive. It was reported that since the last meeting of the committee, Interferon had been licensed for use in the treatment of HCV

<sup>249</sup> Ibid [SGH.004.0803] at 0805

<sup>250</sup> Dr Keel – Day 86, pages 144–147

<sup>251</sup> Mr McIntosh – Day 84, pages 136–137

<sup>252</sup> Agenda for meeting of the SNBTS Medical and Scientific Committee on 10 November 1994 [SNB.009.9436]

<sup>253</sup> SACTTI recommendations on HCV look-back [SNB.009.9512]

<sup>254</sup> Ibid [SNB.009.9512] at 9515

<sup>255</sup> Minutes of ACMSBT meeting held on 15 December 1994 [SNB.008.4820]

chronic liver damage.<sup>256</sup> Dr Robinson's sub-committee's view was that 'there was a duty of care towards the patients who were affected, and the implicated donors'.<sup>257</sup> Dr Robinson reported that it was now estimated that 60–80% of recipients who developed transfusion-transmitted HCV infection would become carriers and that 50% would develop chronic hepatitis. Twenty per cent of infected recipients might develop cirrhosis. There could be serious implications for the transfusion population.

**35.166** The minute noted Dr Robinson's comments that:

The overriding view of members who commented to the subcommittee, and the view of the sub committee was that transfusion recipients, some of whom may have been harmed, would benefit from a lookback exercise. Liaison with hepatologists would be needed to ensure a consistent and harmonious approach across the UK, and the legal and ethical implications would need to be carefully considered.<sup>258</sup>

**35.167** Dr Metters, the chairman, commented that the lawyers would look to the committee for a view on how to carry out the duty of care. The process would aim to do what was reasonable and not go beyond that. Dr Perry commented that recognition of the duty of care was right, and that:

[T]he Committee's position needed to be clear on what had changed since 1991 to allow look back now.<sup>259</sup>

**35.168** Dr Robinson commented that it was only more recently that the seriousness of HCV had been recognised.<sup>260</sup> Dr Metters suggested that the benefit of treatment which was becoming available, and counselling, were factors.<sup>261</sup>

**35.169** There were some voices of dissent. It was minuted that:

Professor Zuckerman shared the view expressed by Dr Mortimer that the question of lookback was driven by lawyers. It was important to distinguish between those infected with HCV through NHS treatment and by other means.<sup>262</sup>

**35.170** The practicalities of look-back were discussed. However, the CMO intervened in the debate and commented that it was in the public interest that there should be an urgent decision on the matters of principle and that the detail, though important, was less urgent. A comment from Dr Keel was noted:

Dr Keel said that the view in Scotland was that the Secretary of State was vulnerable as look back was feasible since donors could be identified and traced, and advice from Scottish Office lawyers was that look back should start immediately. The Chairman stressed the need for maintaining uniformity in the UK, but said that it was for the Secretaries of State, not the Committee to decide on whether Scotland should go ahead early.<sup>263</sup>

---

<sup>256</sup> Licensing was an important development, expressing the official view of the Committee on Medicines that the product passed all regulatory tests for general use. However, as the paper by Makris et al shows, there had been extensive use of the product before licensing.

<sup>257</sup> Minutes of ACVSB/MSBT meeting held on 15 December 1994 [SNB.008.4820] at 4824

<sup>258</sup> Ibid [SNB.008.4820] at 4825

<sup>259</sup> Ibid

<sup>260</sup> Compare Chapter 15, *Knowledge of Viral Hepatitis 2 – 1975 to 1985*, and Chapter 16, *Knowledge of Viral Hepatitis 3 – 1986 Onwards*. The seriousness of NANBH/HCV was increasingly acknowledged by relevant experts from 1985.

<sup>261</sup> Minutes of ACVSB/MSBT meeting held on 15 December 1994 [SNB.008.4820] at 4825

<sup>262</sup> Ibid [SNB.008.4820] at 4825

<sup>263</sup> Ibid [SNB.008.4820] at 4826

**35.171** Dr Keel explained that liability for failing to implement look-back was considered a 'material issue' at the time. Once the SHHD had received legal advice, it had to be taken seriously. She did not remember the issue of liability having dominated discussions until that point but it had now become the main determining factor in the decision to proceed with look-back.<sup>264</sup> It was noted at the meeting that four writs had already been issued against the NBA and that the legal advice received was that the duty of care existed in this case.<sup>265</sup>

**35.172** Paragraph 7.12 of the minutes records the material decision reached at the meeting:

Following the discussion the Committee agreed its advice to Ministers as:

- i. in the Committee's view there is a duty of care towards those infected with HCV as a result of NHS treatment. It follows that procedures should be put in place to identify the patients at risk;
- ii. whatever is done should be done equally and uniformly throughout the UK;
- iii. guidance should be drawn up as soon as possible.<sup>266</sup>

**35.173** At paragraph 7.13 it was noted that the Committee agreed that these conclusions would be passed on to the Secretaries of State of all four health departments.<sup>267</sup>

**35.174** When Dr Keel left the meeting her impression was that the UK Health Departments would advise their Ministers separately that look-back should be undertaken across the UK, that the detail was being worked out by various groups and that this would be based on the results from the south east Scotland 'pilot' study. Her impression was that look-back was now going to be put in place 'pretty quickly', as soon as the blood transfusion services could get the guidance developed and put in place in different parts of the UK.<sup>268</sup>

**35.175** Dr Keel stated that, while the minutes might give an impression of activity, other impressions might be drawn, reading between the lines, which suggested that perhaps things were not going to move as quickly as the SHHD might have desired. She explained that, given Scotland's different position and in view of the legal advice that they had received, there was more pressure on Scotland to move forward than might have been felt in other parts of the UK. In addition, Scotland had some practical experience of running look-back.<sup>269</sup>

**35.176** Professor Cash expressed views on this meeting. He was not present and Dr Metters had reminded members of their duty of confidentiality relating to advice given to Ministers. His interpretation of the course of events at this meeting was that it had been decided that there was no option but to proceed and that 'ministers should be advised to press the button and commence some form of look-back'. Of the many reasons for this, as he saw matters, one was the question of legal liability. He thought that there had been no mention of treatment, for example, though that would have been 'incorporated into the whole concept of legal liability'.<sup>270</sup> It is not appropriate to comment on the stage at

---

<sup>264</sup> Dr Keel – Day 86, pages 150–151

<sup>265</sup> Minutes of ACVSB/MSBT meeting held on 15 December 1994 [SNB.008.4820] at 4825

<sup>266</sup> Ibid [SNB.008.4820] at 4826–27

<sup>267</sup> Ibid [SNB.008.4820] at 4827

<sup>268</sup> Dr Keel – Day 86, page 152

<sup>269</sup> Ibid pages 153–154

<sup>270</sup> Professor Cash – Day 85, pages 108–109



which legal liability might have been triggered by developing forms of treatment. Professor Cash's comment reflects his views that threat of legal liability had been a consideration at least since 1991.

**35.177** Dr Keel thought that she would have come back from the ACVSB/MSBT meeting and briefed departmental colleagues between 15 and 22 December 1994. She would have prepared a note of the meeting, as was her usual habit, and would have noted that she had suggested that Scottish Ministers were vulnerable because of the legal advice that had been received. She met with colleagues to discuss getting on with look-back from a Scottish point of view. She thought that, by this stage, there was a collective view that the SHHD needed to inject a degree of urgency into the matter.<sup>271</sup>

### **The decision in Scotland**

**35.178** Matters came to a head on 22 December 1994 when Lord Fraser of Carmyllie, Minister of State at the Scottish Office covering home and health affairs, wrote to Mr Tom Sackville, the Parliamentary Under Secretary of State at the DoH, intimating that, in the light of the medical and legal advice he had received, he had little choice but to carry forward general look-back which the SNBTS was prepared to implement.<sup>272</sup> Mr Tucker, administrative Head of Division at the SHHD, explained that, as it was his responsibility to formulate and coordinate policy advice to Ministers based on the views of professional experts, he would have put forward a minute to Lord Fraser setting out the advice received and seeking his decision on instituting look-back in Scotland.<sup>273</sup>

**35.179** In 1995 a look-back exercise was commenced throughout the UK to trace patients who had received blood products from donors who were found to have tested positive for HCV.

### **Look-back in place**

**35.180** When look-back began, it identified blood donors who had tested positive for HCV in the years since testing was introduced, covering the period 1991–95. The donor would have tested positive with whichever generation of test was then available and their donation would not have been transfused or used in the preparation of blood products. Previous donations by infected donors, before testing had been introduced, would have been the focus of look-back.<sup>274</sup>

**35.181** The next stage of look-back was an attempt to contact all possible recipients of the infected donor's blood, or blood products, manufactured from that blood at any stage in the preceding years. In some cases that represented a large number of recipients over many years. This was done by contacting the hospital where the transfusion had taken place. Many hospital records were inadequate to match donor and recipient: in the early to mid-1990s records tended not to be retained long-term, with many records having been destroyed in the normal course of records management at the time, and there was no effective, centralised computer system matching donors and recipients. Tracking down the recipient(s) was difficult as they might have moved and there might not have been a clear record of the relevant GP to contact for follow-up.<sup>275</sup>

---

<sup>271</sup> Dr Keel – Day 86, page 153

<sup>272</sup> Lord Fraser's letter to Mr Tom Sackville MP dated 22 December 1994 [SNB.008.4848]

<sup>273</sup> Mr Tucker's statement [PEN.018.0406] at 0406–07

<sup>274</sup> Dr Alexander – Day 85, pages 130–131

<sup>275</sup> Dr Alexander's statement on HCV testing [PEN.018.1360] at 1362–63

**35.182** Where a recipient was identified, a letter was sent by the transfusion service to their GP. The GP may not have had much, if any, experience with HCV and the letters to GPs were carefully drafted to encourage referral and often provided a local contact for further information.<sup>276</sup> It was considered that the GP would be best placed to determine whether any follow-up of the likely infection with HCV should be undertaken or not. (Pursuing the issue of HCV infection might not be helpful for an elderly or infirm patient, or one with a life-shortening disease, for example.)<sup>277</sup> It was then up to the GP to make a referral to a hepatologist or a gastroenterologist with an interest in hepatology.

**35.183** Dr Alexander concluded his statement on HCV look-back by attempting to assess the overall effectiveness of the exercise:

In terms of understanding the disease the exercise has been successful. As a strategy to find all the patients with transfusion related HCV infection retrospectively it has been much less successful. For those individuals found to be positive it has had real benefit. It has allowed those individuals to be processed appropriately and in many circumstances treated effectively. It allowed a large number of them to be compensated financially for developing disease as a consequence of the transfusion.<sup>278</sup>

**35.184** However, professional estimates suggest that only a tiny minority of those who were exposed to HCV have been identified by way of the look-back programme. Research published in 2002 estimated that only five per cent of the total number of HCV infections over the 11-year period to September 1991 have been identified, which represented a higher proportion (13%) of those who were alive in 1995 who had received infected blood.<sup>279</sup> Dr Alexander thought this was a fair assessment of the statistics available on the look-back exercise. Only a small percentage of overall HCV infections were picked up because many of the infected donors stopped coming back, perhaps discouraged by efforts to have high-risk donors remove themselves from blood panels. As he put it, 'if the whole programme is based on a donor coming back and being found to be positive and they don't come back, you are stuck'.<sup>280</sup>

**35.185** In addition, as Professor Cash noted (and as Dr Gillon's exercise had demonstrated several years previously), the numbers of individuals who might have been identified as carrying HCV were diminishing over the period between the introduction of screening and the introduction of look-back. Professor Cash explained that the principal reason for the attrition in terms of finding live patients to treat was death from the 'original pathology ... that had taken them to surgery'.<sup>281</sup>

**35.186** Dr Alexander was asked whether, with the benefit of hindsight, the look-back could have been done differently. He said:

In retrospect and with hindsight one could argue that it would have been more effective to screen all plasma samples that were available from donors (a backlog of three years for the English and longer for the Scottish). However

---

<sup>276</sup> An example of a letter of this type is to be found at [LAI.001.0105]. This was sent to Mr Laing's GP as part of the national look-back programme.

<sup>277</sup> Dr Alexander's statement on HCV testing [PEN.018.1360] at 1363

<sup>278</sup> Ibid [PEN.018.1360] at 1364

<sup>279</sup> Ibid

<sup>280</sup> Dr Alexander – Day 85, page 136

<sup>281</sup> Professor Cash – Day 85, pages 109–110

testing this large number of samples could have crippled the transfusion service from doing its normal every day job.<sup>282</sup>

The English backlog of samples from donors that could have been tested totalled more than six million in 1995. The logistics of testing retrospectively that number of stored donor samples for HCV in England alone, while continuing to run a blood transfusion service, were enormous and would have been very expensive.<sup>283</sup>

**35.187** In oral evidence he added this would have been ‘an enormously difficult exercise’ which would only have been possible with an ‘enormous amount of funding’.<sup>284</sup>

**35.188** Both the practical effectiveness (practicability) and the cost-effectiveness (value for patients) of HCV look-back had been challenged before Dr Gillon’s working group made their recommendation.<sup>285</sup> Later studies, including Dr Gillon’s, reported a low level of recipients of infected blood or blood components, who were alive, testable and HCV-positive.<sup>286</sup> However, as Dr Gillon observed, the measurement of the cost-effectiveness of a look-back programme required monitoring of a wide range of factors relating to mortality, morbidity and prolongation of life that have only recently begun to be fully understood. One outcome of the HCV look-back exercise, the National HCV Register, has followed up as many of the patients identified in look-back as possible, providing a uniquely valuable cohort which was starting to give long-term outcomes in very precise terms.<sup>287</sup>

**35.189** Dr Gillon commented that Danish researchers reporting on the outcome of an HCV look-back programme in their country could demonstrate no significant benefit in terms of mortality compared to non-infected transfused patients; they had, however, shown very considerable morbidity in the HCV-infected patients, which was amenable to treatment in a great many cases. The Danish researchers noted a cure rate of close to 50% for patients who were treated with Interferon, an early indication of emerging evidence of benefit for that group of patients.<sup>288</sup> Dr Gillon commented that the benefit people living with HCV obtained from treatment was an indication in favour of targeted look-back.<sup>289</sup> That appears clearly to be correct: finding NHS patients who had been infected by transfusion of blood and blood components may not have achieved a high success rate, but for every patient identified and treated successfully the potential benefit was considerable.

**35.190** Although a clearly measurable benefit has not yet been demonstrated in terms of overall mortality, Dr Gillon anticipated that a cost-effectiveness analysis may be carried out in the future. The Health Protection Agency Study would be extended long enough to show one way or the other whether patients did benefit.<sup>290</sup>

**35.191** Dr Gillon considered that further, incidental, benefits had been achieved by look-back. He considered that the UK transfusion services had regained a measure of trust with

<sup>282</sup> Dr Alexander’s statement on HCV testing [PEN.018.1360] at 1364

<sup>283</sup> Ibid [PEN.018.1360] at 1361

<sup>284</sup> Dr Alexander – Day 85, pages 136–137

<sup>285</sup> Busch, ‘Let’s look at human immunodeficiency virus look-back before leaping into hepatitis C virus look-back’, *Transfusion*, 1991; 31:655–661 [PEN.017.2307]

<sup>286</sup> For example, Just et al, ‘Long-term follow-up among Danish transfusion recipients identified in the national hepatitis C lookback’, *Transfusion*, 2012; 52(3):582–8 [PEN.018.0507]; Ayob et al, 1994 [LIT.001.3802]

<sup>287</sup> Dr Gillon – Day 86, pages 78–80

<sup>288</sup> Just et al, 2012 [PEN.018.0507]. It has to be noted that the nearly 50% cure rate was not achieved with Interferon alone. It reflected the use of more modern Interferon plus Ribavirin combination treatment after about 1998.

<sup>289</sup> Dr Gillon – Day 86, pages 81–83

<sup>290</sup> Ibid pages 79 and 84

the public. There had been various media campaigns when the decision was taken to start look-back and comments adverse to the reputation of the transfusion service had emerged. It was felt to be important to calm down the atmosphere and show that the SNBTS had done something about the problem. Lessons had been learnt from look-back, as reflected in the response to variant CJD (Creutzfeldt-Jakob disease) and other problems.<sup>291</sup> Dr Gillon accepted that it would have been better to have been preventative rather than reactive, but considered that things had progressed rapidly when it was eventually accepted that look-back had to be implemented.<sup>292</sup>

### The ethical considerations

**35.192** The Inquiry had an interest in investigating why four years elapsed between the commencement of universal HCV screening for blood donors on 1 September 1991 and the introduction of the UK general look-back in mid-1995, and whether any ethical or other issues arose relative to the course of events.

**35.193** Lord Fraser's letter indicated that part of the reason for lack of follow-up action on identifying infected donors had been:

[A] concern that it would be impossible to identify all recipients of infected blood and even if it were possible there was a lack of accepted treatment which would be beneficial. It was accepted that if no effective treatment was available, informing those patients who were unaware of their situation could not be justified, since this would cause further distress and anxiety without any benefit.<sup>293</sup>

**35.194** Against the background of changing perceptions of the doctor/patient relationship discussed in preceding chapters and, in particular, in Chapter 32, *An Investigation into the Systems in Place for Informing Patients about the Risks – Ethical Context*, the advice given to, and repeated by, Lord Fraser might be seen as an example of the paternalism of the 1970s. This attitude continued long after significant changes in opinion initiated by British Medical Association (BMA) and General Medical Council (GMC) publications in the late 1980s. Professor Nathanson, Director of Professional Activities at the BMA, responsible for overseeing the association's work on medical ethics and teacher at the universities of Cambridge and Durham, commented that the passage from Lord Fraser's letter was a common reason given at the time for not going ahead with a look-back programme. She said:

It has ... commonly been argued that where that information would bring them only uncertainty, where there was no treatment available, that you couldn't justify causing distress and anxiety. So that last sentence is a sentence that I would recognise as being one that has been commonly cited.<sup>294</sup>

**35.195** However, from a contemporary ethical perspective, Professor Nathanson asserted that individuals have a right to be told information about their health, about their own body and about infections without any qualification, including of the type set out by Lord Fraser. Further, patients aware of their diagnosis had other potential benefits. They could take steps to take care of themselves, even where no treatment was available,

---

<sup>291</sup> Ibid pages 85–86

<sup>292</sup> Ibid page 85

<sup>293</sup> Lord Fraser's letter to Mr Tom Sackville MP dated 22 December 1994 [SNB.008.4848] at 4848

<sup>294</sup> Professor Nathanson – Day 84, page 53

such as by reducing or abstaining altogether from drinking alcohol. They could also be closely monitored and be offered the opportunity of drug treatment as soon as it became available. If they were monitored, their clinicians did not lose contact and the patient would hopefully be contactable when a treatment became available. Otherwise, when drug treatment became available, the patient might be difficult to locate and valuable time would be lost.<sup>295</sup>

**35.196** In addition, if the medical profession does not give people information they hold about them, trust can be lost. If a patient might require unpleasant and closely monitored treatment in the future, requiring a lot of cooperation between doctor and patient, then the fact that information had previously been withheld could undermine that trust.<sup>296</sup>

**35.197** Less generously, it has to be noted that patients who were not informed of their exposure to virus infection were not in a position to take advice, medical or legal, on the implications of having been infected in the course of medical treatment. Lord Fraser had legal as well as medical advice in forming his views. It is appropriate to discuss the issue more fully.

**35.198** It is not for this Inquiry to provide an answer, as a matter of generality, to the question when legal liability might have crystallised, having regard to the availability on general prescription of drug therapy for liver disease resulting from HCV infection. That may depend on circumstances, including the availability of a drug on a named patient basis prior to licensing, and whether the patient was, or could have been, given a choice whether to accept therapy. Professor Nathanson's evidence (paragraph 35.195) has considerable weight. Instant availability of effective therapy, and the risk of legal liability, are not the only issues relevant to look-back policy. Pharmaceutical research may result in new products, or the refinement of existing products, which are beneficial to those infected with HCV. Look-back provides an opportunity for those infected through infected donations to become aware of their condition and to benefit from such new, or refined, products.

**35.199** Professor Cash stated that he strongly supported all of the reasons that Lord Fraser gave in the letter. The SEBTS study had shown that look-back was 'feasible and practicable'.<sup>297</sup> Treatment for HCV was available for general prescription following licensing. And the letter acknowledged the central argument about potential liability which resulted, in his view, from these conclusions. He was referred to the section of the letter which stated that the matter of a look-back policy for HCV was considered by the ACVSB/MSBT, which had advised that procedures should be put in place to identify those at risk but that 'whatever is done should be done equally and uniformly throughout the UK'.<sup>298</sup> His attention was also drawn to the passage which narrated that the advice that Lord Fraser had received from his medical and legal staff had led him to conclude that 'I consider it is no longer a matter of policy but of legal liability, and that look-back should take place as soon as possible in Scotland'.<sup>299</sup> Professor Cash acknowledged that Lord Fraser was conscious that the advisory committee was not advocating immediate implementation of look-back but that, notwithstanding that, Lord Fraser was planning to go ahead with look-back in Scotland. Professor Cash again supported that approach. He accepted, by reference to this letter, that the position in 1991 when screening was introduced was that

---

<sup>295</sup> Ibid pages 53–54

<sup>296</sup> Ibid page 54

<sup>297</sup> Lord Fraser's letter to Mr Tom Sackville MP dated 22 December 1994 [SNB.008.4848]

<sup>298</sup> Ibid [SNB.008.4848]

<sup>299</sup> Ibid

it was the Scottish Office which had responsibility for deciding whether look-back should be implemented in Scotland. He explained that that was because extra resources were going to be required, and in his view at the time it would have required a CMO letter 'to get things going'. In these respects, the position was the same in 1991 as it was at the time of Lord Fraser's letter.<sup>300</sup>

**35.200** Professor Cash was referred to the section of the letter which suggested that the SNBTS could be considered negligent if it did not proceed with look-back. Dr Mitchell had written to him on 14 May 1990 commenting that Glasgow and West of Scotland RTC at that time had no look-back policy, and that the Service could be considered to be negligent in not advising about potential future use of donor blood.<sup>301</sup> He was asked if this was, perhaps, sounding a 'distant alarm bell'. Professor Cash said that he did not consider that Dr Mitchell was the originator of the alarm bell; he considered that everybody was beginning to think about the implications. He recalled there had been concern in September 1988 at a meeting of a group of people, who included Scottish Office lawyers, about the potential for litigation that would arise from HIV transmission by blood and blood products. Professor Cash considered that this was a landmark meeting at which people 'eventually began to talk about who had the duty of care and legal responsibility'. He explained that they had all been 'fretting' about look-back.<sup>302</sup>

**35.201** The stage at which legal liability crystallised with the general availability of an effective treatment for liver disease may well have been the last point at which to introduce look-back. But it cannot be concluded that that was necessarily the first stage of importance.

## Discussion

### *Policy on look-back*

**35.202** From 1991, there was a clear UK transfusion service policy on HCV look-back, following the advice of the ACVSB/MSBT at its meeting on 25 February of that year. After the introduction of anti-HCV screening, look-back would 'not be undertaken as a service leaving the option for those carrying out research. However all cases of post-transfusion hepatitis should continue to be investigated'.<sup>303</sup>

**35.203** That was a qualification of the agreement between Professor Cash and Dr Gunson recorded in Professor Cash's letter to the Scottish Transfusion Directors dated 9 July 1990, in which it was said that investigation of donors implicated in cases of reported post-transfusion hepatitis would continue in the period before anti-HCV was introduced, but that, from that date, it would not be appropriate to introduce a systematic look-back programme on previous recipients of donations. Witnesses were agreed that the letter referred to reverse look-back and, if so interpreted, it implied a more comprehensive ban on look-back than emerged in February 1991.

**35.204** It would be inappropriate, however, to apply too rigidly the definitions of look-back introduced in paragraphs 35.3 and 35.4 of this chapter. The terms 'targeted look-back' and 'reverse look-back' associated with the definitions do not appear to have been in common use in the UK transfusion service, so far as disclosed by the contemporaneous correspondence and records of committee proceedings recovered by the Inquiry. From a

---

<sup>300</sup> Professor Cash – Day 85, pages 3–5

<sup>301</sup> Dr Mitchell's letter to Professor Cash dated 14 May 1990 [SNB.004.5009]

<sup>302</sup> Professor Cash – Day 85, pages 12–13

<sup>303</sup> Minutes of meeting of the ACVSB/MSBT on 25 February 1991 [SNB.001.8934] at 8939

review of the whole evidence it is generally possible, with the benefit of expert help such as provided by Dr Gillon, or from the context in some cases, to interpret the documentary evidence and form a view whether individual documents referred to 'targeted look-back' or 'reverse look-back' as now defined. Examples have been noted in the narrative of the evidence.

**35.205** However, to adopt the terminology now in use, the advice of the ACVSB/MSBT in February 1991 can be expressed in this way. Following the introduction of anti-HCV screening reverse look-back should continue as it had in the past, providing for the investigation of the source of transmitted infection where a transfusion patient had acquired HCV infection. Otherwise there should be no systematic look-back programme. On that view, systematic targeted look-back would be inconsistent with UK, including Scottish, Health Department policy from February 1991.

**35.206** When Professor Cash read the guidelines prepared by Dr Gillon's group in September 1990 it would have been apparent to him that targeted look-back was proposed, and it would equally have been apparent that that was contrary to the agreement on policy he had reached with Dr Gunson and reported in July 1990. His response was that the SNBTS required to think about the issue carefully. He circulated the report to the Regional Transfusion Directors and to Mr McIntosh in anticipation of the MSC meeting of 6 November 1990. There was no representative of the SHHD at that meeting, though the BTS was represented by the Regional Transfusion Director for Leeds who spoke for Dr Gunson.<sup>304</sup> In the event, the meeting did not make a decision on any matter or principle, but commissioned Dr Gillon to re-draft his proposals as Standard Operational Procedure guidelines.

**35.207** The issue of principle was referred in the first instance to Dr Metters, and the SHHD and professional members of the ACVSB/MSBT were copied into the correspondence.<sup>305</sup> Professor Cash's letter did not disclose Dr Gillon's recommendations. It simply invited Dr Metters to refer to the ACVSB/MSBT the SNBTS Directors' request that a policy of look-back (without further specification) be considered. Consequently, there was nothing to alert Dr McIntyre, of the SHHD, for example, to the fact that any particular departure from UK policy was in contemplation. As indicated in paragraphs 35.62–35.65, the precise sequence of events at the end of 1990 and in early 1991 remains obscure. By the meeting of the MSC on 19 February 1991 'national events' had come into play and led to agreement that no look-back should be introduced at that stage. The advice of the ACVSB/MSBT was more qualified but excluded a systematic look-back programme. That would have excluded the exercise proposed by Dr Gillon and his colleagues as contrary to UK and Scottish departmental policy on look-back. Having regard to later comments about the role of the ACVSB/MSBT in relation to look-back, it is significant that even at this early stage in events the committee was engaged in discussion as, effectively, the source of authoritative guidance on issues around look-back.

**35.208** Consistently with the policy position adopted, Professor Cash wrote to Dr Gillon on 12 March 1991 advising that the guidelines should be amended to exclude the references to targeted look-back. The outcome was that Professor Cash had 'tested the water' with Dr Metters and through him the ACVSB/MSBT without disclosing Dr Gillon's proposals and without compromising the agreement he had reached with Dr Gunson.

<sup>304</sup> Minutes of the first meeting of the SNBTS Medical and Scientific Committee on 6 November 1990 [SNB.009.5513]

<sup>305</sup> Referred to at paragraph 35.60 above

**35.209** As narrated above, when confronted with Professor Cash's letter dated 12 March 1991, Dr Gillon, with the support of Dr McClelland, resolved to go ahead with targeted look-back in the SEBTS region. This can be seen, in hindsight, as a highly principled act, in defiance of national policy, and it should be said immediately that in the view of this Inquiry Dr Gillon's actions were highly commendable.

**35.210** Dr Gillon considered that the SEBTS ought, and should be able, to carry out a look-back exercise from September 1991, the date upon which donor screening for HCV was to commence. Suitable second-generation tests were becoming available and a confirmatory PCR test for HCV was in the later stages of development. From Dr Gillon's point of view, the initiatives taken in south east Scotland reflected the correct ethical response to donors following the introduction of HCV testing. It is important to note the basis for that view. His experience of the HIV era was a material consideration. In relation to HCV, the dilemma arose for him as a doctor as soon as a donation was confirmed as HCV-positive: by the following day he would have the donor's records on his desk with information showing whether there were previous donations and, therefore, whether the donor might have transmitted HCV infection. From that point he had means of obtaining access to information about previous recipients.<sup>306</sup>

**35.211** He accepted that there were important differences between HCV and HIV. Consequently, one could not necessarily compare the decision immediately to institute targeted look-back for HIV with the long process before a similar procedure was instituted for HCV. The health implications of positive diagnoses for the two diseases were very different. The prevention of the secondary spread of HIV, despite the absence of treatment, could have been a reason for proceeding with HIV look-back. With HCV, for a long time there was no information on its sexual transmission and once such information became available it demonstrated much lower levels of sexual transmission.<sup>307</sup>

**35.212** He explained, however, that to his mind 'previous donations' translated directly into 'previous recipients' and he felt that he could not in all conscience ignore that information. He saw it as part of his duty of care to the recipients of potentially infected blood to ensure that their clinicians had that information, irrespective of whether there was any treatment available at that time.<sup>308</sup> Dr Gillon's views on this matter accord with the ethical duties that Professor Nathanson considered incumbent on a doctor in the doctor/patient context in the early 1990s.

**35.213** Dr Gillon's first report to Professor Cash was dated 20 September 1990, and the ethical dilemma was clearly expressed in it.<sup>309</sup> There were logistical difficulties, sufficient at the time to persuade the AABB that look-back should not be recommended. (However, as highlighted above, it was perceived in the USA that surrogate testing had limited the risk of infected individuals continuing to donate blood.) As noted in paragraph 35.48 above, Dr Gillon's group considered the AABB position to be untenable, given the desirability of informing recipients so that they could protect others, and also receive treatment with Interferon if the benefits of this form of therapy were confirmed.

---

<sup>306</sup> Dr Gillon – Day 86, page 97

<sup>307</sup> Ibid pages 98 and 100

<sup>308</sup> Ibid pages 97–98

<sup>309</sup> Letter from Dr Gillon to Professor Cash dated 20 September 1990 [SNB.004.5074]



### *Dr Gillon's look-back project*

**35.214** The screen samples used in the SEBTS exercise were obtained between 1 September 1991 and 29 February 1992. The Ayob paper reporting on the exercise in the SEBTS was published in 1994. It had been submitted for publication in November 1993 and accepted for publication on 21 July 1994. It disclosed the time taken for the exercise in terms of medical and secretarial hours. But it did not disclose the time taken for the analysis of the study for the paper or for the preparation of the report itself. However, a brief account of the project had been included in Dr Gillon's paper for the College of Physicians symposium in October 1993 (albeit mis-described). Professor Cash alerted Transfusion Directors to the need to review the policy on look-back in his letter dated 15 October 1993, with particular reference to the views of Dr Dusheiko. The MSC debated the issue at its meeting in November 1993.

**35.215** By autumn 1993 therefore, it was highly likely that the SEBTS initiative would become known to a wider constituency. Subsequently, it must also have become clear to those concerned with UK and Scottish Health Department policy, as they came to appreciate what had been done, that the report related to an activity that was in fairly flagrant breach of national policy guidelines. The Ayob paper stated that UK policy, in common with American policy, was against look-back. However, before looking at the evidence relating to the official response, it is necessary to consider what was known about the SEBTS initiative between 1991 and mid 1994, and by whom.

**35.216** Dr Gillon said that he thought that he informed Professor Cash of the look-back exercise at some point between March 1991 and September 1991. That evidence is accepted. Professor Cash's own recollection of events was imprecise and, in any event, he stated that he was prepared to defer to Dr Gillon on the matter. When the exercise began, it seems likely that anyone alert to what was happening in the SEBTS would have understood that some initiative was in hand. Of the 42,697 donors screened routinely, 20 were identified as HCV-positive. Fifteen had given previous donations from which 83 components had been prepared. All of these were investigated. It was a major exercise involving accessing a large number of records and involving a significant investment of time. It was not carried out in secret, and given its scale it could hardly have been clandestine, but it seems highly likely that there was no attempt to publicise the exercise while it was in progress. Dr Gillon may have informed Professor Cash of the exercise for any number of possible reasons, one of which may have been that it was a prudent precaution to take in order to ensure that there would be no interference with it once it had begun.

**35.217** On the other hand, it appears likely that other SNBTS Transfusion Directors were not informed of it until at or after the October 1993 symposium, depending on whether or not they heard Dr Gillon's address. That is not surprising. As discussed throughout this report, the several regions of the SNBTS largely operated as separate autonomous organisations, each implementing their own policies which might coincide with or differ from others' on an uncoordinated basis. Professor Cash's letter of 15 October 1993 did not mention Dr Gillon's work in raising the issue of look-back with the Transfusion Directors. As matters transpired at the MSC meeting on 9–10 November 1993, the Directors wanted further information from Dr McClelland, and time to think. Accordingly, it appears likely that they had not been kept informed of the SEBTS initiative before that point. It is likely that it was as a result of that meeting that the Directors became 'generally aware' of Dr Gillon's work, in Professor Cash's words (see paragraph 35.107).

**35.218** Mr McIntosh considered that he had been 'duped'. At some stage he had been informed by Professor Cash that the SEBTS was conducting a 'pilot study' of look-back procedures. Professor Cash said that he had suggested the title and his evidence on this matter is accepted. The title was devised in order to avoid questions about the SEBTS project. It is likely that it was a matter of indifference to Dr Gillon how the project was described so long as he could get on with the work. A 'pilot study' on look-back was less of a challenge to national policy than a systematic targeted look-back investigation of all anti-HCV screen positive returning donors and the recipients of blood or components obtained from their donations. Professor Cash had an interest in representing the exercise as one limited in scope. And, as Dr Gillon's anecdote at paragraph 35.109 makes apparent, Professor Cash appears to have been concerned to make it clear to others that the initiative was not an SNBTS pilot, but strictly an SEBTS matter. In his oral evidence, Professor Cash explained his position: there was a great deal of sensitivity in government circles about look-back, and opposition in some quarters. In the circumstances described, it is reasonable to infer that if action against Dr Gillon's initiative were to be avoided, it was necessary to resort to a degree of subterfuge. And it succeeded. Dr Gillon was able to proceed to complete the project without interference. The CSA, as represented by Mr McIntosh, did not understand the nature of the project, and there was no adverse reaction from any agency.

**35.219** It appears likely that the SHHD had no knowledge of the project until the autumn of 1993 at the earliest. As understood by Dr Keel, the position of the SHHD from the time she joined the service until early 1994 was that Scotland should not be implementing look-back because it was not thought feasible and because there was no evidence-based therapy available for treating infected individuals. Those views were shaped and influenced by statements by the SNBTS Directors, by UK committees, and by the department's understanding of expert opinion 'across the UK and abroad'. Broadly the SHHD reasons for believing that look-back was not appropriate reflected the views of the ACVSB/MSBT.

**35.220** It is apparent from Dr Keel's evidence that the feasibility of a look-back exercise in Scotland, generally, became clear to her on 18 May 1994. Several features of her recorded actions on that day demonstrate that she was unprepared for what Dr Gillon had to say. She was in error in suggesting that the SHHD might not have a locus, given their role in policy matters, but that may have resulted from her inexperience in her post. Her anxiety to return to base and discuss what she had heard with SHHD colleagues was indicative of the fact that she had come to the meeting unprepared by such discussion in advance of the meeting.

**35.221** It is slightly less easy to understand why Dr Keel should have been in that position. Dr Keel was at the October symposium at which look-back was aired, to some extent at least, by Dr Gillon. Even if one discounts Professor Cash's more exuberant observations on the impact of Dr Dusheiko's contribution, Dr Gillon's paper did disclose that look-back had been explored in the SESBT region. However, it may be, as Dr Gillon suggested, that despite his airing of the subject only Dr Dusheiko and 'one or two others' had their interest caught by it. Professor Cash, who had arranged the symposium and, apparently, had a particular interest in look-back at the time, also had no recollection of the subject matter of Dr Gillon's talk. Dr Keel was not copied in on Professor Cash's letter of 15 October 1993 to transfusion colleagues, which indicates that he was not then ready to open up the policy issue directly with SHHD colleagues before he had discussed it at the MSC. However, Dr Keel was present at the MSC discussion.

**35.222** The MSC discussed look-back on 10 November 1993, as anticipated in Professor Cash's letter. The minute of that meeting records that full discussion took place of what was clearly a targeted look-back scheme (see paragraph 35.128). Dr Keel is recorded as having been present for item 4.6 which included the discussion of 'Lookback: HCV' as a new agenda item but Dr Gillon was not present. Consequently no presentation by him, such as Dr Keel witnessed on 18 May 1994, was then made. The record indicates clearly that, while decision was postponed, what had been envisaged was a policy decision on the item. It may be that the consensus to postpone the decision together with the concerns expressed by the directors in relation to the potential difficulties with the practicalities likely to be encountered in Inverness, Aberdeen, Dundee and the west of Scotland reinforced her then extant view that look-back was not feasible for Scotland as a whole or considered an urgent matter. Undoubtedly, the SEBTS was uniquely well-placed within Scotland to carry out a look-back exercise due to its blood banking system, the expert assistance available to it and the IT resources that it commanded. The action log following from the meeting, which provided background to the agenda for the meeting on 18 May 1994,<sup>310</sup> indicated that Professor Cash was to ensure that 'look-back-HCV' received further discussion. The 'Discussion Topics For Future MSC Meetings', attached to the agenda for the 18 May 1994 meeting, included 'HCV confirmed positive donors-look-back'.<sup>311</sup> No name or initials were provided for any 'presenter' and no priority rating had been allotted to the item. The action log, also attached to the agenda of 18 May 1994, suggested that the ACTTD/I were then discussing look-back. The SHHD was not represented on the ACTTD/I. Dr Keel was at the issues meeting on 16 May 1994. At that meeting targeted look-back was discussed. The minute records that Mr McIntosh would send a draft policy statement to the Department for clearance.

**35.223** If Dr Keel had sought the advice of other medical and policy colleagues before the meeting of 18 May, it seems reasonable to speculate that, despite her relative inexperience, she would not have inadvertently misrepresented the SHHD position at it. However, in the absence of any reference to HCV look-back on the agenda, it is not surprising that she did not consider that there was any need to do so. At the meeting on 24 May, arranged after the issues meeting of 16 May 'following further developments after the meeting', it was indicated that the SNBTS proposals for targeted look-back got a sympathetic hearing, but the decision was that the DoH would be consulted before a final decision was reached. Notwithstanding the impact of Dr Gillon's presentation, the SHHD still required to consult with the DoH and it seems likely that that would have been the attitude of SHHD officials whenever confronted with SNBTS proposals for targeted look-back.

**35.224** It is worth noting that in the autumn of 1993, Professor Cash's approach to targeted look-back, in recorded exchanges, appears to have been decidedly low-key. The records of the MSC meetings of November 1993 and May 1994 indicate clearly that, within the SNBTS community, Professor Cash was at pains to ensure that look-back was kept on the agenda. However, there is no indication in any of the correspondence that he was a passionate advocate held in check by more cautious transfusion directors.

**35.225** At the meeting of the ACTTD/I on 18 January 1994, Professor Cash explicitly relied on Dr Dusheiko's advocacy of targeted look-back. He did not then disclose Dr Gillon's completed work, and his proposal for action emphasised the need for research,

<sup>310</sup> List of action points attached to agenda for meeting of SNBTS Medical and Scientific Committee on 18 May 1994 [SNB.009.9172] at 9173

<sup>311</sup> Discussion Topics for Future MSC Meetings [SNB.009.9175]

probably involving a research grant application. Interestingly, it was remitted to Professor Tedder and Dr Barbara to examine protocol options for look-back. Scottish experience and capacity were not mentioned. But a corner had been turned: the committee supported the concept and encouraged grant seeking for the undertaking. It is against this background that the proceedings of the MSC on 18 May 1994 have to be considered, and the wider publication of Dr Gillon's programme has to be understood. It was, at very least, consistent with the thrust of the decision of the ACTTD/I, though not as yet the ACVSB/MSBT.

**35.226** The ACVSB/MSBT met on 10 February 1994. The minutes of that meeting have not been recovered. But it is clear that the matter was referred to the SACTTI. On 29 September 1994, Dr Robinson presented the SACTTI recommendations to the ACVSB/MSBT. Members of the SACTTI included Professor Cash and Dr Gillon. The recommendation was that there was a serious case for considering a look-back policy for HCV. Dr Gillon's work was not relied on in the report which dealt with the position of the NBTS and noted that the facilities were available to undertake tracing, counselling and referral, with a potential case load of 3000 (the number estimated by Dr Gillon for the rest of UK other than Scotland). The outcome on 29 September 1994 was a further postponement of any decision for members to submit written comments. The disposal of the issue of principle took place at the next meeting of the ACVSB/MSBT on 15 December 1994, and is narrated in paragraphs 35.165–35.173. Practical implementation of look-back was in the event accelerated by the actions of Lord Fraser of Carmyllie on 22 December 1994, and took place in 1995.

#### *Earlier implement of targeted look-back in Scotland*

**35.227** Lord Fraser of Carmyllie's letter answers conclusively the question whether Scotland was prevented by wider UK policy considerations from proceeding with targeted look-back from 1 September 1991. The Inquiry was not directed to any change in the law between 1990 and December 1994 that would have had a bearing on the advice Lord Fraser might have had from his legal advisers on the obligation to pursue look-back. There may, however, be questions as to whether the factual, circumstantial, context had changed over that period such as might have affected the enforceability of the general duty of care. Any relevant questions would then have related to the known facts, including those relating to the feasibility of look-back in Scotland. Crucial facts would have included:

- The reliability of available screening tests.
- The traceability of prior donations by a donor testing positive for anti-HCV after confirmation testing.
- The identification of potentially infective prior donations.
- The traceability of recipients of those donations.
- The availability or likely availability of treatment.

**35.228** The logistical difficulties associated with look-back have been rehearsed above: they were real and substantial and, as events were to prove, the relative failure of look-back when it was implemented was in part due to those difficulties. But by 1 September 1991, Scotland was in a particularly favourable position. The use of first-generation screening tests might have caused difficulties in some regions of England and Wales, as would the late and patchy availability of PCR tests, as described by Dr Alexander. However, prior to the introduction of routine screening in September 1991, it was known in Scotland, firstly, that the more sensitive and specific second-generation ELISA tests would be available

for routine screening and, secondly, that the RIBA confirmatory tests would also then be available. Furthermore, Professor Simmonds' PCR test was known to be available from the turn of 1990–91. As Dr Gillon explained, Scotland was one of the very few countries, and might have been the only country, that had PCR testing available as part of their confirmatory algorithm right from the outset, substantially ensuring reliable diagnosis for those found positive. When a donor was confirmed anti-HCV positive after 1 September 1991, they *knew* they were positive and this together with the excellent IT resources, assistance and blood banking system put the south east region of Scotland where Dr Gillon operated, in a particularly favourable, and possibly unique, position to initiate look-back from the very outset of screening as he had advocated. However, that was not the case for the rest of Scotland as became apparent at the MSC meeting at the end of 1993. A number of logistical difficulties, some of which are likely to have been exacerbated by the passage of time, had to be overcome when the UK look-back exercise began in 1995.

**35.229** Whenever precisely the feasibility of a look-back exercise in Scotland as a whole was, or should have been, established, a further matter which requires to be addressed relates to the availability of effective treatment. On his own evidence, Professor Cash, among others, became convinced of the inevitability of a look-back exercise as a result of Dr Dusheiko's address at the HCV symposium in October 1993 at which the use of Interferon was advocated as an effective therapy. Even if, contrary to the views of Professor Nathanson and Dr Gillon, the availability of a remedy could legitimately be considered central to the policy issue, there was strong evidence from that point onwards that Interferon was a possible candidate. However, at the MSC meeting in November 1994 Professor Cash reported on the discussions at the SACTTI, which included those relating to the early results of the Interferon and Ribavirin combination pilot study, the lack of a licence for Interferon and the lack of evidence as to whether the therapy would affect the long term natural history of the condition, including preventing relapse after therapy was discontinued.

**35.230** Further, it is a material consideration that Interferon was not licensed until November 1994. The licensing procedure did not prevent the use of the drug on a named patient basis, and Dr Dusheiko made it clear that there had been extensive use of it. On the other hand, it is highly unlikely that the SHHD or the DoH would, or could, have formulated and implemented a national policy that depended on treatment with the use of a drug that was still in the course of assessment by the Committee on Safety of Medicines as part of the licensing procedure. Apart from any risk to patients, the integrity of the licensing procedure itself would have been challenged if either had done so. Whether a decision on licensing of Interferon could have been accelerated would depend on pure speculation.

**35.231** As matters transpired, the Chief Medical Officer's intervention at the meeting of the ACVSB/MSTB on 15 December 1994, and Lord Fraser's letter to Mr Sackville on 22 December 1994 followed the licensing of Interferon. On all the evidence available to the Inquiry, it is not possible to conclude that an earlier decision on UK-wide or Scottish policy could have been reached.

**35.232** It is unfortunate that matters were so long drawn out. Time was the enemy of effective identification of patients who might benefit from management that took account of their infection. Not only was there a risk of progression beyond the stage at which intervention by therapy was likely to be effective, but patients also were lost

through death or the breakdown of communication links. However, it must also be borne in mind, as Dr Gillon noted in his evidence, that the look-back exercise undertaken in 1995 in the UK was one of the earliest comprehensive look-backs instituted in the world

## Conclusions

**35.233** Targeted look-back could not have begun before the commencement of routine screening. In Chapter 31, *The Introduction of Screening of Donated Blood for Hepatitis C*, it is concluded that a decision to recommend to Scottish Ministers that government policy should include a commitment to routine screening of blood donations for anti-HCV should have been taken by the middle of May 1990, with implementation unlikely much before autumn 1990, having regard to the supplies of test kits available.

**35.234** There were no scientific or medical grounds on which routine screening of blood donations in Scotland required to be started simultaneously with the rest of the UK. Successive delays in the uniform start date were influenced largely by problems relating to introducing screening in England and Wales, which had no parallel in Scotland. Scottish Office Health Ministers and the Secretary of State were not informed that financial and other problems affecting only England and Wales were delaying the start date, and advised that the policy of a uniform start date ought to be reviewed. Action, or inaction, on the part of a number of individuals (as more fully set out in Chapter 31) resulted in the opportunity being lost for a more prompt introduction of screening in Scotland. Consequently, Scottish patients lost, firstly, the benefit that would have accrued to them from the early introduction of screening and, secondly, the reduction in the risk of acquiring HCV by transfusion of unscreened, infected blood. What Scottish Office Health Ministers or the Secretary of State would have done with such information can only be a matter of speculation, but in its absence they were deprived of the opportunity to consider the issue and resolve it as they saw fit. In the event, 1 September 1991 became the earliest date at which look-back could have been commenced.

**35.235** If routine screening had been introduced earlier in Scotland, Dr Gillon would probably have gone ahead with the SEBTS project earlier, and the feasibility of look-back for the SEBTS at least would probably have been established earlier. However, as Dr Gillon noted, the work involved in the introduction of universal screening put the look-back debate on the back seat as the development of confirmatory procedures, time required to deal with false positives and the counselling of genuine positives kept people 'pretty busy'. That consideration would have applied whenever screening was introduced. In any event, none of these matters would have affected the licensing process for Interferon. Though from the introduction of Interferon treatment on a named patient basis in England in 1989 and in Scotland in 1990, therapeutic use was a reality, and there was the prospect of improved products being introduced in the ordinary course of research and development by pharmaceutical companies, the licensing of the product was an unavoidable aspect of the regulatory regime in the UK and applied in Scotland as it did in the rest of the UK.

**35.236** At the ACVSB/MSBT meeting in December 1994, Dr Perry expressed his concern that the committee should make clear what had changed between 1991 and that meeting to justify the decision on 15 December to 'allow look-back now'. The report of Dr Robinson's sub-committee provides part of the answer, so far as the ACVSB/MSBT is concerned.<sup>312</sup> However, the Inquiry does not have sufficient evidence about the situation

---

<sup>312</sup> Paragraphs 35.166–35.167 above

in England and Wales to provide an analysis or critique of the deliberations and decisions of the ACVSB/MSBT in relation to those parts of the UK over this critical period. So far as Scotland is concerned, Dr Keel emphasised that the ACVSB/MSBT was the principal UK Advisory Committee and that it would have been the committee that the SHHD 'would have looked to for a steer on this look-back'.<sup>313</sup> It is clear, however, that the sequence of events leading up to Lord Fraser's initiative did not reflect the outcome of requests from the SHHD for advice from the ACVSB/MSBT. On this occasion, Lord Fraser proceeded on Scottish advice.

**35.237** Lord Fraser's letter simply reflected the independent obligation of the Scottish Office Health Ministers to act in the best interests of Scottish patients, an obligation that existed throughout the relevant period and beyond. The clear expression of the legal obligation was not a new factor: the advice of law officers on that issue would have been the same whenever the question was put to them. As far as medical advice is concerned, Dr Keel was the main medical advisor at this point in time. She provided counsel on the medical and clinical benefits of look-back. Her own view had been formed by meetings that took place in the months preceding Lord Fraser's letter, as well as by SNBTS advice, particularly in relation to the SEBTS study. Latterly, she had also met with experts including hepatologists. In May 1994 she, and thereafter the SHHD, became convinced that look-back should be carried out in Scotland as a whole, and the SNBTS and the SHHD worked towards that end.

**35.238** The potential seriousness of NANB Hepatitis, and therefore of HCV infection, had been established in the second half of the 1980s. The suggestion at the ACVSB/MSBT meeting on 15 December 1994, reported at paragraph 35.168 above, that it was 'recently' recognised that HCV was potentially a serious condition is inconsistent with the evidence obtained by the Inquiry. The research of Dr Hay's Sheffield group using biopsy showing a high prevalence of serious morbidity in patients with NANB Hepatitis infection, was published in 1985. The Sheffield findings did not become generally accepted opinion immediately. However, the analysis of the clinical manifestations of infection in the eighth edition of Sherlock's *Diseases of the Liver and Biliary System*, 1989, and indeed Professor Zuckerman's 1988 paper on 'Unresolved issues in non-A, non-B hepatitis' reflected the general acceptance by 1989 of the potential seriousness of NANB Hepatitis/HCV infection.<sup>314</sup> The topic is discussed in Chapter 15, *Knowledge of Viral Hepatitis 2 – 1975 to 1985* and Chapter 16, *Knowledge of Viral Hepatitis 3 – 1986 Onwards*.

**35.239** The feasibility of look-back for Scotland as a whole was accepted by mid-1994, and the potential seriousness of the infection had been acknowledged before the beginning of that decade. The logistics of the look-back exercise were burdensome, partly because of problems with record-keeping and the limitations in the computer systems then available, both of which contributed to the difficulty in tracing patients – not an easy task in itself as a result of name changes and changes of address. But those difficulties had to be resolved in 1995, and the resolution of them is unlikely to have become less difficult with the passage of time. The effectiveness of the treatment, or treatments, available for HCV continued to be discussed by expert committees until almost the end of 1994.

<sup>313</sup> Dr Keel – Day 86, pages 107–108

<sup>314</sup> Chapter 16, *Knowledge of Viral Hepatitis 3 – 1986 Onwards*, paragraphs 16.37–16.39

**35.240** In 1993 and 1994 Interferon therapy was controversial. It is not clear that very many individuals, in fact, lost a chance of treatment. It was widely held that the prospects of effective treatment with Interferon, certainly alone, were poor. Furthermore, treatment was unpleasant and poorly tolerated by patients. However, as any treatment options developed, in terms of the range of product and their effectiveness, information of HCV status would have been of interest to patients and might have affected their receptivity to treatment, notwithstanding the risk of side-effects. For patients who were informed of their exposure to HCV, such information might have encouraged them to abstain from alcohol entirely, or reduce their consumption of it, and adopt a different lifestyle despite the absence of effective treatment for their condition.

**35.241** So far as the direct responsibility of Scottish Ministers is concerned, Lord Fraser of Carmyllie responded with reasonable speed to the advice tendered by Dr Keel and her legal colleagues. That was advice generated in Scotland, and underscored the responsibility of Scottish Ministers for health policy north of the border. However, in the final analysis, the availability of safe and effective treatment was always going to be a crucial factor. The SACTTI report presented to the ACVSB/MSBT on 10 November 1994 did not resolve matters to the satisfaction of that expert committee. Only when Interferon was licensed in November 1994 was the way clear. In all the circumstances prevailing, it cannot be said that look-back should have been introduced generally in Scotland before November 1994.

**35.242** As concluded in Chapter 3, *Statistics*, the investigations made by the Inquiry suggest that further epidemiological study will not produce a more reliable estimate of the number of people in Scotland who have been infected with HCV as a result of transfusion with blood or blood components. The number infected can only be estimated, and the Inquiry's best estimate can be found in Table 3.21 of that chapter. Whatever the number, every one of those still alive is likely to benefit from identification, testing and treatment. Some may have already so benefitted, but others will not have done so. Accordingly, the more pressing practical problem is how to identify all of those so infected in order to ensure that all may be offered effective medical care.

**35.243** The SNBTS look-back exercise, described in this chapter, ran until 1998 using data available following the introduction of anti-HCV screening in September 1991. That look-back exercise had necessary limitations. First, any HCV positive donors who had donated before screening began would not be screened unless they returned to donate after September 1991. Secondly, the look-back study lacked the highly efficient patient tracking systems available today. Early donor card records were not searchable and different transfusion centres and hospitals had different record keeping systems. Difficulties were encountered in cross referencing donation numbers and recipients and vice a versa. Medical records had been lost or destroyed. Some recipients had changed their names through marriage or other causes. Some recipients had changed addresses.

**35.244** Due to the inevitable limitations of the look-back exercise as described above, there will still be recipients of HCV positive blood who remained, or remain, unaware of that fact. Some of those will have cleared the virus naturally. Some will have died either as a result of age, the life-threatening condition that resulted in transfusion being required, HCV itself or from other causes. However, a number of the recipients will not have cleared the virus, will be alive and at risk of the disease progressing and of infecting others. Some of those who are symptomatic among that group may have sought medical attention,



have had their condition diagnosed and be receiving treatment for it. However, a number will remain who are either asymptomatic or whose condition has not yet been diagnosed despite their symptoms, particularly if they received a transfusion in the years leading up to the introduction of screening. Dr Mutimer, Consultant Hepatologist, suggested that the median time from infection to cirrhosis in younger patients was about 30 years.

**35.246** Significant symptoms are likely to manifest themselves as the condition progresses. Treatment is available which might arrest the development of the disease, and it tends to be more effective if given prior to the onset of cirrhosis and related complications. Attempts have been made to alert individuals thought to be at risk of HCV through a number of government initiatives including the *Hepatitis C Action Plan for Scotland*.<sup>315</sup> That plan has been much praised and was described by the World Hepatitis Alliance recently as 'a model of best practice'.<sup>316</sup> On 25 August 2011 the Scottish Government brought together sexual health, HIV, Hepatitis C and Hepatitis B into the *Sexual Health and Blood Borne Virus Framework 2011–2015*.<sup>317</sup> The framework built on the success of the *Hepatitis C Action Plan for Scotland: Phase II*<sup>318</sup> and *Respect and Responsibility*<sup>319</sup> as well as further developing the *HIV Action Plan in Scotland*.<sup>320</sup> However, as the majority of Scottish patients suffering from HCV have tended, historically, to become infected through drug use, the bulk of the practical measures outlined in the *Action Plan* and in the *Framework* are aimed at that cohort. Unfortunately, a stigma is attached to the condition in consequence of its drug related and substance abuse association, and the framework acknowledges that raising awareness of Hepatitis C among health professionals is also a significant challenge.

**35.247** Patients with bleeding disorders, registered with UKHCDO on the National Haemophilia Database, are also affected by the transmission of HCV. They are a well-defined group of individuals. Those who test HCV positive are being managed by, and receiving treatment from, haemophilia clinicians and other specialists as required. Their condition is subject to routine monitoring including by liver function tests.

**35.248** The transfusion patients have only one common characteristic namely that they received an infected transfusion at some date prior to September 1991 in the course of medical or surgical treatment. As previously indicated, not all recipients of HCV positive blood were traced by the look-back exercise. There are therefore individuals who may well remain unaware of their HCV positive status. Any measures designed to reach those suffering drug use-related HCV are less likely to reach, or identify, these individuals. These people are, however, likely to benefit from testing and, if appropriate, modern anti-viral treatment.

<sup>315</sup> Scottish Government (2006) *Hepatitis C Action Plan for Scotland – Phase I: September 2006 – August 2008*. Available: <http://www.scotland.gov.uk/Publications/2006/09/15093626/13> Last accessed 26 January 2015.

<sup>316</sup> Health Protection Scotland (2010) *Hepatitis Action Plan for Scotland: Phase II: Second Year Annual Report*. Available: <http://www.hepatitis-scotland.org.uk/media/50321/happii-second-yr-annual-report-2010-11.pdf>. Last accessed 26 January 2015.

<sup>317</sup> Scottish Government (2011) *The Sexual Health and Blood Borne Virus Framework 2011–2015*. Available: <http://www.scotland.gov.uk/Publications/2011/08/24085708/0> Last accessed 26 January 2015.

<sup>318</sup> Scottish Government (2008) *Hepatitis C Action Plan for Scotland: Phase II: May 2008 – March 2011*. Available: <http://www.scotland.gov.uk/Publications/2008/05/13103055/17> Last accessed 26 January 2015

<sup>319</sup> Scottish Government (2005) *Respect and Responsibility: Strategy and Action Plan for Improving Sexual Health*. Available: <http://www.scotland.gov.uk/Publications/2005/01/20603/content> Last accessed 26 January 2015

<sup>320</sup> Scottish Government (2009) *HIV Action Plan in Scotland: December 2009 to March 2014* Available: <http://www.scotland.gov.uk/Publications/2009/11/24105426/0> Last accessed 26 January 2015

## **Recommendation**

The Inquiry recommends:

That the Scottish Government takes all reasonable steps to offer an HCV test to everyone in Scotland who had a blood transfusion before September 1991 and who has not been tested for HCV.

# APPENDIX 1

## INQUIRY PROCEDURES

### Terms of Reference

The Terms of Reference for the Inquiry were agreed between the Scottish Ministers and Lord Penrose. By letter to Lord Penrose dated 12 January 2009 the then Cabinet Secretary for Health and Wellbeing, Nicola Sturgeon MSP, provided further explanation of certain aspects of the Terms of Reference. An amendment to the Terms of Reference for the Inquiry was announced on 13 November 2009 to include three additional deaths which were to be investigated and a further amendment to them was made on 22 February 2011 to remove one of those individuals from the investigation. The Terms of Reference as amended are:

#### Term of Reference 1:

To investigate the systems in place in Scotland for the collection, treatment, licensing, testing, preparation for supply and supply for use by the NHS of blood and blood products with particular reference to the risks of transmission of the Hepatitis C virus and HIV to patients treated by the NHS in Scotland, including the role of government in regulation and setting guidelines and standards.

#### Term of Reference 2:

To investigate the systems in place for informing patients treated by the NHS in Scotland of the risks associated with the use in their treatment of blood or blood products, with particular reference to the risks of infection with the Hepatitis C virus and HIV.

#### Term of Reference 3:

To investigate the systems in place in Scotland for obtaining consent from, and testing for infection with Hepatitis C and HIV, patients treated with blood or blood products, and informing any patients found to be so infected.

#### Term of Reference 4:

To investigate the systems for recording and monitoring the numbers of NHS patients in Scotland treated with blood and blood products, with particular reference to the numbers exposed to risk of infection with the Hepatitis C virus and HIV and the numbers contracting either or both such infections as a consequence of such treatment.

#### Term of Reference 5:

To examine the circumstances generally in which patients treated by the NHS in Scotland became infected with Hepatitis C, HIV, or both through the use of blood or blood products in the course of their treatment, taking account of the development of scientific and clinical understanding and evidence internationally.

#### Term of Reference 6:

To investigate the deaths of Reverend David Black, Mrs Eileen O'Hara, Alexander Black Laing and Victor Tamburrini, with particular reference to the circumstances in which they became infected with the Hepatitis C virus, HIV or both.

#### Term of Reference 7:

To investigate the steps taken by those involved in, and those responsible for, the NHS in Scotland, including NHS Boards and the Scottish National Blood Transfusion Service

(SNBTS), their officers and employees and associated agencies, once Hepatitis C and HIV were identified, to trace individuals who might have become infected with one or both of them as a result of receiving blood or blood products; and to identify any other or further steps that might reasonably have been taken to trace such individuals.

Term of Reference 8:

To investigate the steps taken by those involved in, and those responsible for, the NHS in Scotland including NHS Boards and the SNBTS, their officers and employees and associated agencies, to prevent the provision of infected blood and blood products.

Term of Reference 9:

To investigate the steps taken by those involved in, and those responsible for, the NHS in Scotland including NHS Boards and the SNBTS, their officers, employees and associated agencies to inform individuals who might have received infected blood or blood products of the risks associated with their treatment for themselves and their families; and to offer treatment to any individual at risk, and to identify any other or further steps that might reasonably have been taken to inform and to treat such individuals.

Term of Reference 10:

To examine any particular adverse consequences for patients treated by the NHS in Scotland, and their families, of infection through blood and blood products with Hepatitis C and HIV, including the treatment offered.

Term of Reference 11:

To identify any lessons and implications for the future, and make recommendations.

Term of Reference 12:

To report as soon as practicable.

### **The Inquiries Act 2005 and the Inquiries (Scotland) Rules 2007**

The Inquiry was established under the Inquiries Act 2005 ('the 2005 Act'). Inquiry procedures were governed by the 2005 Act and the Inquiries (Scotland) Rules 2007 ('the 2007 Rules').

### **Procedure Directions, Guidance Notes and Restriction Orders**

Section 17 of the 2005 Act states that, subject to the provisions of the Act itself or of the 2007 Rules, the Chairman of the Inquiry may make his own directions as to the procedure and conduct of the Inquiry. Under this section, Lord Penrose issued a number of procedure directions and guidance notes which were published on the Inquiry's website. These are listed in Appendix 5.

Sections 19 and 20 of the 2005 Act provide that restriction may be imposed on attendance at an Inquiry or any particular part of it and on disclosure or publication of any evidence or documents given, produced or provided to an inquiry. Under these sections of the 2005 Act the Chairman made the restriction orders listed in Appendix 5.

### **Preliminary hearing and the two phases of the Inquiry**

On 31 March 2009 a preliminary hearing was held at which the Chairman outlined the approach he intended to take to the conduct of the Inquiry and in fulfilling his remit.

The Inquiry was conducted in two broad phases.

The purpose of phase 1 was to focus the issues which the Inquiry required to consider at the public hearings and, having regard to the Chairman's obligations under section 17(3) of the 2005 Act (duty to act with fairness and to avoid any unnecessary cost), to reduce the length of these hearings.

Phase 1 of the Inquiry consisted of:

- The gathering of documentary evidence from various sources.
- The taking of witness statements.
- The consideration of the evidence with the aim of establishing as much as possible of the medical and scientific background and identifying the controversial facts and issues which required further investigation.
- The drafting and publishing of the Preliminary Report.

Due to the volume of documentation which the Inquiry examined, the complexity of the medical and scientific background and the extent of the time period covered by the Inquiry's Terms of Reference, a decision was made early in the Inquiry process that it was both appropriate and necessary for the Inquiry to produce a Preliminary Report. The aim of the Preliminary Report was to provide the results of the Inquiry's research and analysis of the information received and the evidential background to the topics identified in the Terms of Reference in order to provide a basis on which to move forward and examine the areas of controversy at the public hearings.

Phase 2 of the Inquiry involved:

- The gathering of further evidence.
- Holding public hearings into the issues which had been identified as requiring further investigation (see 'List of topics ...' section below).
- Sending warning letters and considering the responses to these.
- Writing the Final Report containing a detailed analysis of the evidence on the topics and the conclusions reached in respect of these.

### **Call for evidence**

On 24 June 2009 the Inquiry issued a public call for documents and witness statements relating to the Inquiry's Terms of Reference. This call for evidence was made in a press release to the national, local, online and broadcast media (including all health correspondents). All persons and organisations holding documents relevant to the Terms of Reference were invited to contact the Inquiry Secretary to discuss the documents held and the best means of producing them. In addition, patients who contracted Hepatitis C and/or HIV through receiving blood and/or blood products from the NHS in Scotland, and the relatives of such patients, who wished to provide a statement were asked to contact the Inquiry.

The Inquiry also sought to reach potential witnesses with a call for evidence on its own website, in a Google advert, by Twitter and on Facebook. The Inquiry distributed a poster and leaflet to all haemophilia centres in Scotland and to all health boards asking that they be distributed to all GP practices. With the help of Community Pharmacy Scotland the posters and leaflets were also sent to all pharmacies in Scotland. Haemophilia Scotland distributed the leaflets through its membership newsletter and promoted the Inquiry through its website and through membership meetings.

On 18 March 2010 Lord Penrose made a radio broadcast on Radio Scotland to appeal for more witnesses to come forward. At this time a further call for witnesses was made in local newspapers across Scotland.

### **Notices for, and request for, production of evidence**

Section 21(2) of the 2005 Act gives the Chairman the power to require a person to provide evidence to the Inquiry in the form of a written statement and to provide any documents in his or her custody or under his or her control that relate to a matter in question at the inquiry.

As this is a Scottish inquiry, section 28(4) of the 2005 Act provides that those powers are not exercisable so as to require any evidence document or other thing to be given, produced or provided by or on behalf of, amongst others, Her Majesty's Government in the United Kingdom.

The use of these statutory powers to recover documents did not necessarily mean that an organisation was unwilling to assist the Inquiry. Where an organisation held documents containing personal data or which were confidential, then providing the documents to the Inquiry in response to a Section 21 Notice meant that the data were lawfully processed.

On 17 September 2009 Lord Penrose served a notice under section 21 of the 2005 Act on Scottish Ministers requiring production of all documents in their custody or under their control relating to the Inquiry's Terms of Reference and dating from the period from 1 January 1974 to 31 December 2006. In response to that notice, the Scottish Government produced over 37,000 documents to the Inquiry. At the request of the Inquiry, two officials from the Scottish Government provided written witness statements in relation to the procedures for the identification and production of those documents and to explain the position as regards documents that had been destroyed or were being withheld by reason of legal professional privilege.

On 2 October 2009 Lord Penrose served a notice under section 21 of the 2005 Act on the Common Services Agency for the Scottish Health Service requiring the production of 482 Scottish National Blood Transfusion Service files listed in the Appendix to the Notice. The 482 files in question were selected by the Inquiry Team from an index, referred to as 'the documentation account', which had been prepared by the SNBTS in anticipation of requests for production of documents from its records. In view of the importance of the documentation account in the identification of the files to be produced to the Inquiry, a request was made to the SNBTS for a witness statement on various issues arising in relation to its preparation. Such a statement was provided by the SNBTS Public Inquiry Team Co-ordinator.

In 2006 the Department of Health commissioned a review of all documents held between 1970 and 1985 in relation to blood safety. The *Review of documentation relating to the safety of blood products 1970-1985 (Non A non B hepatitis)* was issued on 22 May 2007. Early in 2009 the Inquiry advised the Department of Health that it would require files relating to blood and blood products between 1986 and 1991. In September 2009 the Department of Health produced a list of about 166 files they had identified as possibly relevant to the Inquiry. Many such files ran to several volumes. On 26 October 2009 the Inquiry requested copies of documents previously disclosed by the Department of Health in terms of Freedom of Information releases. After further correspondence with

the Department of Health in June 2010 the Inquiry advised the Department of Health that it was particularly interested in files between 1 January 1989 and 1 September 1991 relating to the testing of donated blood for Hepatitis C. The Inquiry indicated 50 files which appeared to it to be of relevance and these files, together with some others, were made available for inspection by the Inquiry. Between 1 and 4 November 2010 two members of the Inquiry Team visited the Department of Health to review files of potential relevance to the Inquiry. As a result of this visit the Inquiry was provided with 63 documents.

### **Documentary evidence**

Nearly 120,000 documents were recovered from both public and private sources. The majority came from the records of the Scottish Government and various NHS bodies.

In addition, statements were provided by patients and their relatives, clinicians and others. These statements were often accompanied by supporting documents.

Appendix 2 gives further information about how the documentary evidence was processed and used by the Inquiry.

### **Annual summaries and framework document**

Much of the Inquiry's work during the first year consisted of the team considering the documentary material as it was recovered. This task was undertaken by means of summarising the relevant documents and then inserting references to the documents in summaries prepared for each of the key years – the annual summaries. Within each annual summary, documents were referred to under three separate headings: developments in respect of HIV; developments in respect of HCV; and developments in respect of blood products. From these annual summaries the main events relevant to the Terms of Reference were extracted. The Inquiry drafted a framework document containing the references of all documents relevant to the Terms of Reference. This framework document ran to 107 pages and became a timeline reference for subsequent work of the Inquiry.

### **Taking of statements from patients and relative witnesses**

The Inquiry engaged three statement takers to meet with and take statements from the patient and relative witnesses. These statement takers were provided with specific training for this purpose.

Those witnesses who attended the Inquiry for the purpose of giving their witness statements were entitled to apply for an award of travel and subsistence expenses and/or for compensation for loss of time, under Procedure Direction No. 2.2 – Award of Travel and Subsistence Expenses 1 April 2011 (original direction dated 22 June 2009) and Procedure Direction No. 4.1 – Award of Compensation for Loss of Time 17 February 2011 (original direction dated 22 June 2009).

Seventy-eight patient and relative statements were finalised prior to the publication of the Preliminary Report. These 78 statements were reported on in Chapter 4 of the Preliminary Report. A further 81 patient and relative statements were finalised after the Preliminary Report was published. This figure excludes the witness statements taken from the relatives of those whose deaths were specifically referred to the Inquiry under Term of Reference 6. The witness statements are summarised in Chapter 4. The identities of these witnesses were not disclosed to any other party.

## Core Participants

Rule 4 of the 2007 Rules provides that the Chairman may designate a person as a Core Participant in the Inquiry. A 'Core Participant' is usually understood to refer to a participant who will be expected to have a key role during the inquiry, attending for all or substantial parts of the proceedings, either personally or by their recognised legal representatives, and participating actively in the proceedings by making statements or asking questions, subject to the control of the Chairman.

In deciding whether to designate a person as a Core Participant, the Chairman must have particular regard to the desirability of including persons who fall within certain categories stated in Rule 4(2). These categories include those who have a significant interest in an important aspect of the matters to which the Inquiry relates.

It was impracticable and inconsistent with the Chairman's duties under section 17(3) of the 2005 Act (duty to act with fairness and to avoid any unnecessary cost) to designate as a Core Participant every person who had a significant interest in the Inquiry. Given the number of people infected with Hepatitis C or HIV and their family members, such an approach could have resulted in a substantial number of people being designated as Core Participants. Instead, the Chairman considered that a process of selection was required to ensure that the main groups of those with an interest in the subject matter of the Inquiry were represented as Core Participants.

A public invitation was extended to those interested to apply, by 7 July 2010, for designation as a Core Participant. Over 70 applications were received from patients and relatives of patients. Applications were also received from the personal representatives of the five deceased named in Term of Reference 6, the Scottish Ministers, the Common Services Agency for the Scottish Health Service on behalf of the SNBTS, the 14 Scottish Area Health Boards and the Haemophilia Society (known in Scotland as 'Haemophilia Scotland').

All the patients and relatives who applied for designation as Core Participants were represented by Thompsons, Solicitors. On 16 July 2010 the Chairman gave further guidance to these applicants on how he proposed to select those to be designated as Core Participants. He stated that he proposed to designate Core Participants (a) to reflect the distinct interests that could be identified from the circumstances set out in the applications and any relevant witness statements, and (b) to ensure that no more Core Participants were designated than were sufficient to ensure that Thompsons was adequately instructed to represent those interests at the hearings. A hearing was held on 10 August 2010 to consider submissions on this proposed approach.

Following the hearing, the Chairman decided that patient and relative Core Participants should be selected under appropriate groupings of interests, namely:

- Transfusion cases up to and including 1979.
- Transfusion cases in the 1980s.
- Transfusion cases in the 1990s.
- Hepatitis C cases associated with Haemophilia A up to and including 1979.
- Hepatitis C cases associated with Haemophilia A in the 1980s.
- Hepatitis C cases associated with Haemophilia B up to and including 1979.



- Hepatitis C cases associated with Haemophilia B in the 1980s.
- HIV cases associated with Haemophilia A or B.

Fourteen patients and relatives who fell within these groupings were provisionally designated as Core Participants, subject to these persons consenting to being so designated. An issue arose as to whether it was necessary for the identities of those who were designated Core Participants to be published. Having considered representations made on behalf of the provisional Core Participants the Chairman decided that only the initials of the Core Participants and the class of interest under which they had been selected would be published. He also decided, to ensure fairness to all concerned, that their identities would only be disclosed to the other Core Participants, subject to explicit undertakings of confidentiality. On that basis, on 30 September 2010, all 14 provisionally designated Core Participants consented to their designation. One further Core Participant was designated in December 2010 to illustrate two of the groupings listed above.

Those designated as Core Participants and their recognised legal representatives are listed in Appendix 3.

### **Funding of Core Participants**

All the individual Core Participants were awarded the expenses of their legal representation. Section 40 of the 2005 Act provides that the Chairman may award reasonable amounts in respect of legal representation in relation to the Inquiry. This section provides that such awards may be made to those attending the Inquiry to give evidence or to produce documents and to persons, including Core Participants, whether individuals or representative bodies, considered by Lord Penrose to have a sufficient interest to justify an award. Rules 17 to 20 of the 2007 Rules make detailed provision in relation to awards. Rule 18 provides that the Chairman has to take into account the financial resources of the applicant and the public interest so far as relating to the making of an award. In addition, a Determination by Scottish Ministers made under section 40(4) of the Act stated certain qualifications and conditions on the Chairman's power to make such awards. The Chairman issued an Inquiry Procedure Direction No 3.1, Applications for legal representation at public expense, in which he provided details about the procedure and conditions for applying for and being awarded such expenses.

### **Publication of Preliminary Report**

On 8 September 2010 the Inquiry published its Preliminary Report. The Preliminary Report set out the evidential background to the topics identified in the Terms of Reference. It did not reach any conclusions on matters of fact. It identified matters that appeared to be controversial and which required further investigation.

### **List of topics for investigation at the public hearings**

The Preliminary Report contained a draft list of topics which the Chairman considered should be examined at the public hearings in light of the Inquiry investigations to date. Responses to this list, including proposed additions or modifications to it, were invited from anyone who had suggestions to make. Fifteen submissions were received and considered. In February 2011 the draft list of topics was finalised taking account of these submissions. The list of topics investigated at the public hearings was as follows:

## **Part A**

The deaths of Reverend David Black, Mrs Eileen O'Hara, Alexander Black Laing and Victor Tamburrini, with particular reference to the circumstances in which they became infected with the Hepatitis C virus, HIV or both.

## **Part B – HIV/AIDS**

B1) The efforts made to discourage 'higher risk' donors from giving blood (by the dissemination of information, including leaflets); whether these efforts went far enough and began early enough.

B2) The use of blood product concentrates in Scotland, including any perceived disadvantages of such products, from their introduction in or around 1974; the continuation of the use of commercial concentrates in particular after:

- International realisation that these carried a risk of AIDS.
- The proposal by Dr Galbraith of the Public Health Laboratory Service in May 1983 that use in the UK should be stopped.
- Significant progress towards self-sufficiency in the manufacture of blood products by the NHS in Scotland had been made.

B3) The implementation of heat treatment against LAV/HTLV-III by the Protein Fractionation Centre in Scotland in December 1984, and the technological background to such implementation, including the history and exploration of methods of heat inactivation by the Scottish National Blood Transfusion Service.

B4) The decision not to use kits from the United States of America for testing donated blood for the virus as soon as they became available but, instead, to follow a process of evaluation of the kits before any such use.

B5a) The information given to patients (or their parents) about the risk of AIDS before their treatment with blood or blood products.

B5b) The tracing and testing of patients who might have been exposed to the virus through their treatment with blood or blood products.

B5c) The information given to patients who might have been infected, or who were found to be infected, and their families.

B5d) In particular, the circumstances in which those patients known collectively as the Edinburgh Cohort became infected with HIV, the testing of such patients for HIV and the information given to them about their infection.

B6) The effects of infection with HIV, including the effects of treatment, on patients and their families.

## **Part C – Hepatitis C**

C1) The acceptance of blood from 'higher risk' donors, in particular:

C1a) Prisoners.

C1b) Donors who had a history of jaundice, and who were negative for Hepatitis B when the existence of Non-A Non-B Hepatitis was known and its presence could not be excluded.

C2) The non-introduction in Scotland of surrogate testing for Non-A Non-B Hepatitis.

C3) The implementation of heat treatment sufficient to inactivate Hepatitis C in blood products by the Protein Fractionation Centre in Scotland in 1987, and the technological background to such implementation, including the achievement of this objective by the National Blood Transfusion Service in England and Wales in 1985.

C3a) The use of blood product concentrates in Scotland in the period between the introduction of NHS heat-treated products in 1984 and the supply of NHS products sufficiently treated to inactivate Hepatitis C.

C4) The interval between the availability of tests for the Hepatitis C virus in 1989 and the introduction of screening of donated blood for the virus in the United Kingdom in September 1991.

C5a) The information given to patients (or their parents) about the risk of non-A, non-B Hepatitis and the severity of the condition before their treatment with blood or blood products.

C5b) The tracing and testing of patients who might have been exposed to the virus through their treatment with blood or blood products.

C5c) The information given to patients who might have been infected, or who were found to be infected, and their families.

C6) The effects of infection with Hepatitis C, including the effects of treatment, on patients and their families.

Topic C3A was added to the list of topics in August 2011, in response to representations from Core Participants.

### **Preparation of topics for public hearings**

Each topic was assigned to one of the Inquiry Counsel and a paralegal. They were responsible for the preparation of each topic for the public hearings and leading the evidence on it.

Inquiry Counsel prepared notes on the line of evidence for most topics detailing the matters which required further investigation at the public hearings, the evidence required for this – namely, the witnesses and the documentary evidence – and any further investigations to be undertaken.

The paralegals sent requests for statements to witnesses. These requests asked the witnesses to provide a written statement of their evidence to the Inquiry and stated the specific matters about which the Inquiry wished the witnesses to provide information. Such requests often included documentary evidence which the Inquiry considered would assist the witnesses in this task and which the witness could consider before providing his or her statement.

Once such statements were finalised the witnesses were asked to provide a signed statement. These statements were then shared with the Core Participants on a confidential basis in advance of the public hearings. Usually they were published on the Inquiry's website.

A few witnesses were either unable or unwilling to provide a statement.

## **Procedure at the public hearings**

The Inquiry produced a document *Guidance on the Oral Hearings* which set out guidance on what the Inquiry expected from Core Participants and their legal representatives and from witnesses giving oral evidence to the Inquiry and on what could be expected from the Inquiry Team.

The Inquiry heard evidence and submissions on 89 days between 8 March 2011 and 30 March 2012. Hearings were generally held from Tuesday to Friday with a morning and a lunch break each day. They were arranged in blocks with the Inquiry endeavouring to hear all evidence on individual topics together within a block.

A further procedural hearing was held on 29 October 2012 to allow Lord Penrose to hear submissions on behalf of the patients, relatives and the Haemophilia Society that certain witnesses be called to give further evidence on the topic of Statistics.

In terms of Inquiry Procedure Direction No. 6 the Chairman directed that no opening statements be made by Inquiry Counsel or by, or on behalf of, the Core Participants.

All witnesses who were required to attend the hearings were sent a notice by the Chairman under section 21(1) of the 2005 Act. 67 witnesses gave evidence at the hearings. These witnesses are detailed in Appendix 4. Each witness took the oath or made an affirmation before giving their evidence.

The Inquiry endeavoured to release to the Core Participants a list of all witnesses required to attend to give evidence related to a topic four weeks before the commencement of the respective hearings.

The Inquiry endeavoured to produce to the legal representatives of Core Participants and, where considered necessary, to witnesses the documents relied on in each topic four weeks before the start of the evidence in respect of that topic. There was a database – Courtbook – of such documents for the use of the legal representatives of the Core Participants. Appendix 2 provides further information about Courtbook. Within Courtbook documents were grouped and inventoried according to each topic. Witnesses who wished to refer to a document during their evidence were asked to produce such a document to the Inquiry no later than two weeks prior to the start of the evidence on that topic.

Questioning of witnesses was primarily carried out by Inquiry Counsel. Counsel for the Core Participants questioned witnesses on areas of importance. Initially, they were required to have obtained the Chairman's approval to do so but more flexible arrangements were introduced as the hearings progressed.

During the hearings special applications were made by the Core Participants and on behalf of witnesses to allow further documents, including additional statements and comments, to be received in evidence. In addition at times supplementary written information was requested from some witnesses.

## **Evidence of patient and relative witnesses**

Thirteen individuals were selected from all the patient and relative witnesses to give oral evidence at the public hearings for Topics B6 and C6 (the effects of infection with HIV and Hepatitis C) as being representative of, or at least as illustrating, some of the main themes that emerged from the initial statement gathering exercise. The Inquiry selected

those it considered would paint as clear and as wide a picture as possible of the severe side-effects of infection with either HIV or Hepatitis C, including the effects of treatment, on themselves and their families. Factors which were taken account of in selecting these witnesses included:

- The means by which a person was infected with the virus(es).
- The severity of the effects of infection and the effects of treatment.
- The nature and range of the effects of infections and the effects of treatment.
- Where a patient or relative lived and where he or she received treatment.
- The sex of the patient or relative.
- The age of the patient or relative.
- The occupation of the patient or relative.
- Whether the patient suffered from a pre-existing or other medical condition which meant that it was difficult to distinguish the effects of the infection with the virus.

After identifying potential witnesses to give evidence, the Inquiry wrote to these witnesses asking them if they would be prepared to do so. At the time they were asked to give evidence each of these witnesses was sent a copy of the Inquiry's *Guidance on the Oral Hearings*. In addition to being provided with information about giving evidence anonymously (see section on anonymity below), each witness was offered the opportunity to give evidence by video conferencing or from behind a screen. None of the witnesses chose to do so.

Those asked to give evidence were also advised that, as a person attending the Inquiry to give evidence, they might be entitled to legal representation and advice at Inquiry expense. Some of these witnesses chose to be legally represented and they were represented by Thompsons, Solicitors.

The Inquiry recovered all the medical records of those witnesses who agreed to give evidence. These medical records were then considered with the witness's statement before a final decision was made about that witness giving evidence.

### **Anonymity and protection of identity of patient and relative witnesses**

It was decided that all patient and relative witnesses giving evidence at the hearings would not have their names or identities disclosed, even if they had no objection to this. This meant that the evidence of these witnesses could be heard on an equal basis.

In order to preserve anonymity, the Inquiry redacted copies of the statements and medical records of these witnesses. All details from which the witness could be identified were redacted from these documents. Each witness had the final say on the information which was redacted.

The redacted witness statements and medical records were made available only to the legal representatives of Core Participants and were provided only after they had given confidentiality undertakings.

Restriction Orders were made restricting those who could attend the hearings at which these witnesses gave evidence to members of the Inquiry Team, Counsel and one representative of the solicitors representing the designated Core Participants and any person authorised by the Chairman to accompany the witness during the hearing of that witness's evidence. The Restriction Orders also prevented the disclosure or publication of their oral evidence or documents revealing their names and identities.

Each witness chose a pseudonym under which they gave evidence and by which they are referred to in the Final Report.

### **Evidence of relatives of Mr Tamburrini and Mrs O'Hara**

Two family members gave oral evidence at the hearings during the investigations into the specific deaths. These were Mrs Jean Tamburrini and Mrs Roseleen Kennedy. Both witnesses were identified and their unredacted witness statements were made available to Core Participants and put on the Inquiry's website.

### **Final written submissions and final hearing**

Core Participants were directed to submit their final written submissions to the Inquiry and to intimate them to the legal representatives of other Core Participants by 5pm on 26 March 2012. Inquiry Counsel did not prepare submissions but set out a list of 67 questions which they suggested fell to be answered.

The final hearing took place on 30 March 2012. The hearing was divided into two parts. During the first part of the hearing, Counsel appearing for the Core Participants each made a brief statement explaining the approach adopted in relation to their written submissions and highlighting any points considered to be of particular importance. During the second part of the hearing Counsel for the Core Participants made closing statements in terms of Rule 10 of the 2007 Rules.

### **Warning letters procedure**

Rule 12(7) of the 2007 Rules provides that the Inquiry must not include any significant or explicit criticism of a person in the report unless the Chairman has sent that person a warning letter and given that person a reasonable opportunity to respond to it. Neither the 2005 Act nor the 2007 Rules define what is meant by a 'significant or explicit criticism' and so the Inquiry gave these words their common sense meanings.

In terms of Rule 12(2) a warning letter must –

- (a) state what the criticism or proposed criticism is;
- (b) contain a statement of any facts that the Chairman considers may substantiate the criticism or proposed criticism;
- (c) refer to any evidence or documents which may support those facts;
- (d) invite the person to make a written statement if the person wishes; and
- (e) note that the information is subject to confidentiality restrictions.

Rule 12(3) provides that the Chairman may send copies of any evidence or documents referred to with the warning letters if he considers it appropriate to do so.

The Inquiry sent 103 warning letters under Rule 12(7) of the 2007 Rules. The Inquiry sent warning letters to those persons criticised in the final report and to those persons who were subject to criticism by another person when that criticism was narrated in the Report.

Recipients of these letters were allowed 28 days and in a few cases, on cause shown, a longer period to respond. The Inquiry received 100 responses to warning letters. The responses included supporting documentation and together these totalled over 1000 pages.

All responses were carefully considered and, if it was deemed appropriate and/or necessary, the Report was amended to take account of information provided in them.

### **Keeper of the Records of Scotland**

At an early stage of the Inquiry the Chairman consulted the Keeper of the Records of Scotland on the manner and format of creating, maintaining and transferring the records of the Inquiry to the National Records of Scotland (NRS).

In terms of Rule 16(3) of the 2007 Rules at the end of the Inquiry the Chairman will transfer the records of the Inquiry to the NRS.





## APPENDIX 2

### INQUIRY ORGANISATION AND ADMINISTRATION

#### The Inquiry Team

As Chairman of the Inquiry, Lord Penrose was independent of government or any other body or organisation. He alone was appointed to investigate the matters raised by the Terms of Reference.

Oliver James, Emeritus Professor of Medicine at the University of Newcastle, was appointed to act as the medical assessor to the Inquiry under section 11 of the 2005 Act. He was the principal adviser to the Inquiry on medical matters. He had 30 years' experience as a Consultant Physician and was a former Senior Vice President of the Royal College of Physicians (London).

Senior Counsel to the Inquiry was Laura Dunlop QC who was assisted by Euan Mackenzie, Nick Gardiner and Jane Patrick, Advocates. They did not represent any organisation or person appearing before the Inquiry. Their role was strictly impartial, assisting Lord Penrose to investigate the facts, examining witnesses at the hearings, providing advice on questions of law, evidence and procedure, liaising with Counsel for the Core Participants and assisting with the drafting of the Inquiry reports and other documents produced by the Inquiry.

Gillian Gibson (Galbraith), Advocate, assisted the Inquiry with the warning letters process and with the drafting of the Final Report.

The Solicitor to the Inquiry was Douglas Tullis assisted until June 2014 by Louyse McConnell-Trevillion, the Deputy Solicitor. They were responsible for the provision of legal advice, liaising with solicitors for the Core Participants, dealing with claims for expenses and drafting procedural documentation. Heike Gading and then Andrea Summers took on the role of Solicitor to the Inquiry after Douglas Tullis retired in December 2013.

The Secretary to the Inquiry was Maria McCann, assisted by Diane Barr and then Sarah Noble as Deputy Secretary. The Secretary was responsible for all administrative arrangements for example: commissioning an Inquiry office and hearings venue, the organisation of IT support, recruitment and management of paralegal and administrative staff, handling the Inquiry's finances, drawing up and implementing the Inquiry's communication strategy, including maintenance of the Inquiry's website. The Secretary and her team were also responsible for managing the publication of the Preliminary and Final Reports. The Documents and Evidence Manager was Neil MacFarlane assisted by Oliver Stempt and Keith Fleming. Neil and Keith also contributed to the drafting of the Final Report. At different times, members of the administrative team included: Fraser Paterson, Meg Orr, Kate Miguda, Sheila Renton, Rhona Carr, Samantha Doherty, Philip Brough, Lorna Gibson, Claire Stapley, Edin Omanovich, Kimberley Meikle, Kristina Hanson, Fiona McLean and Helen Fleming.

The Inquiry employed a number of paralegals, many of whom were, in fact, qualified lawyers. They developed expertise in particular subject areas of the Inquiry and used this expertise during different stages of the Inquiry, including to code documents and to assist Inquiry Counsel in preparing for and during the public hearings. Those who assisted the Inquiry as paralegals at various stages of the Inquiry were Angus Evans, Jenny Livingstone, Gemma

Lovell, Stuart McWilliams, Gregor Mair, Janet Marsh, Jennifer Murphy, Teri Pidgeon, Lindsey Robertson, Charles Rogers, Yasmin Shepherd, Lorna Young and Laura Weir.

Sascha Cochran, Margaret Fraser and Jane Patrick were the statement takers responsible for taking the statements from patients and relatives. Margaret Fraser was appointed Witness Liaison Manager for the public hearings.

Mary Jane Bennett provided editing and proofreading services for the Preliminary Report and the Final Report. Murray Earle and Stefania Greci provided proofreading services for the Final Report.

### **Accommodation**

The Inquiry leased office accommodation within the Scottish Legal Aid Board ('SLAB') premises at 44 Drumsheugh Gardens in Edinburgh. Due to the relocation of SLAB, on 29 September 2014 the Inquiry moved to Victoria Quay, Edinburgh.

The preliminary hearing on 31 March 2009 took place at Edinburgh International Conference Centre, The Exchange, Edinburgh. The public hearings were held at accommodation specifically leased for that purpose at Clydesdale Bank Plaza, 50 Lothian Road, Edinburgh. The procedural hearings on 10 October 2010 and on 29 October 2012 were held at the Apex International Hotel, 31-35 Grassmarket, Edinburgh.

### **Inquiry IT**

The Inquiry's basic administrative IT systems were supplied by the Scottish Government as part of their SCOTSLite service, a service made available to smaller Scottish public bodies.

The Inquiry was very conscious from the outset that it could expect to receive a large quantity of documentary evidence. It was clear that IT systems would be required that were specifically designed for the handling and presentation of large numbers of documents.

Mike Taylor of i-Lit Ltd, an expert on IT for litigation and inquiries, provided advice on the selection of IT systems.

Tenders were invited through an Office of Government Commerce (OGC) framework agreement: Specialist Solutions – Electronic Document and Records Management Solutions. Framework Agreement Code A217837/L11.

The successful contractor was Computacenter (UK) Ltd. Working through a number of partners, Computacenter provided the Inquiry with a range of document processing services including initial processing, a document management system, and hearing room display systems.

### **Inquiry's website and bulletins**

The Inquiry's website was launched on 10 February 2009. It was set up and maintained by Whitespace. It contained background information, key documents relating to the Inquiry, a witness timetable showing which witnesses were scheduled to give their evidence on a particular day, transcripts of the evidence heard at the public hearings, frequently asked questions and the preliminary report. It was updated regularly during the course of the Inquiry. This report is available on the Inquiry's website.

The Inquiry issued four bulletins during the course of the Inquiry to provide the public with a progress report and an insight into the work of the Inquiry Team.

## **Document storage**

The Inquiry made use of Systematics Signature Delium database ('Signature database'). Over 118,000 documents were entered into this database. In addition to the material obtained from the Scottish Ministers, the SNBTS, the Department of Health and Lothian Health Board, over 1600 documents were collected in the course of the Inquiry including witness statements, documents provided by witnesses, medical records, scientific papers and journal articles. Assistance in configuring and managing the database was provided through the Computacenter contract by Elizabeth Miller and Alexander Parkes.

The initial processing of documents was carried out by Hobs Legal Docs in London. Services covered the scanning of paper files, the preparation of images and searchable versions of documents, and the inputting of various basic pieces of descriptive information for each document. In the event, most of the documents recovered by the Inquiry had already been scanned by the organisations providing them. This meant that there was little need to transport files to London for scanning, and Hobs were able to concentrate on the preparation of image files and descriptive data for loading into the Signature database.

It was clear to the Inquiry that the bulk of document recovery would occur in the early stages of the Inquiry and that there would need to be a system in place that could quickly assess documents for evidential significance. It was decided that there would be an initial coding exercise for these documents.

Once documents had been loaded into the Signature database the Inquiry Team undertook a subjective coding exercise to identify the issues that a document addressed and to assess the relative importance of the document.

Documents thought to be of interest were put through a second review undertaken by members of the Inquiry Team who had developed more detailed knowledge of the key issues during particular time periods. This review considered the importance level assigned to documents. Those documents which were still considered to be important after the second review were linked into the database's Chronology Manager which allowed a timeline to be developed. These documents were then passed to Inquiry Counsel.

It is important to note that documents not considered directly relevant at this stage remained in the Signature database and would still appear in search results. This ensured that documents whose significance might not have been obvious at an early stage of investigations would be available during more detailed investigation of particular topics.

As noted above, the subjective coding process was designed to deal with the initial receipt of large numbers of documents at the one time. Once these bulk deliveries had been completed, it was no longer considered necessary to formally have documents subjectively coded, as the smaller numbers of documents being received meant that they could be assessed for relevance directly. They were still looked at by Inquiry Counsel.

The main Signature database was only available to members of the Inquiry Team.

## **Public hearings: sharing documents**

In preparation for the public hearings the Inquiry Team set up a separate version of the Signature database which would be available to the legal representatives of the Core Participants and which would also support the display of documents in the hearing room. Courtbook, as it was known, was initially set up with all the documents published

with the Inquiry's Preliminary Report. Documents and witness statements for each of the topics to be examined during the public hearings were exported from the Signature database and imported to Courtbook so that the Core Participants' legal representatives could use them to prepare for hearings. Core Participants' legal representatives were also able to ask for documents to be added to Courtbook.

Documents were checked before copying them to Courtbook so that sensitive personal data could be redacted.

By the end of the Inquiry nearly 5000 documents had been placed into Courtbook.

The Inquiry Team provided training to Core Participants' legal representatives on the use of Courtbook and helped them to configure their IT systems to allow access to the database.

### **Hearing room systems**

The specification for the hearing room systems was drawn up by Elizabeth Miller and the work of building and installing the systems was subcontracted by Computacenter to the NVT Group.

The server for the Courtbook database was installed in the hearing room premises throughout the period of public hearings. This was done to reduce the number of possible points of failure between the server and the hearing room when documents were being displayed.

Courtbook included tools for publishing documents as they were used in the hearings, and these tools were used to display Courtbook documents to Counsel, witnesses and the general public in the hearing room. The database allowed the Inquiry Team to record which documents had actually been exhibited and the witnesses with whom the documents had been used. At the end of each day's hearings any documents shown for the first time were exported from Courtbook and uploaded to the Inquiry's public website so that in due course they could be linked to the published transcript of the day's proceedings.

During the hearings, Counsel would read out the reference of any documents that they wished to show to a witness. The hearing room operator would call up the document on his PC and then publish it to monitors in front of the Chairman, the witness and the legal teams. Two large plasma screens were installed at the front of the public seating area so that members of the public could see the documents as they were being put to witnesses.

The hearing room network provided wired and Wi-Fi internet connections for the Inquiry Team and for Core Participants' legal representatives. Wi-Fi was also available for the press and the general public.

### **Hearing transcripts**

A live transcription service was provided throughout the hearings by Merrill Legal Solutions. The stenographer was Catherine Anderson and the Editor was Stuart Marshall.

The Chairman and the legal teams were able to access the live transcript as it was created, allowing them to refer back quickly to earlier passages of evidence. The legal representatives could highlight or annotate sections of evidence for future reference. At the end of each day a corrected and checked version of the transcript was provided to the Inquiry Team, who then uploaded it to the Inquiry's website. The following day active links

were added to the transcript on the website so that readers could open up any documents that were referred to during the hearing.

The transcripts of the evidence of those patient and relative witnesses who gave evidence anonymously were redacted prior to being uploaded onto the Inquiry's website. Each patient and relative approved the redactions made.

### **Video conferencing**

Video conferencing facilities were set up in the hearing room to allow the Inquiry to take evidence from witnesses who would otherwise have found it difficult to take part. It also made it possible for a witness who was appearing in connection with more than one topic to give his or her evidence in separate video conferences to fit in with the logical order of the evidence rather than appearing in person for a whole day to deal with a range of topics.

### **Data protection**

The Inquiry was registered under the Data Protection Act 1998.

### **Public relations**

Media and public relations support was provided to the Inquiry by Golley Slater under a Scottish Government Marketing Services Framework agreement.

### **Report**

This report is published on behalf of the Inquiry by APS Group Scotland Ltd under the Scottish Government contract for supply of design, print, publishing and associated services.



## APPENDIX 3 CORE PARTICIPANTS

The following individuals and organisations were designated by the Inquiry Chairman under Rule 4 of the Inquiries (Scotland) Rules 2007, which provides that:

(1) The chairman may designate a person as a core participant at any time during the course of the inquiry (but only with the consent of that person).

(2) In deciding whether to designate a person as a core participant the chairman must have particular regard for the desirability of including as core participants persons who-

....

(b) have a significant interest in an important aspect of the matters to which the inquiry relates....

Legal representatives of Core Participants are noted at the top of each table.

<b>Personal representative of those whose deaths were investigated under Term of Reference 6</b>	<b>Legal Representative: Thompsons Solicitors</b>
Mrs Jeanie Black as personal representative of the Reverend David Black	
Mrs Roseleen Kennedy as personal representative of Mrs Eileen O'Hara	
Mrs Annie Laing as personal representative of Alexander Black Laing	
Mrs Jean Tamburrini as personal representative of Victor Tamburrini	
<b>Anonymised Core Participants, designated by Chairman to illustrate different grouping of interests</b>	<b>Legal Representative: Thompsons Solicitors</b>
Transfusion cases up to and including 1979 – JF	
Transfusion cases in the 1980s – EF; KM	
Transfusion cases in the 1990s – No designation [Mrs Annie Laing, as representative of Alexander Black Laing, deceased, is already designated and covers that interest]	
Hepatitis C cases associated with Haemophilia A up to and including 1979 – FM; PD	
Hepatitis C cases associated with Haemophilia A in the 1980s – MM; BW; JM2	
Hepatitis C cases associated with Haemophilia B up to and including 1979 – DB; IB; JD	
Hepatitis C cases associated with Haemophilia B in the 1980s – RM	
HIV cases associated with Haemophilia A or B – JM; GM; KM2; JM2	
<b>Patient interest organisations designated as core participants under rule 4 (2) (b)</b>	<b>Legal Representative: Thompsons Solicitors</b>
The Haemophilia Society	
Haemophilia Scotland (designated February 2014)	

The Common Services Agency, the 14 area Health Boards and Scottish Ministers were designated under the other provisions of rule 4 (2) of the Inquiries (Scotland) Rules 2007.

<b>Designated as Core Participants under provisions of rule 4 (2)</b>	<b>Legal Representative: Directorate for Legal Services (Solicitor to the Scottish Government)</b>
The Scottish Ministers	
<b>Designated as Core Participants under provisions of rule 4 (2)</b>	<b>Legal Representative: Central Legal Office (CLO)</b>
The Common Services Agency for the Scottish Health Service (on behalf of the Scottish National Blood Transfusion Service)	
Ayrshire and Arran Health Board	
Borders Health Board	
Dumfries & Galloway Health Board	
Fife Health Board	
Forth Valley Health Board	
Grampian Health Board	
Greater Glasgow Health Board	
Highland Health Board	
Lanarkshire Health Board	
Lothian Health Board	
Orkney Health Board	
Shetland Health Board	
Tayside Health Board	
Western Islands Health Board	



## APPENDIX 4 INQUIRY WITNESSES

Witness name	Topic(s)	Oral evidence	Written statement
Alex	C6	10 January 2012	Confidential
Amy	B5 and B6	8 June 2011	Confidential
Anne	C6	15 December 2011	Confidential
AKEN, Professor Willem van	Mr Tamburrini	9 March 2011	PEN.001.0306 (Report)
"	"	"	PEN.011.0001 (Supplementary Report)
"	B3	15 September 2011	PEN.012.1932 (Statement)
"	"	"	PEN.012.1928 (Second Statement)
"	C3	4 November 2011	PEN.017.1597 (Statement)
ALEXANDER, Dr Graeme	Mr Laing	11 March 2011	LAI.001.1125 (Report)
"	C5	17 January 2012	PEN.018.1360 (Statement)
Bridie	C6	9 December 2011	Confidential
BATHGATE, Dr Andrew	Mr Tamburrini	8 March 2011	TAM.001.2380 (Report)
BOULTON, Dr Frank	B2	12 May 2011	PEN.015.0226 (Addendum statement)
BROWN, Geraldine	B5 and B6	16 June 2011	PEN.012.0401 (Statement)
Christine	B5 and B6	7 June 2011	Confidential
Colin	C6	13 December 2011	Confidential
CACHIA, Dr Philip	C5	12 January 2012	PEN.018.0853 (Statement)
"		"	PEN.018.1239 (Response to the Reports of Dr Hay and Dr Nathanson)
CASH, Professor John	C1	23 March 2011	WIT.003.0120 (Statement)
"	B2	13 May 2011	PEN.015.0273 (Updated statement)
"	B3	8 September 2011	PEN.012.1912 (Statement)
"	B4	27 September 2011	PEN.017.1038 (Statement)

<b>Witness name</b>	<b>Topic(s)</b>	<b>Oral evidence</b>	<b>Written statement</b>
CASH, Professor John	C3	27 October 2011	PEN.017.1085 (Statement)
"	C2	16 November 2011	None referred
"	C2	29 November 2011	None referred
"	C4	1 December 2011	PEN.017.1741 (Statement) PEN.017.1885 (Supplementary statement) PEN.017.2094 (Statement)
"	C4	11 January 2011	PEN.017.2094 (Statement) PEN.017.2779 (Supplementary Statement)
"	C5	17 January 2011	PEN.018.0353 (Statement)
COLVIN, Dr Brian	Reverend Black	9 March 2011	BLA.001.2281 (Report)
"	C3A	14 October 2011	PEN.017.1674 (Report)
"	C3A	7 December 2011	PEN.017.1674 (Report)
CUTHBERTSON, Dr Bruce	Mr Tamburrini	8 March 2011	PEN.011.0048 (Statement of clarification – joint with Dr Perry)
"	"	"	PEN.011.0004 (Response to questions posed by the Inquiry on SPPS batch 1194)
"	B3	14 September 2011	PEN.013.0025 (Statement)
"	C3	27 October 2011	PEN.017.1200 (Statement)
David	B5 and B6	9 June 2011	Confidential
DOW, Dr Brian	Mr Laing	11 March 2011	PEN.001.0016 (Statement/Paper)
"	C1	18 March 2011	WIT.003.0094
"	C1	12 May 2011	WIT.003.0094
"	C2 and C4	22 November 2011	PEN.017.1925 (C2 statement) PEN.017.1915 (C4 statement)
DUNN, Dr Frank G	Mrs O'Hara	10 March 2011	PEN.010.0114 (Statement)

<b>Witness name</b>	<b>Topic(s)</b>	<b>Oral evidence</b>	<b>Written statement</b>
Elaine	B5 and B6	10 June 2011	Confidential
Frances	B5 and B6	9 June 2011	Confidential
FORBES, Professor Charles	B2	28 April 2011	PEN.015.0254 (Statement)
"	B5	15 June 2011	PEN.012.0411 (Statement)
"		"	PEN.012.1328 (Statement)
FORRESTER, Dr John	C2	21 November 2011	PEN.017.1752 (Statement) PEN.017.2052 (Supplementary statement)
FOSTER, Dr Peter	B2	10 May 2011	PEN.015.0101 (Statement) PEN.013.1125 (Supplementary paper)
"	B2	11 May 2011	PEN.015.0101 (Statement)
"	B3	6 September 2011	PEN.012.1852 (Statement)
"	B3	7 September 2011	PEN.012.1438 (Statement)
"	C3	26 October 2011	PEN.017.1556 (Statement)
Gordon	C6	13 December 2011	Confidential
GILLON, Dr John	Statistics	16 March 2011	PEN.001.0043 PEN.013.1557 PEN.001.0038 PEN.001.0043 (Statements)
"	C1	24 March 2011	WIT.003.0129 (Statement)
"	B5	24 June 2011	PEN.012.0862 (Statement)
"	C2	17 November 2011	PEN.017.1931 (Statement)
"	C5	18 January 2012	PEN.018.0410 (Statement)
GOLDBERG, Professor David	Statistics	16 March 2011	PEN.013.0014 PEN.001.0206 (Statements)

Witness name	Topic(s)	Oral evidence	Written statement
HANN, Professor Ian	B2 and B5	6 May 2011	PEN.015.0370 (Statement)
"	"	"	PEN.012.0205 (Statement)
"	"	"	PEN.012.0203 (Statement)
"	"	"	PEN.015.0035 (Statement)
"	"	"	PEN.015.0353 (Statement)
"	"	"	PEN.012.0270 (Statement)
"	B2 and B5	10 June 2011	None referred
HAY, Dr Charles	Statistics	18 March 2011	None referred
	C5	12 January 2012	PEN.018.1186 (Statement)
HAYES, Professor Peter	C6	14 December 2011	PEN.018.0240 (Report)
KEEL, Dr Aileen	C5	18 January 2012	PEN.018.0396 (Statement)
KENNEDY, Mrs Roseleen	Mrs O'Hara	10 March 2011	WIT.003.0420 (Witness statement)
Laura	C6	15 December 2011	Confidential
LEEN, Professor Clifford	B6	15 June 2011	PEN.012.1044 (Report)
LEIKOLA, Professor Erkki Juhani	C1	29 March 2011	WIT.003.0001 WIT.003.0027 (Statements)
"	C2 and C4	30 November 2011	PEN.017.1837 (C2 statement) PEN.017.1957 PEN.017.1961 (C4 statements)
LEITCH, Ms Christina	B5 and B6	24 June 2011	PEN.012.1430 (Statement)
LEVER, Professor Andrew	B2	17 May 2011	PEN.015.0517 (Report)
"	B2	18 May 2011	PEN.015.0517 (Report)
LOWE, Professor Gordon	B5	28 June 2011	PEN.016.1250 (Statement)
"	B5	30 June 2011	PEN.016.1250 (Statement)
"	C3A	13 October 2011	PEN.017.1471 (Statement)
"	C5	16 December 2011	PEN.018.0649 (“Collective response”)

Witness name	Topic(s)	Oral evidence	Written statement
LUDLAM, Professor Christopher	Statistics	30 March 2011	None referred
"	B2	3 May 2011	PEN.015.0445 (Statement) PEN.015.0468 PEN.015.0385 PEN.015.0375 (Supplementary Statements)
"	B2	4 May 2011	PEN.015.0445 (Statement)
"	B5	17 June 2011	PEN.012.0351 (Statement) PEN.012.0774 (Note of meeting)
"	B5	21 June 2011	None referred
"	B5	28 June 2011	None referred
"	B3	9 September 2011	PEN.012.1688 (Statement)
"	C3A	13 October 2011	PEN.017.1790 (Statement)
"	C3A	14 October 2011	Not referred to by number
"	C3	28 October 2011	PEN.017.1620
Mark	B5 and B6	14 June 2011	Confidential
MACDONALD, Dr Iain	C2	21 November 2011	PEN.017.1702 PEN.017.2048 (Statements)
MACNIVEN, Mr Duncan	C3	3 November 2011	PEN.017.1604 (Statement) PEN.017.1866 (Compensation statement)
"	C2	17 November 2011	PEN.017.2053 (Statement)
"	C2	14 December 2011	None referred
McCLELLAND, Dr Brian	C1	22 March 2011	WIT.003.0072 (Statement)
"	B1	25 March 2011	WIT.003.0036 (Statement)
"	B2	6 May 2011	PEN.015.0307 (Statement)
"	B5 and B2	30 June 2011	PEN.016.1239 (Statement) PEN.012.1426 (Supplementary statement)

<b>Witness name</b>	<b>Topic(s)</b>	<b>Oral evidence</b>	<b>Written statement</b>
McCLELLAND, Dr Brian	B4	29 September 2011	PEN.017.1337 (Statement)
"	C2	15 November 2011	PEN.017.0754 (Statement)
"	C2	16 November 2011	PEN.017.0754 (Statement)
"	C4	23 November 2011	PEN.017.2491 (Statement)
"	C4	24 November 2011	PEN.017.2491 (Statement)
McINTOSH, Mr David	C4	29 November 2011	PEN.017.2126 (Statement)
"	C5	13 January 2012	PEN.018.0358 (Statement)
McINTOSH, Dr Ronald V	C3	3 November 2011	PEN.017.1234 (Statement)
MITCHELL, Dr Ruthven	C1	22 March 2011	WIT.003.0106 (Statement)
"	B4	30 September 2011	PEN.017.1002 (Statement)
"	C2	17 November 2011	WIT.003.0116 (Statement) PEN.017.1897 (Statement)
"	C4	24 November 2011	PEN.017.1901 (Statement)
MURRAY, Mr Alexander	C3	3 November 2011	PEN.017.1868 (Statement)
MUTIMER, Dr David	Mr Tamburrini	8 March 2011	PEN.010.0310 (Report)
"	Reverend Black	9 March 2011	BLA.001.2277 (Report)
"	Mrs O'Hara	10 March 2011	BLA.001.2298 (Report)
NATHANSON, Dr Vivienne	B5	23 June 2011	PEN.012.0330 (Report)
	C5	13 January 2012	PEN.018.0419 (Supplementary statement)
NORFOLK, Dr Derek	Use of Blood	17 March 2011	PEN.010.0048 (Statement)

Witness name	Topic(s)	Oral evidence	Written statement
PERRY, Dr Robert J	C1	24 March 2011	WIT.003.0050 (Statement)
"	B2	13 May 2011	PEN.016.0460 (Statement)
"	B5	24 June 2011	PEN.012.1331 (Supplementary statement)
"	B3	13 September 2011	PEN.012.1759 (Statement)
"	C3	28 October 2011	PEN.017.1219 (Statement)
"	C4	23 November 2011	PEN.017.2108 (Statement)
"	C3A	7 December 2011	PEN.017.1244 PEN.017.1843 (Statements)
PETERKIN, Dr Myrtle	Mr Tamburrini	9 March 2011	PEN.001.0306 (Report)
PETTIGREW, Dr Anna	B2 and B5	5 May 2011	PEN.015.0486 (B2 statement) PEN.012.0277 (Statement)
RICHARDSON, Dr Alison	B5 and B6	8 June 2011	PEN.016.1284 (Statement)
ROBERTSON, Dr Kevin	Mrs O'Hara	10 March 2011	PEN.010.0170 (Statement)
Stephen	C6	8 December 2011	Confidential
SCOTT, Dr Graham A	C1	24 March 2011	WIT.003.0019 (Statement)
"	B4	28 September 2011	PEN.017.0513 (Statement)
SMITH, Dr James K	B3	1 November 2011	PEN.012.1551 (Statement)
"	C3	2 November 2011	PEN.017.2198 (Statement)
TAIT, Dr Campbell	Statistics	30 March 2011	None referred
TAMBURRINI, Mrs Jean	Mr Tamburrini	8 March 2011	PEN.001.0309 (Statement)
THOMAS, Professor Howard	Introduction to hepatitis	11 October 2011	PEN.017.1071 (Report)
"	Introduction to hepatitis	12 October 2011	PEN.017.1071 (Report)
TUCKER, Mr George	C4	24 November 2011	PEN.017.2060 (Statement)

---

<b>Witness name</b>	<b>Topic(s)</b>	<b>Oral evidence</b>	<b>Written statement</b>
TURNER, Professor Marc	Collection of Blood	17 March 2011	PEN.002.0452 (Statement)
WATTERS, Mr David	B2, B5 and C5	19 January 2012	None referred
WEISS, Professor Robin	B4	27 September 2011	PEN.017.1261 (Letter)
WILKIE, Dr Patricia	B5 and B6	14 June 2011	PEN.016.1297 (Statement)
WINTER, Dr Mark	B2	26 April 2011	PEN.015.0292 (Statement)
"	B2 and B5	27 April 2011	PEN.015.0292 (Statement)



## **APPENDIX 5**

### **INQUIRY PROCEDURE DIRECTIONS, GUIDANCE NOTES AND RESTRICTION ORDERS**

#### *Procedure Directions*

- Procedure Direction No. 1 – Production of documents to the Inquiry – 27 June 2009
- Procedure Direction No. 2.2 – Award of Travel and Subsistence Expenses for providing a witness statement or documents – 1 April 2011 (replaced Direction 2.1, dated 2 February 2011, which had itself replaced Direction 2, dated 22 June 2009)
- Procedure Direction No. 3.1 – Applications for legal representation at public expense – 17 November 2009 (replaced Direction 3, dated 22 June 2009)
- Procedure Direction No. 4.1 – Award of Compensation for Loss of Time – 2 February 2011 (replaced Direction 4 dated 22 June 2009)
- Procedure Direction No. 5 – Core Participants – 16 June 2010
- Procedure Direction No. 6 – Opening Statements – 16 February 2011
- Procedure Direction No. 7 – Oral Evidence by Video Link – Dr Mutimer and Professor Hann – 24 February 2011
- Procedure Direction No. 8 – Pseudonyms – 6 May 2011
- Procedure Direction No. 8 – Oral Evidence by Video Link – Professor Weiss – 26 September 2011
- Procedure Direction No. 9 – Pseudonyms – 28 October 2011
- Procedure Direction No. 10 – Pseudonyms – 3 November 2011
- Procedure Direction No. 11 – Pseudonyms – 15 November 2011
- Procedure Direction No. 12 – Oral Evidence by Video Link – Mr David Watters – 12 January 2012
- Procedures in relation to Final Hearing – 24 February 2012

#### *Guidance Notes*

- Guidance on Travel and Subsistence Expenses
- Note on Designation of Core Participants
- Guidance Note on Core Participants
- Guidance on Written Statements Provided Voluntarily
- Guidance on Providing a Witness Statement or Documents to the Inquiry
- Guidance on the Oral Hearings
- Guidance Note in Relation to Warning Letters

### ***Restriction Orders***

- Restriction Order – 6 May 2011 – restricting the right of attendance at certain hearings of the Inquiry and prohibiting the disclosure of the evidence of certain witnesses
- Amended Restriction Order – 20 May 2011 – restricting the right of attendance at certain hearings of the Inquiry and prohibiting the disclosure of the evidence of certain witnesses
- Restriction Order – 28 October 2011 – restricting the right of attendance at certain hearings of the Inquiry and prohibiting the disclosure of the evidence of certain witnesses
- Restriction Order – 3 November 2011 – restricting the right of attendance at certain hearings of the Inquiry and prohibiting the disclosure of the evidence of certain witnesses
- Restriction Order – 9 January 2012 – restricting the right of attendance at the hearing of the Inquiry on 10 January 2012 and prohibiting disclosure or publication of the applications, evidence and the transcript of this hearing
- Restriction Order – 11 January 2012 – revoking the Restriction Order dated 9 January 2012 and prohibiting disclosure or publication of the applications, evidence and the transcript of the hearing held on 10 January 2012

© Crown copyright 2015

An online version of the report is available at [www.penroseinquiry.org.uk](http://www.penroseinquiry.org.uk)

**ISBN: 978-0-85759-022-0 (Volume 5 of 5)**

**This Inquiry Report comprises an Executive Summary (ISBN: 978-0-85759-023-7), five volumes and a DVD**

Published on behalf of The Penrose Inquiry by APS Group Scotland, 21 Tennant Street, Edinburgh EH6 5NA  
DPPAS43828 (03/15)